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IDENTIFYING THE MARIHUANA USER

by

Forest S. Tennant, Jr., M.D., Dr. P.H.

Veract, Inc.

Dedicated To The
California Highway Patrol
Who Have Been The
Inspiration For This Handbook

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NOTE FROM THE AUTHOR

This is one of a series of manuals on specific drugs which are abused and/or may cause dependence. Much of it is based on observations made on my patients who have drug problems and from personal research studies. Since research on drug abuse is a relatively new field of endeavor, one can expect future changes in some of the information presented here. I have attempted to give the reader the most current information. As new information becomes available these manuals will be updated.

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SECTION I
BACKGROUND ON MARIHUANA USE

PURPOSE AND INTRODUCTION

- This manual is for law enforcement, medical, correctional, legal, and mental health professionals, as well as employers, teachers, and parents who must competently and accurately identify a drug user in his/her various stages of use.

- Much of the information given here comes from observations and studies conducted with drug users who have been treated in the author's facilities.

- This is the first edition of this manual. It will be updated when enough new information warrants it.

- The format of this manual is intended to help the reader to rapidly review the material, and to be used as a quick reference guide.

- Some material is presented in detailed tables to provide answers to specific questions.

- This manual was written in collaboration with many experienced drug abuse clinicians in order to provide as much scientific accuracy as possible.

- A list of scientific references is provided because there is considerable research that gives the scientific grounding for the identification procedures described here.

THREE CATEGORIES OF IDENTIFICATION

1. ***Acute Marihuana Influence***
   This category is of the most interest to law enforcement and medical personnel who must determine which drug someone has recently taken. For example, identification of the acute user is especially applicable when a person is publicly intoxicated, obviously sedated, driving poorly, or has had an accident or injury.

2 ***Chronic and Covert Marihuana Use***
This category is of great interest to employers, teachers and parents, who must recognize the covert or non-obvious user. For example, this situation is applicable to a person who is performing poorly in work or in school, behaving abnormally, or who has certain specific medical symptoms.

3 ***Marihuana Addiction or Dependence***
This category is of most interest to medical, penal, and mental health personnel who must determine if addiction or dependence is present and must be medically treated. For example, this situation is applicable to a person who is admitted to a penal or medical institution, and a decision must be made whether medical withdrawal treatment is necessary.

WHAT IS MARIHUANA?

- Marihuana is the plant, Cannabis sativa.
- Hashish is the resin from Cannabis sativa. It is becoming more popular in the United States.
- The active ingredient in marihuana is delta-9-tetrahydrocannabinol (THC).
- THC is used medicinally to help relieve nausea and vomiting produced by anti-cancer drugs. THC is taken as a capsule or tablet when used for medical purposes.

HOW IS MARIHUANA USED?

- It is usually smoked as a cigarette or joint
- Hashish is smoked in a pipe.

POTENCY AND HAZARDS OF TODAY'S MARIHUANA

- Beginning in about 1983, the potency of the marijuana sold in the United States dramatically increased from 1-2% THC to 5-15% THC content. Some areas report a 27% THC level in marihuana.
- The increase in potency has made today's marihuana much more hazardous relative to causing impairment, addiction, and medical complications.
- Many persons in the United States have had personal experiences or have observed other persons during the 1960's and 1970's who smoked marihuana joints containing 1-2% THC. These persons are still under the impression that marihuana is quite harmless due to these experiences, and are not aware of the differences in marihuana today.
- Although the potency difference between 1 and 10% marihuana is a mathematical difference of only 9%, the human brain recognizes this as a 900% difference.
- In the late 1960's and early 1970's, the author observed that U.S. Army soldiers in Europe and Vietnam who smoked potent marihuana and hashish developed many medical complications. The same medical problems are now being observed in the United States in persons using marihuana.
- The high potency marihuana now being smoked is responsible for many accidents, injuries, addiction, and health complications. This new development is the primary reason this handbook has been developed.

HOW DOES MARIHUANA WORK IN THE BODY?

- The THC that is smoked partially changes into two other compounds after it enters the human blood stream. These two compounds are chemically known as 11-hydroxy-$\triangle$9-tetrahydrocannabinol (OH-THC) and 11-Nor$\triangle$9-tetrahydrocannabinol-9-carboxylic acid (C-THC).
- THC is detectable in the human blood stream (plasma) for only about two hours. It produces euphoria and may cause visual, mental, and muscle (motor) impairment during this time period. OH-THC stays in the plasma 4 to 6 hours and may cause a small amount of euphoria. Depending on the amount smoked, C-THC may remain in the plasma for as long as 3 to 6 days. It causes no euphoria but may produce visual, mental and motor impairment. Consequently, users have no perception that they may be impaired.
- C-THC stays in human plasma for so long because it is lipophillic or fat-soluble. It goes into fatty tissue and "sticks" until it is released back into the plasma. Because of the fat-solubility of C-THC, it can be found in the urine for many days after one has stopped smoking marihuana. C-THC has been found in urine for up to about 45 days in chronic or addicted marihuana users.

SUMMARY OF MARIHUANA METABOLITES

Metabolite	Approximate Length of Time in Plasma	Causes Euphoria	Causes Visual, Mental, and Motor Impairment
THC	2-3 hours	Yes	Yes
OH-THC	4-6 hours	Mild, if any	Yes
C-THC	3-6 days	No	Yes

EVIDENCE OF IMPAIRMENT

- A study at Stanford University in California was done with 10 licensed, commercial pilots who smoked a marihuana joint and then were tested on a flight simulator 24 hours later. Pilots made landing errors and one even missed the runway!
- The author has detected strabismus of the eye (non-convergence) and non-or slow-reacting pupils up to one week after chronic marihuana smoking was stopped. These findings were present as long as C-THC was detected in the plasma.
- Due to new research, it is clear that one may remain legally and medically under the influence of marihuana for up to a few days after smoking it.

EFFECT OF MARIHUANA ON NEUROTRANSMITTERS AND THE IMMUNE SYSTEM

- Many controlled research studies have shown that marihuana has both stimulant and sedative effects on the body. Until recently, the cause of this has not been understood. Marihuana has been shown to reduce levels of the body's internal stimulant, norepinephrine, and the body's internal opioid, endorphin.
- These findings help explain why marihuana smoking causes an increase in pulse rate and blood pressure while at the same time may produce muscle relaxation, slow speech and sedation. In simple terms, marihuana has many of the simultaneous, combined effects of cocaine and heroin.
- The sex hormones, follicle stimulating hormone and luteinizing hormone, may be suppressed by chronic marihuana use.
- It is marihuana's effects on neurotransmitters, neurohormones, and the immune system that provide many of the physical signs and behaviors that allow for the medical and legal identification of acute and chronic marihuana use.

WHO ABUSES MARIHUANA?

- Marihuana was once known as a drug for the college student. Its use is now widespread in all age groups and socioeconomic classes. Today most users start using marihuana in their early teenage years, but use below age 10 years is not uncommon.
- Recent surveys of high school seniors in the United States reveal that as many as 60-70% have reportedly tried marihuana at least one time and about 5 to 7% report daily use.

- Drug addicts of various types frequently use marihuana as a second drug. This is particularly common in cocaine, amphetamine, and phencyclidine (PCP) addicts.
- Persons with the underlying psychiatric disorders of depression and schizophrenia often find marihuana particularly desirable.
- Most marihuana users are also cigarette smokers.

GENERAL PATTERNS OF MARIHUANA USE

Classification	Usual Frequency of Use	Chief Characteristic
Intermittent or occasional	1 to 4 times per month	Sometimes called social, casual, or "recreational" users. Also used to control stress.
Binge	Every few hours for a short period.	A great amount used in a short time period (weekend or evening)
Addiction or dependence	Type 1—6 to 12 times per day	Probably dependent upon THC or OH-THC. Withdrawal symptoms begin the day of cessation (when THC or OH-THC leaves the blood stream).
	Type 2—Daily or every other day	Probably dependent upon C-THC Withdrawal symptoms occur about three days after cessation (when C-THC leaves the blood stream)

SECTION II

IDENTIFICATION OF ACUTE MARIHUANA INFLUENCE

ACUTE EFFECTS OF MARIHUANA

- Marihuana has four basic effects, although all four may not exist in one person at the same time.

Stimulation
- Increase in Pulse Rate
- Increase in Temperature
- Increase in Blood Pressure
- Decreased Attention Span
- Sweating
- Craving for Sweets
- Mood Elevation
- Poor Concentration

Sedation / Muscle Relaxation
- Droopy Eyelid
- Strabismus (non-convergence)
- Slow or Non-reactive Pupil
- Inability to Maintain Pupil Constriction
- Giggly or Giddy
- Visual-Perception Disturbance
- Poor Muscle Coordination
- Mouth-Breather (dry lips/mouth)
- Slow Gait
- Poor Balance
- Sleepy Appearance
- Slow Speech

Anesthesia/Analgesia
- Pain Relief
- Increased Hearing Threshold
- Memory Loss
- Time Distortion

Hallucinogenic
(Usually only with high doses or combined with other drugs)
- Hallucinations
- Paranoia
- Delusion

- Marihuana is commonly used with alcohol (a sedative), cocaine (a stimulant), PCP, or other drug which may potentiate some of its effects and reactions.

- Most of these effects last about 2 to 5 hours after smoking marihuana. Some effects, particularly vision, motor and mental may last for more than 24 hours, depending on the dosage taken.

GENERAL PHYSICAL AND BEHAVIORAL SIGNS OF ACUTE DRUG INFLUENCE

- All psychoactive drugs, when consumed in a high enough dose, will produce abnormal physical and behavioral signs in an individual who is not tolerant to the drug. Many of these signs are generic in that they are similar regardless of which drug, including marihuana, is taken. For example, a common misconception is that stimulants and sedatives cause very different acute physical and behavioral signs. Although there are some specific differences in the acute drug effects of stimulants and sedatives, both classes of drugs produce many identical symptoms. More importantly, low and high dosages of the same drug may produce different signs and symptoms. The degree of tolerance that a user may have will also influence symptoms. Further, persons in withdrawal from a stimulant, e.g., cocaine, may exhibit symptoms associated with the acute use of a sedative, e.g. heroin and vice versa.

- A problem in the physical examination and evaluation of the drug user is that the evaluator may not know the terminology to apply to what he/she observes. Listed here are a number of terms which may be used to describe the various generic symptoms and behaviors that are commonly observed with most types of acute drug influence, including acute marihuana influence.

- It is not essential that the evaluator or examiner memorize or even be able to recognize all of the signs and symptoms listed here to make a proper medical and legal diagnosis. The presence of only some of the following, when combined with laboratory confirmation of body fluid, (i.e. blood or urine) is sufficient to make a medical and legal diagnosis of acute drug influence.

TABLE OF GENERAL SIGNS AND SYMPTOMS FOUND IN ACUTE DRUG INFLUENCE

Accommodating
Agitated
Aggressive
Alert
Angry
Anesthetized
Anorexic
Anxious
Antagonistic
Antisocial
Argumentative
Befuddled
Belligerent
Bizarre
Boisterous
Bubbling
Cautious
Cocky
Combative
Confused
Contentious
Contradictive
Dazed
Deliberate
Denies
Depressed
Disheveled
Disjointed Speech
Disoriented
Distracted
Drowsy
Eager
Erratic
Euphoric
Evasive
Excited
Expressionless
Flat
Forgetful
Giddy
Giggly
Happy
Hesitant
Hostile
Hyperactive
Hysterical
Impatient
Inappropriate
Inattentive
Incoherent
Inconsistent
Indecisive
Indifferent
Irrational
Irritable
Insolent
Intoxicated
Jittery
Jovial
Jumbled Speech
Laughing
Lethargic
Loud
Mellow
Monotone
Moody
Mute
Nervous
Non-responsive
Non-communicative
Obstreperous
Over-confident
Paranoid
Passive
Persnickety
Pesky
Rambling
Redundant
Relaxed
Remorseful
Repetitive
Resistive
Restless
Rigid
Ruffled
Sedated
Silly
Sleepy
Sluggish
Somnolent
Stumbling
Stuperous
Subdued
Submissive
Talkative
Tense
Uncertain
Uncooperative
Uneasy
Uncaring
Unconcerned
Unkempt
Unresponsive
Unsteady
Violent
Withdrawn

NOTE. Some of these terms mean the same thing and there may be other terms that are acceptable.

PHYSICAL EVALUATION/EXAMINATION OF A PERSON SUSPECTED OF ACUTE MARIHUANA INFLUENCE

- Below is a list of physical evaluation procedures to be used when a person is suspected of acute marihuana influence. It is not necessary to do every procedure to make a correct medical and legal identification. Most of these procedures can be done by a non-medical person:
  1. Listen for speech rate.
  2. Observe gait and balance.
  3. Look for sleepy apparance, droopy eyelids, mouth breathing, dry lips, and green tongue.
  4. Smell for odor of alcohol and marihuana.
  5. Assess responses for attention span, concentration, and giddiness.
  6. Assess depth perception by asking person to estimate a distance.
  7. Examine eyes for droopy eyelid, pupil reaction, strabismus (non-convergence), and redness.
  8. Determine muscle coordination and balance by finger-to finger, finger-to-nose, step test, and/or one leg balance-count test (divided attention)
  9. Take pulse, blood pressure, and respiratory rate.
  10. Feel skin for sweating and tremor.
  11. Note if hallucinations, delusions, or paranoia is present.
  12. Instruct to give correct time, date, and place.
  13. Observe for general physical and behavorial signs of acute drug influence (see previous table)

LEGAL DIAGNOSIS OF DRUG INFLUENCE

- The elements required to make a ***legal*** diagnosis of acute drug influence are well established in case law. Furthermore, the elements are identical to the ***medical*** diagnosis of acute drug influence. Put simply, the elements required for a proper diagnosis of acute drug influence are the same in a medical clinic, emergency room, work place, police department, or on a highway. There are three basic elements required to make a medical and legal diagnosis.
  1. Reason to investigate further
  2. Physical evidence
  3. Laboratory confirmation

Professionals may differ in the terms that they use to describe the three elements. Some of the terms are listed here.

- **ELEMENT NO. 1 — Reason to Investigate Further**

Some Common Descriptive Terms	Some Common Reasons
Probable Cause (Law Enforcement) Just or "For" Cause (Industry) Reasonable Suspicion (Industry) Index of Suspicion (Medicine)	accident, injury, illegal activity, improper driving, abnormal behavior, psychosis, absenteeism, walk or talk

- **ELEMENT NO. 2 — Physical Evidence**

Some Common Descriptive Terms	Some Common Evidence
Supporting Evidence (Legal) Specific Objective Facts (Legal) Abnormal Physical Finding (Medicine)	abnormal walk, speech, balance, visual perception, blood pressure, pulse, mental state, eye signs, mental response

- **ELEMENT NO. 3 — Laboratory Confirmation**

Sometimes called "essential evidence," this element requires that the drug be found in a body fluid which can be blood, urine, breath, saliva, eye fluid (vitreous), hair, or feces. Urine is the most common fluid that is analyzed with blood ranking second. Alcohol is usually measured in breath.

LABORATORY FINDINGS AND CORRELATIONS WITH DEGREE OF ACUTE INFLUENCE

Only in the case of alcohol does the body fluid concentration reflect any predictable degree of impairment of acute influence. Most states use a blood alcohol concentration of 100mg/100 ml, or 10 mg% as the legal criteria for acute alcohol influence because this level is known to cause significant physical impairment in persons who are not tolerant to alcohol. At this time, it is not scientifically possible to determine the degree of acute influence or impairment by the concentration of other drugs of abuse present in blood or urine. Therefore, qualitiative, not

quantitative urine and blood tests are the most appropriate to confirm a diagnosis of acute influence of marihuana, cocaine, heroin, amphetamines, and phencyclidine. It is also emphasized that the presence of abnormal physical signs, symptoms, and behaviors are the primary determinants of acute influence — not the laboratory test, which is only capable of confirmation.

LEGAL DIAGNOSIS OF ACUTE MARIHUANA INFLUENCE

- Recommended criteria are listed here for the medical and legal diagnosis of acute marihuana influence. Note that all three elements as described above are included.

- **ELEMENT NO. 1 — Reason to Investigate Further**
  One of the Following Must be Present

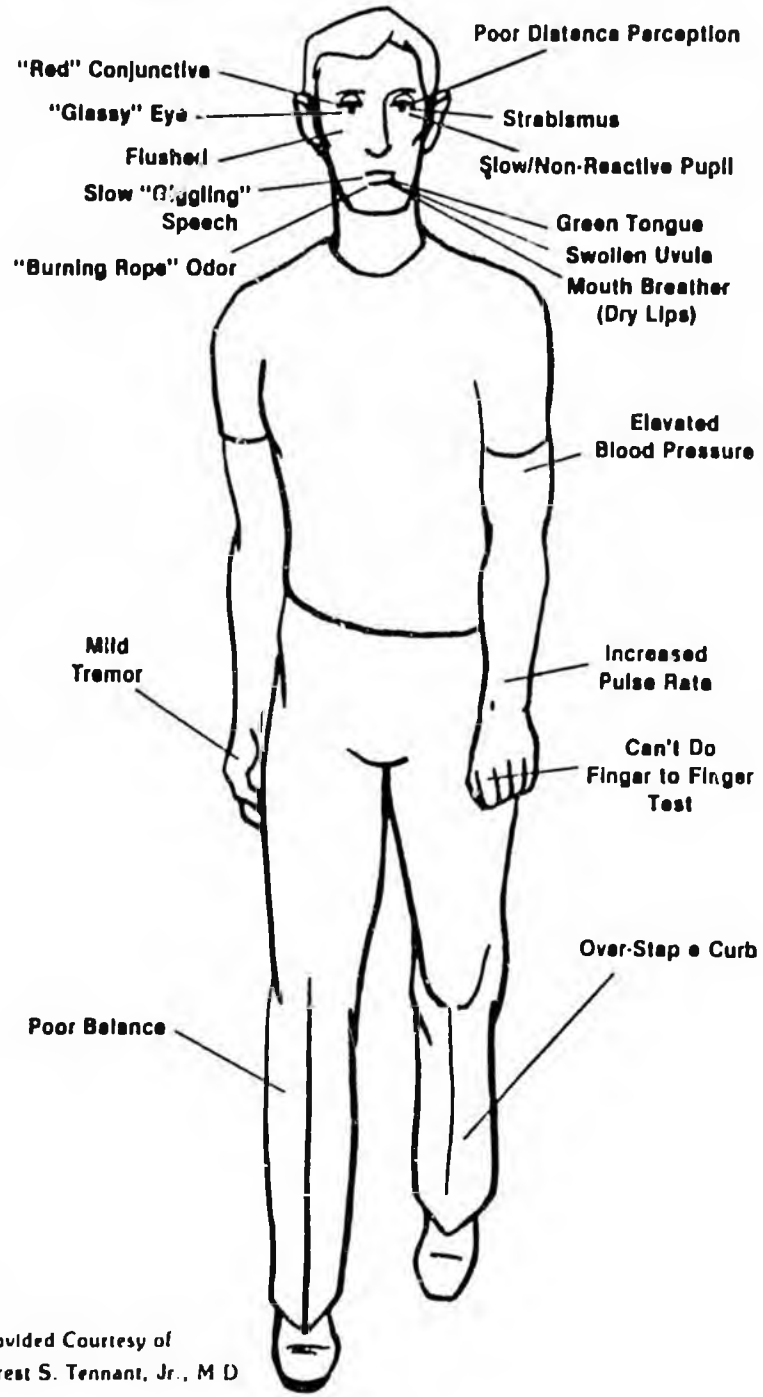
Accident
Injury
Illegal Activity
Recurrent Infections/Illness
Progressive Change in Mood, Mental Ability, or Memory
Deterioration of Work or School Performance
Psychiatric Symptoms
Abnormal Gait or Speech
Improper Driving
Sudden Disappearance from Work/Home
Other Unusual Behavior
Smell of Marihuana Smoke

ELEMENT NO. 2 – Physical Evidence – Supporting Evidence
Two or More of the Following Must Be Present

Slow or Non-Reacting Pupil
Pupil Cannot Hold Constriction in Direct Light
(Rebound Dilation)
Strabismus (Non-Convergence)
Abnormal Walk or Stumbling
Green Tongue
Elevated Pulse
Slow or Slurred Speech
Abnormal Finger-to-Finger Test
Unattentive or Unresponsive to Questions
Does Not Know Current Time, Date, or Place
Inappropriate Laughter or Giggling
Other Acute General Influence Signs (See Table on page 8)
Red Eye (Sclera)
Dilated Pupil
Droopy Eyelid
Mouth Breathing and Dry Lips
Abnormal Distance Perception
Elevated Blood Pressure
Abnormal Divided-Attention Test
(One Leg-Count Test)
Poor Balance/Coordination
Excess Sweating
Tremor
Abnormal Step Test

ELEMENT NO. 3 –
Laboratory Confirmation – Essential Evidence
Presence of marihuana metabolite in urine, blood, or saliva.

Physical Signs of a Non-Tolerant Person Under Marihuana Influence



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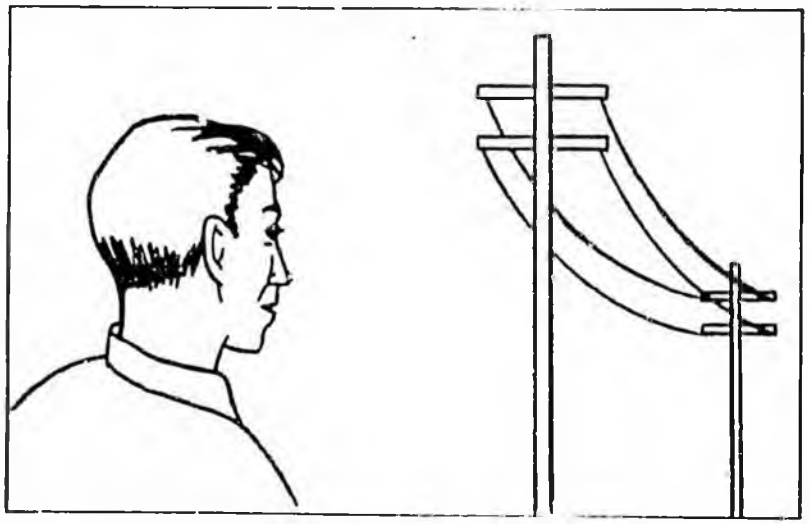
SPECIFIC PHYSICAL TESTS FOR ACUTE MARIHUANA INFLUENCE

Physical tests can be conducted which demonstrate evidence of acute marihuana influence. These tests access one or more of the basic physical determinants or drug influence, i.e., perception, balance, coordination, and attention span. Not all of these tests need to be positive to establish the diagnosis of acute influence. Seldom are all the tests abnormal at the same time. Not all of these tests need to be done to establish a diagnosis of acute marihuana influence. In addition, there may be other tests or variants of these which can be utilized since the object of the physical tests is to document that marihuana is present in the body and that it is producing some physical effect.

Test #1 – Distance Perception Test

Procedure: Ask how far away an object is, such as a wall, telephone pole, etc.



Normal
Can estimate distance

Abnormal
Estimate is off 20% or more

Test #2 – Step Test

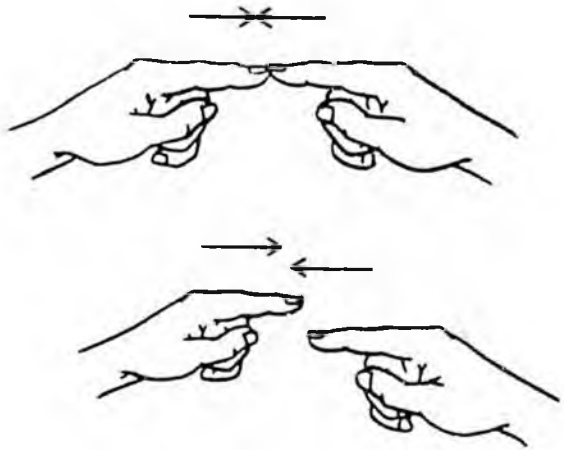
Procedure: Have subject attempt to step up a curb or stairs.

Normal
Can step up accurately

Abnormal
Over-steps or under-reaches

Test #3 – Finger-to-Finger Test

Procedure: With eyes open and arms extended, have the subject touch his index fingers. Then have subject shut his eyes and again try to touch his index fingers.



Normal
Less than 2" off and usually in a vertical plane

Abnormal
More than 2" off and usually in a horizontal plane

Test #4 — One Leg-Count-Balance Test (Divided Attention)

Procedure: Have subject stand on one leg, close eyes, and count to 10.

Normal	Abnormal
Can accomplish	Cannot stand on one leg and complete the count

Test #5 — Strabismus or Non-Convergence Test

Procedure: Ask subject to focus eyes on a finger or object at the end of the subject's nose.

Normal	Abnormal
Can "cross eyes" and gaze at object	One or both eyes will be unable to converge and will drift outward

Test #6 — Time Test

Procedure: Ask subject what time it is.

Normal	Abnormal
Will know correct time	Will be off at least 15 to 30 minutes

Test #7 — Pupillary Reaction

Procedure (A): Shine a light on the pupil and quickly remove it. Observe reaction. Then shine the light on the pupil to see if the pupil can maintain its constriction.

Normal	Abnormal
Pupil rapidly reacts. With constant light it will maintain constriction for at least 5 to 10 seconds.	Pupil reacts slowly or not at all. With constant light, the pupil will not hold its constriction and will dilate to its original size or slightly bigger (rebound dilation).

Procedure (B): Measure pupil size in room light and then put individual in darkness for five minutes.

Normal	Abnormal
Pupil will dilate	Pupil will not dilate

CHANGES IN VITAL SIGNS WITH ACUTE MARIHUANA INFLUENCE

Marihuana has stimulant properties due to its effects on norepinephrine. Consequently, vital signs may show stimulatory effects.

PUPIL SIZE —	Over 5.0 mm in diameter
PULSE —	Over 100 beats per minute (Normal - 72/minute)
BLOOD PRESSURE —	Systolic over 140 mm Hg (Normal - 120 mm Hg) Diastolic over 100 mm Hg (Normal - 90 mm Hg)
RESPIRATORY RATE —	Over 25 respirations per minute (Normal - 20/ minute)
TEMPERATURE —	Over 100°F (Normal 98.6°F)
SPECIAL NOTE:	If two of the above are present and there is marihuana derivative in plasma, urine, or saliva, acute marihuana influence should be considered to be present

VISION EFFECTS WITH MARIHUANA

There is growing evidence that some eye abnormalities and possibly other neuro muscular effects are present as long as marihuana's long-acting metabolite, C-THC, remains in the blood stream (plasma). Basically this means that marihuana may produce impairment and meet the criteria for acute influence for possbily as long as three to six days after the last dose of marihuana. For example, a study was conducted at Stanford University in which ten licensed pilots were given a marihuana joint containing 19 mg of THC. Twenty four hours later they were tested on a flight simulator, and all made landing errors, including one pilot who missed the runway. Other examples of vision effects of marihuana include numerous drivers driving erratically who are routinely arrested by the California Highway Patrol. Upon examination they show eye findings of strabismus and slow or non-reactive pupil but claim to have not smoked marihuana for three to four days. However, they show marihuana metabolite in their urine but no evidence of alcohol or other drug use.

The author has now studied some chronic marihuana users to correlate eye and other physical abnormalities with the presence of C-THC in plasma. Although strabismus (non-convergence) and slow, or non-reactive pupils were not present in every user, they were found in some marihuana users 3 to 6 days after they claimed to have ceased

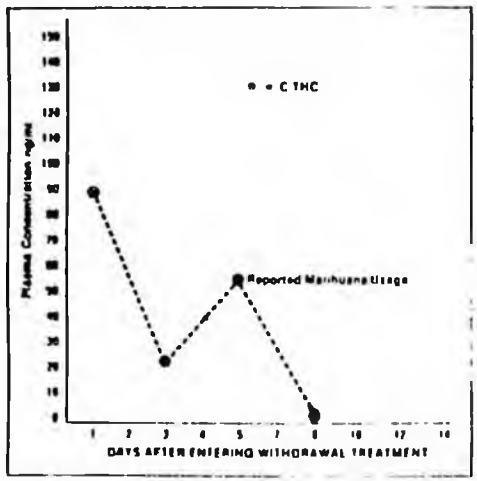
use. Figures in Example 1 show the plasma levels of C-THC in two chronic marihuana users who were treated by the author. In both cases one-sided strabismus and non-reactive pupil were present until C-THC was undetectable in plasma. The importance of this finding is that drug influence and impairment may remain for several days after marihuana was last used even though the user has no feeling of euphoria or perception of impairment. The presence of strabismus and a non-reactive pupil can impair visual tracking ability which may produce accidents and injuries.

CASE EXAMPLES OF PLASMA CONCENTRATIONS AND EYE ABNORMALITIES

To document whether eye abnormalities exist after cessation of marihuana use, the author has studied chronic users by determining the presence of C-THC in plasma while, at the same time, determining the presence of strabismus and non or slow-reactive pupils. Shown are two examples. In both cases C-THC remained in plasma for three days following the user's last reported use. In addition, strabismus and a non-reactive pupil were present during this time. Additionally, these persons experienced mild withdrawal symptoms when the plasma no longer showed C-THC.

EXAMPLE NO. 1

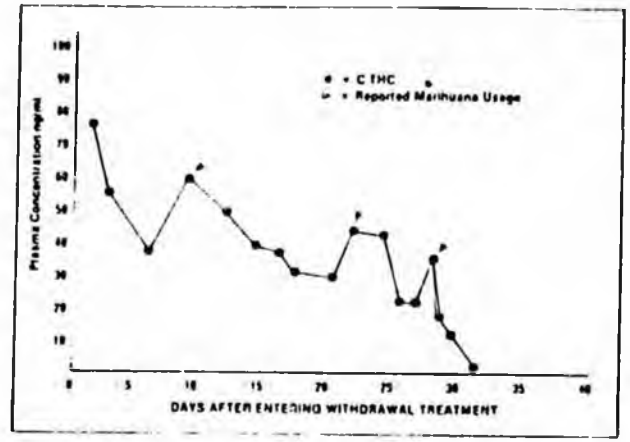
PLASMA CONCENTRATIONS OF C-THC DURING WITHDRAWAL IN A 3 TO 5 TIMES PER DAY MARIHUANA USER.



Strabismus and non-reactive pupil were present during the eight days that C-THC was detected in the plasma

EXAMPLE NO. 2

PLASMA CONCENTRATIONS OF C-THC DURING WITHDRAWAL IN A ONE TIME PER DAY MARIHUANA USER



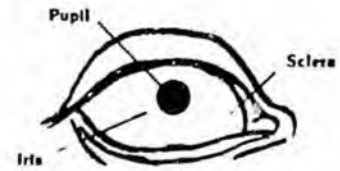
Strabismus and a non-reactive pupil were present during the 32 days that C-THC was detected in plasma

DETERMINATION OF PRESENCE OF PUPILLARY DILATION OR CONSTRICTION

In normal room light, the pupil of an adult is usually between 2.9 and 6.5 mm in diameter. About 1 to 3% of the adult population may have a congenital dilation or constriction.

A rapid way to determine if dilation or constriction is present is to measure the pupil diameter against one side of the iris.

Normal Size Pupil



Pupil diameter about same width as one side of iris

Constricted Pupil

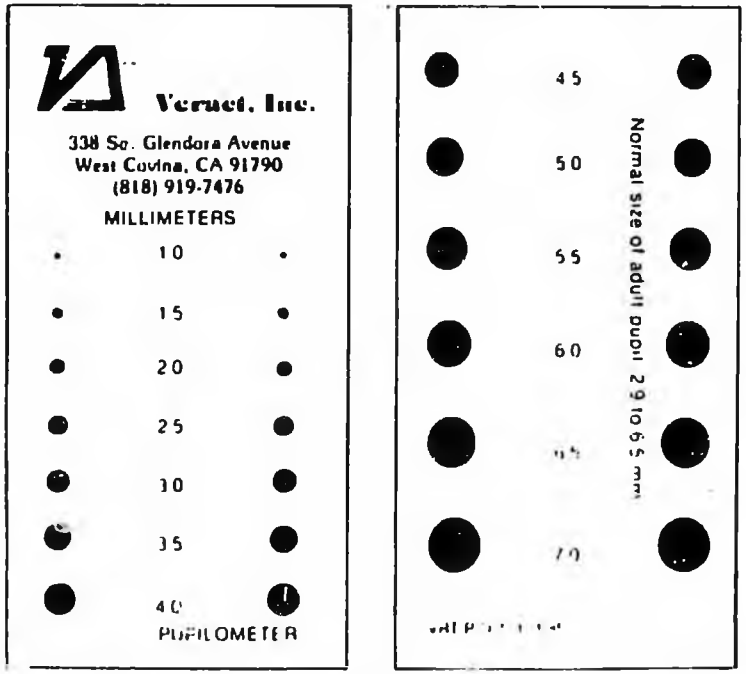
Diameter much smaller than width of one side of iris

Dilated Pupil

Diameter much larger than width of one side of iris

MEASUREMENT OF PUPIL SIZE AND REACTION

Use a standard pupilometer for measuring of pupil size. Pictured here is an actual-size example which can be copied for use.



Dilated pupil of type observed with acute cocaine-amphetamine influence. Sometimes observed with acute marihuana influence.

Reddish sclera (dilated veins) of acute marihuana smoker.

Constricted pupil and reddish eye in person under acute influence of marihuana and heroin.

Droopy eye lid, constricted pupil and reddish sclera of person under the acute influence of phencyclidine (PCP) and marihuana.

PUPIL MEASUREMENT GUIDELINES

1 During the day, test subject away from bright sun. At night, test the subject in light. Plain room lighting is best.

2 Measure pupil size by holding a flashlight at a 45° angle from the subject's lateral side. Never shine the light directly into the eye from the front, or the pupil will constrict and destroy the measurement.

3 Compare subject's pupil size to a pupilometer. Note sizes in millimeters.

4 Keep flashlight about one foot away.

5 Note the reaction or absence of reaction in subject's pupils by "flicking" the light beam on and off the pupil.

6 Repeat above procedures on at least one non-drug-using person in the same light and note results for comparison.

7. A few persons with a very dark iris surrounding the pupil cannot be adequately measured.

PHOTOGRAPHIC DOCUMENTATION OF PUPIL SIZE AND REACTION

There are some specific legal occasions when photographic evidence of pupil size and/or reaction may be advantageous. The following are key points when using this procedure.

1 A standard camera with a flash is sufficient since it reacts faster than the pupil can.

2. Take photograph with pupilometer next to the eye for comparison.

3. Room light is satisfactory. Avoid bright light or darkness.

4. To document non-reactivity by photograph, take a picture in room light. Then place the subject in a very dark room for 5 minutes and repeat the same photograph. A non-reactive pupil will not dilate in darkness. It is advisable to take photographs of a control subject at the same time and in the same light to demonstrate the difference.

SUMMARY OF EYE EFFECTS WITH MARIHUANA

Finding	How Often Present	Usual Approximate* Time May last After Smoking
Redness	Frequent	4 to 6 hours
Dilated Pupil	Sometimes	2 to 4 hours
Non- or Slow-Reacting Pupil	Usual	1 to 3 days
Failure to Hold Constriction (Rebound Dilation)	Sometimes	4 to 6 hours
Strabismus (non-convergence)	Frequent	1 to 3 days
Droopy Eyelid	Frequent	2 to 4 hours
Failure to Estimate Distance	Frequent	4 to 6 hours

**Approximate means that the time may be shorter or longer*

LEGAL CASE EXAMPLES OF ACUTE MARIHUANA INFLUENCE

There are many legal challenges currently in process with employees who have been disciplined for marihuana use and/or detection in urine. In most of these caes, there was a claim of acute marihuana influence by the employer, but one of the three key elements was missing, i.e., cause for suspicion, physical evidence, or laboratory confirmation. Courts in California have now had considerable experience with drivers who are under the acute influence of marihuana and case law is now well established. The California Highway Patrol has developed the methodology to accurately identify the driver under marihuana influence and some of the information in this handbook is based on their experience. Following are two typical case examples.

CASE EXAMPLE #1 – California High Patrol

Element #1	Finding(s)
Cause to investigate	Weaving on road

Green coated tongue of marihuana-hashish smoker.

Glazed eye and droopy eye-lid of acute marihuana influence.

Reddish, glazed eye of acute marihuana influence. Normal size pupil and mild drooping of eye-lid.

Element #2
Physical Examination

Reddish eye
Strabismus (one-side)
Poor distance perception
Non reactive pupil
Animated
Anxious
Evasive
Giddy
Indifferent

Element #3
Laboratory Confirmation

Negative Alcohol Breath Test
Marihuana metabolite in urine

CASE EXAMPLE #2 – Industrial Accident

Element #1	**Findings**
Cause to investigate	Accident involving machinery
Element #2	
Physical Examination	Glassy Eye
	Flushed
	Sleepy
	Non-responsive
	Inconsistent
	Unsteady
	Inappropriate
	Stumbling
Element #3	
Laboratory Confirmation	Marihuana metabolite in urine

In the latter case, two lay persons made the physical observations and carefully recorded this in writing

Section III

IDENTIFICATION OF CHRONIC OR COVERT MARIHUANA USE

HOW TO MAKE A DIAGNOSIS OF CHRONIC MARIHUANA USE

- There are two major criteria used in order to make a diagnosis of covert or chronic marihuana use when a person doesn't admit use.
  1 Presence of suggestive behaviors and signs
  2 Marihuana derivative in blood or urine
- The major problem of chronic marihuana use is to know when to suspect someone.
- When someone is suspected of chronic marihuana use, they can be confronted by telling them the signs and behaviors that make you suspicious. Once confronted, it may be appropriate for a physician, employer, parent, teacher, coach, etc., to ask for a urine test for definitive proof.

WHY MAKE A DIAGNOSIS OF CHRONIC OR COVERT MARIHUANA USE?

Chronic marihuana use has so many debilitating and negative consequences that it needs to be identified as early as possible in order to prevent it's numerous medical complications and social problems.

In contrast to most other drug or alcohol abusers, marihuana users, in the author's experience, have a higher success rate in stopping and maintaining abstinence. Early identification and intervention usually produces good results. Consequently, the best way to help a chronic or covert marihuana user is to identify him, her as soon as possible.

WHEN TO SUSPECT CHRONIC OR COVERT MARIHUANA USE

Only a blood or urine test will definitely diagnose marihuana use. However, you should suspect chronic marihuana use if you observe a combination of some of marihuana's chronic effects. Some of marihuana's long-term effects can be scientifically attributed to its ability to adversely affect the brain's norepinephrine, or endorphin systems. In addition, chronic marihuana smoking causes irritation of the respiratory system, instability of glucose metabolism, and occasionally, abnormalities of sex hormones. These hormone and respiratory changes can provide clues to chronic covert marihuana use if one knows the basic signs and behaviors associated with them.

BASIC SIGNS AND BEHAVIORS ASSOCIATED WITH CHRONIC AND COVERT MARIHUANA USE

- Frequent absences from school or work
- Time distortion, including tardiness, unusual meal times
- Frequent missed appointments
- Constant use of eye drops (usually Visine®)
- Wears marihuana-leaf jewelry, insignia, or have clips to hold cigarettes
- Wear sunglasses indoors
- Abnormal sleep pattern such as staying up after midnight or daytime sleeping
- Repetitive forgetfulness or broken promises
- Frequent accidents, injuries, and/or traffic violations
- Loss of interest or motivation in job/school/relationships
- Deterioration of work or school performance
- Careless in hygiene and grooming habits. Females stop polishing their nails or wearing lipstick and make-up. Males skip shaving. Fail to brush teeth
- Recurrent respiratory infections
- Poor pain and stress tolerance
- Acne worsens
- Sudden personality changes. Becomes dull, bland, humorless
- Binge eating of sweets and snacks between meals

TIME DISTORTION WITH MARIHUANA

Chronic use of marihuana and many other stimulant drugs alters the brain chemistry so that normal time patterns are not maintained. To illustrate, the normal person tends to know when three meals per day should be eaten, when to go to sleep at night, take a 15-minute coffee break, or when to leave for school or work to arrive on time. A person whose internal time clock has been disturbed by chronic drug use will have distorted behaviors, including inability to keep appointments and meet time deadlines. They will also tend to stay up late at night or sleep during the day.

MOTIVATION DISTURBANCES

Marihuana may disrupt the brain chemicals that allow one to be motivated to carry out normal day to day activities. Lack of motivation exhibits itself in a number of rather typical ways. Particularly affected are such common motivations, such as eating a proper diet, maintaining

normal hygiene, and treating one's fellow man in a civil and decent manner. A chronic or covert marihuana user may be unable to maintain a sufficient level of motivation to carry out these routine daily functions.

ABNORMAL SELF-PERCEPTION OF JOB OR SCHOOL PERFORMANCE

Cocaine, marihuana, and PCF may markedly impair a person's job or school performance. For unknown reasons, however, the drug user may have little or no accurate perception of this. They may insist that they are "doing fine" and that they do not deserve criticism in spite of failing grades or poor athletic or job performance. Unfortunately, the loss of accurate perception of self-performance may persist after drug use is stopped.

PERSONS MOST LIKELY TO SUSPECT

Cigarette smoking is the single, biggest indicator that a person may be using illegal drugs. Approximately one-third of the adult population over age 18 years smoke cigarettes, and of these, about 25% abuse drugs and/or alcohol. These figures may be higher for youth. The percentage of youth who are between 13 and 19 years of age, who smoke cigarettes and frequently use marihuana is probably over 50%. One reason youth who smoke cigarettes are likely candidates to use illegal drugs is because they are already knowledgeable about inhaling and are tolerant to the heat irritation produced by ordinary cigarettes. Physically and psychologicaly, it is a short step from cigarette smoking to marihuana or cocaine inhalation. Over 99% of heroin users smoke cigarettes. In the author's experience well over 90% of PCP and amphetamine users smoke cigarettes.

CRAVING FOR SWEETS

Constant ingestion of sweets is a behavior that many chronic marihuana users exhibit. Marihuana releases norepinephrine from neurons which can reduce blood sugar and cause craving for sweets. Extremely poor dental hygiene is often observed in chronic marihuana users and this may be related to the constant ingestion of sweets

ANESTHETIC AND ANALGESIC EFFECTS OF MARIHUANA

Marihuana has some pain relieving effects It was even used for this purpose in ancient medical practice It is probably anesthesia of the auditory (hearing) mechanism that enables drug users to listen to

Swollen uvula and poor dentition in a chronic marihuana-hashish user.

Blackened gums of chronic marihuana-cocaine smoker.

excessively loud music that irritates most normal people. The author has observed that many industrial accidents occur because either the victim or propagator was a marihuana user and apparently did not hear machinery, a vehicle, or even a verbal warning.

WORK PROBLEMS OF THE HIGHLY-TRAINED WORKER

Numerous research studies document that marihuana, particularly the high potency forms now sold in the United States can impair tasks that require superior mental and physical skills. Also, impairments can be demonstrated many hours after the euphoria or "high" has subsided. Specifically, marihuana may impair immediate recall, glare recovery, peripheral vision, and time sense. Visual illusions and inappropriate or incorrect memory may intrude into consciousness, leading to an interruption of correct mental sequencing of events in time called, "temporal disorganization." While simple, repetitive and well known tasks can usually be performed properly, work requiring a high level of cognitive integration may be adversely affected. An example is a chronic marihuana user who operates a machine competently until it malfunctions at which time the person may not be able to recall or remember the appropriate safety measures. Put another way, when a person is under the influence of drugs, routine tasks usually get accomplished, but dealing appropriately with the unexpected or the unusual is quite another matter. Other adverse effects of chronic marihuana influence on the job include diminution of visual tracking, complex reaction time, hand steadiness, complicated signal interpretation, and attention span. Deficiencies in perception, memory and cognition make learning difficult which handicaps all but workers doing the simplest tasks.

The author has observed many middle-management personnel, who began smoking marihuana many years ago when it was only a 1-2% grade of potency. They now find they cannot achieve the level of skill called for in their jobs due to the impairment produced by the more potent marihuana.

SOME SIGNS OF DETERIORATING WORK PERFORMANCE

Work Patterns

- Inconsistency in quality of work
- High/low periods of productivity
- Poor judgment/more mistakes than usual and general carelessness
- Lapses in concentration
- Difficulty in recalling instructions
- Difficulty in remembering own mistakes
- Using more time to complete work, missing deadlines
- Increased difficulty in handling complex situations

Absenteeism

- Acceleration of absenteeism and tardiness, especially Mondays, Fridays, before and after holidays
- Frequent unreported absences, later explained as "emergencies"
- Unusually high incidence of colds, flu, upset stomach, headaches
- Frequent use of unscheduled vacation time
- Leaving work area more than necessary (e.g., frequent trips to water fountain and bathroom)
- Unexplained disappearance from the job with difficulty in locating employee
- Requesting to leave work early for various reasons

Accidents

- Taking of needless risks
- Disregard for safety of others
- Higher than average accident rate on the job

Mood/Actions

- Appears to be depressed or anxious
- Irritable
- Suspicious
- Complains about others
- Emotional unsteadiness / mood changes
- Withdrawn or improperly talkative
- Spends excessive amount of time on the telephone
- Argumentative
- Exaggerated sense of self-importance
- Violent
- Avoids talking with supervisor regarding work issues

Relationship to Others On the Job

- Overreaction to real or imagined criticism
- Avoiding and withdrawing from peers/supervisors
- Complaints from co-workers
- Borrowing money from fellow employees
- Complaints of problems at home such as separation, divorce and child discipline problems
- Persistent job transfer requests

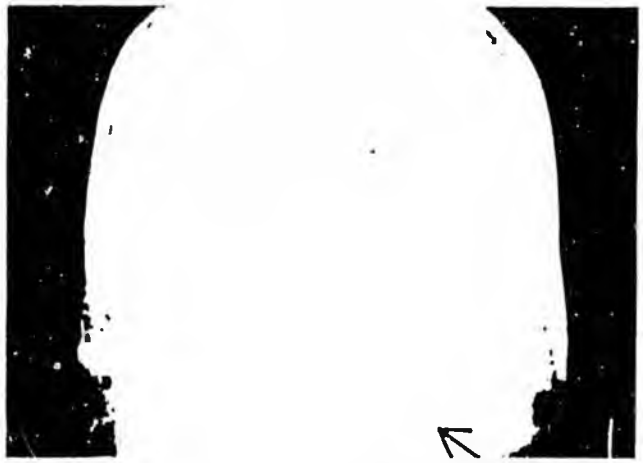
Physical Signs or Condition

- Weariness, exhaustion
- Untidiness
- Yawning excessively
- Blank stare
- Slurred speech
- Sleepiness (nodding)
- Unsteady walk
- Sunglasses worn at inappropriate times
- Changes in appearance after lunch or break

MEDICAL PATIENTS WHO SHOULD ESPECIALLY BE SCREENED FOR COVERT MARIHUANA USE

- Psychiatric patients under age 25
- Teenagers Young Adults with Chronic Respiratory Infections and Allergies/Urticaria
- Pregnant Women under age 25
- Males with gynecomastia (enlarged breasts)
- Weight loss (indicating poor nutrition)

Allergic rash due to marihuana smoking.



Sinusitis in a marihuana-hashish smoker.

WORKERS WHO SHOULD ESPECIALLY BE SCREENED FOR COVERT MARIHUANA USE

- Chronically Absent
- Job Deterioration
- Frequently Tardy
- Accident or Injury Prone
- Memory Lapses
- Repeatedly Miss Deadlines
- Excessively Sick
- Poor Hearing
- Sleeping on Job

TEST TO DETERMINE IF SOMEONE YOU KNOW IS LIKELY TAKING MARIHUANA AND/OR OTHER DRUGS

Following is a self-test to determine if a person might be covertly taking marihuana and/or other drugs. If you complete this test and it suggests drug use, you may want to confirm or deny your suspicion with a urine test.

1. Does the person eat three meals per day at the normal eating times? YES NO
2. Does the person make it to school work on time practically every day? YES NO
3. Does the peson voluntarily go to bed on weekdays by 11:00 p.m.? YES NO
4. Can you easily awaken the person in the morning? YES NO
5. Does the person meet curfews/or deadlines the vast majority of time? YES NO
6. Is the person's weight holding steady or slightly increasing? YES NO
7. Does the person comb his or her hair every morning? YES NO
8. Does the person brush his or her teeth at least morning and evening? YES NO
9. Does the person attend Church or Sunday School at least once a month? YES NO
10. Does the person invite friends to the house whose behavior is open and normal? YES NO
11. Does the person smoke cigarettes? YES NO
12. Does the person have a good attention span? YES NO
13. Does the person take responsibility for household chores? YES NO
14. Does the person take care to appear neat and clean? YES NO
15. Does the person frequently play loud rock music after midnight? YES NO

16. Does the person play "heavy metal" music or engage in other cult-like activities? YES NO
17. Has the person's acne worsened in the past 90 days? YES NO
18. Has the person lost interest in a school/work activity he/she used to enjoy? YES NO
19. Is the person having trouble getting along with teachers, coaches, friends, fellow workers, or spouse? YES NO
20. Is the person having trouble getting along with you? YES NO
21. Has the person lost interest in the clothes that he/she wears or changed the type of clothing worn (for example, "dressing down")? YES NO
22. Has the person suddenly had a drop in grades or work performance? YES NO
23. Has the person had over three colds, sinus infections, or other respiratory ailments in the past one year? YES NO
24. Does the person sniff a great deal or have a chronic reddened appearance under the nose? YES NO
25. Does the person smoke a brown type cigarette? YES NO
26. Has the person failed to come home at night on more than one occasion during the past 90 days? YES NO
27. Does the person complain that a lot of people don't see things his or her way? YES NO
28. Does the person constantly complain that people including the family don't understand him/her? YES NO
29. Has the person had more than two motor vehicle accidents or other traffic violations in the past one year? YES NO

INTERPRETATION OF TEST TO SUSPECT COVERT DRUG USE

Questions 1 through 14:

A Answer "No" to three or less: Drug use doubtful
B Answer "No" to four to six: Drug abuse very likely
C Answer "No" to seven or more: Drug abuse almost certain

Questions 15 through 29:

A Answer "Yes" to three or less: Drug abuse doubtful
B Answer "Yes" to four to six: Drug abuse likely
C Answer "Yes" to seven or more: Drug abuse almost certain

THE WORST THING TO DO IF YOU SUSPECT MARIHUANA USE

The worst thing to do is to do nothing because a person may have little time left in which to continue drug use without risking permanent neurochemical changes. If you suspect drug use, it is important to take action that will either confirm or discount your suspicions.

INFORMING THE SUSPECTED USER

Step one is to find a quiet, uninterrupted time to inform the suspected user of your suspicion. There is one common downfall when most persons do this. That is to fail to tell the drug user the precise reasons drug use is suspected. In other words, don't simply say, "I think you are using drugs." Say, "Here is a list of specific reasons that make me think you are using drugs." Then read the list. Be specific and include all the behavior and physical symptoms that make you suspicious. Refer to the above table, to make your list.

WHAT IF MARIHUANA USE IS DENIED?

1. Tell the individual all the behaviors you want changed so that you will not longer be suspicious.

2. If the individual is an employee and your personnel policies allow for a medical evaluation and/or urine test for drugs, obtain these for confirmation.

LEGAL RIGHT TO TERMINATE AN EMPLOYEE FOR COVERT MARIHUANA USE

Many private companies and public organizations are now identifying marihuana users by a urine test. In some cases, the test is done for a cause such as previously listed or it is done as part of routine testing at an annual physical examination or other periodic testing time. At the present time, there are numerous law suits and arbitrations going on throughout the United States over the issue of whether an employer may legally terminate an employee for covert marihuana use. Most of the litigation has been brought about because the mere presence of marihuana metabolite in blood or urine, regardless of amount, does not prove there was any job impairment or hazard. In addition, the precise time of marihuana ingestion cannot be pinpointed by a urine test, and

marihuana can even enter urine in small amounts through passive (being near others smoking) inhalation. The author has now reviewed, been consulted, or appeared in arbitration hearings for several dozen cases of marihuana detection by employers. Although future court judgments and/or legislation could modify current trends, the author passes on the following observations to serve as legal guidelines for employers regarding marihuana use by employees.

- Companies should not urine test anyone unless there are written policies regarding procedures and penalties. Unionized organizations must have prior joint labor-management agreements.
- Pre-employment urine screening and disallowing employment for marihuana in the urine is now routinely done in many companies, and it is rarely challenged.
- Termination is rarely challenged if the three elements of acute marihuana influence, as described in this handbook are present and carefully recorded in writing, i.e., reasons to investigate further, physical evidence, and laboratory confirmation.
- Employees who may endanger others by virtue of their marihuana use, such as transportation personnel, machinery operators, or physicians, may often be successfully terminated or lose their license by virtue of marihuana detection, even though all of the criteria for acute influence is not present.
- Suspension or temporary termination for the purpose of treatment or documenting clearance of marihuana from blood and/or urine is essentially never challenged on legal grounds.
- Repeated positive urine tests, even without meeting criteria for acute influence is rarely challenged.

RECOMMENDED GUIDELINES FOR EMPLOYERS WHO DETECT MARIHUANA USE

Unless there are purely business or other non-drug related reasons, the author generally recommends that employers not terminate marihuana users. Why? My experience clearly shows that marihuana users can be withdrawn and remain abstinent much easier than the vast majority of alcoholics and other drug (cocaine, heroin, etc.) users, provided they are periodically urine tested. Since marihuana may be detected in urine for many days after a single usage, periodic urine testing can insure abstinence. In contrast, cocaine and alcohol cannot be detected in urine for more than about 24 to 36 hours post use which makes relapse difficult to detect until it is full-blown.

For reasons not clearly understood by the author, he seldom sees marihuana users relapse if they remain abstinent for four consecutive months (120 days). In addition, the withdrawal symptoms of marihuana addiction are relatively mild and don't require hospitalization.

SPECIFIC STEPS TO RETAIN A MARIHUANA-DETECTED EMPLOYEE

1. Suspend or temporarily terminate the employee for purposes of clearing the urine of marihuana.

2. Don't hospitalize unless the employee requests it.

3. Have attending physician take a marihuana urine test weekly until clear.

   If you need precise documentation that marihuana is leaving the body in a timely, sequential fashion, plasma testing or quantitative urine testing can be done.

4. Return employee to regular duty when the attending physician certifies that the employee is fit for duty based on the following:

   a. No marihuana or other drug in urine
   b. No presence of strabismus and the pupil is reactive
   c. Has normal physical and mental abilities

5. Upon return to work, give employee in writing:

   a. List of all prior job deficiencies which were likely drug related
   b. Treatment and monitoring plan
   c. Penalty if there is future drug use

6. Urine test weekly for 90 to 120 days

7. Optional:

   a. Eye examination and alcohol breath test by trained person at time of each urine collection
   b. Drug education classes
   c. Counseling
   d. Self-help group
   e. Additional urine tests for one year

SECTION IV
IDENTIFICATION OF MARIHUANA DEPENDENCE OR ADDICTION

WHAT IS ADDICTION OR DEPENDENCE

- A modern definition of an addict or dependent person is someone who desires to keep a minimal quantity of drug in the blood stream at all times.

- When the drug quantity in the blood stream drops below a critical level, the addict will automatically take another dose to raise the blood level. The most common example is the person addicted or dependent on nicotine who will almost be unconscious of reaching for another cigarette in order to raise his or her blood level of nicotine. The minimal level in a marihuana addict is about 5-10 ng/ml of C-THC.

- It is necessary for the blood stream to maintain a minimal level of drug in order to saturate target areas of the brain. If a saturated area suddenly becomes unsaturated, withdrawal sets in. In the case of opioids and benzodiazepines, the target areas are known as "receptor sites."

- The concepts of physical and psychological dependence are archaic in light of new research on blood concentrations, receptor sites, brain chemistry, and withdrawal syndromes. All mind altering drugs, including nicotine, marihuana, and cocaine, can produce addiction or dependence, develop tolerance, and induce a withdrawal syndrome after cessation of chronic use. The author recommends the term "biologic" addiction or dependence rather than the terms "physical" or "psychologic" since both of these factors are always present to at least a limited degree.

- Addiction or dependence can be essentially diagnosed by simply knowing how long a specific drug stays in the blood stream and finding out from the user how often he/she uses it.

BACKGROUND EVIDENCE FOR MARIHUANA ADDICTION

Marihauna addiction was described in the United States over 40 years ago. In 1944, 35 "confirmed marihuana addicts" were admitted to a military hospital and developed withdrawal symptoms. Since this time, marihuana addiction has been reported in other countries. In addition, animals have demonstrated addiction to marihuana and there has been

one carefully controlled trial where humans were given known quantities of THC, and they developed withdrawal symptoms when marihuana was abruptly discontinued. Animals that are addicted to marihuana have demonstrated withdrawal symptoms when given naloxone, and the author has recently demonstrated this in a human marihuana addict. When naloxone precipitates withdrawal symptoms, it means that the addicting drug has opioid (i.e., heroin, morphine, etc.) activity. To complement these findings, another recent study in animals has demonstrated that THC will deplete endorphins in the nervous system. Furthermore, marihuana may also adversely affect the neurotransmitters, norepinephrine and serotonin. Current evidence suggests that marihuana addiction exists, at least in part, as a result of depleted endorphin, norepinephrine, and possibly other neurotransmitters.

COMMONLY OBSERVED MARIHUANA WITHDRAWAL SYMPTOMS

The following symptoms have been reported in animal and human studies

Insomnia	*Anorexia*
Nausea	*Photophobia*
Myalgia	*Cannabis craving*
Anxiety	*Depression*
Restlessness	*Mental confusion*
Irritability	*Yawning*
Chills	*Anergy*

TWO TYPES OF CLINICAL MARIHUANA DEPENDENCE

Two types of marihuana dependence are seen today. Type One is an individual who will self-administer marihuana several times per day, usually at an interval of about two to four hours unless asleep. This individual may voluntarily present to the clinician with the complaint that their daily dosage has escalated and that they are unable to cease use without medical assistance. The patient may or may not relate mental impairment primarily related to memory, motivation, time-keeping, abnormal thoughts, and work or school performance. In addition, they may relate a number of withdrawal symptoms that occur when they attempt abrupt cessation. The precise relapse rate following withdrawal is unknown, but it occurs.

CASE EXAMPLE: Voluntary Treatment

MV was a 25-year old male who presented with the complaint that he could not "stop marihuana by myself." He was a 12-year user having begun marihuana smoking at 13 years of age. He had used marihuana daily for about five years and was using two to three joints per day at the time of admission to outpatient treatment. The patient was married and held a regular job as a warehouse superintendent. He claimed he was having considerable conflicts with his wife and employer. In addition, he had noticed in the two months just prior to admission that he occasionally heard voices that were not real, did not always have total "control over his mind," and had some thoughts of suicide. He denied use of any other drug or excessive alcohol intake. His treatment admission breath alcohol was negative, and his urine contained marihuana metabolite, but no other abusable drug. The patient was administered desipramine, 25 mg. three times per day and was given weekly phsychotherapy for approximately six months. During the first ten days of treatment, he reported insomnia, abdominal cramps, diaphoresis, tachycardia, and anxiety. These symptoms subsided, and he submitted a urine void of marihuana approximately 30 days after admission. Most of the thought disturbances noted above disappeared after about two to six weeks of treatment. He denied any marihuana use during the six months after entering treatment, and he submitted monthly urine tests that showed no marihuana.

Type Two form of marihuana dependence is primarily being identified as a result of mandatory urine screening and treatment referral in the workplace. Seldom does a Type Two voluntarily present for treatment, although it may occur. In this form, the patient is usually self-administering marihuana every 24 to 36 hours and may give a history of carrying on this habit for several years. As in Type One, reported impairment relative to memory, motivation, time keeping, and job performance is variable. In contrast to Type One, however, the patient may report few if any symptoms of withdrawal upon abrupt cessation. Relapse, however, is common.

CASE EXAMPLE: Identification On Job and Mandatory Treatment

HS was a 37-year-old male salesperson. He was reported to the management of his company to be a marihuana user who also sold it to other employees while on company premises. A mandatory urine test revealed the presence of marihuana metabolite, and in order to retain employment he was required to undergo withdrawal and enter a periodic urine-testing program. Upon interview, he stated that he had used marihuana every evening for approximately 22 years. He believed this habit had not been injurious to himself until approximately three months prior to treatment when he began to notice some defects in his short term memory. Physical examination was normal. Plasma analysis showed 80 ng/ml of C-THC. He was administered desipramine, 25 mg. three times per day and tyrosine. During the first three weeks following cessation of marihuana, he reported mild insomnia, depression, anergy, and craving. Urine analysis showed no marihuana metabolite after about 50 days. After six weeks of abstinence, he reported improvement of short term memory and improved job performance.

METABOLIC BASIS FOR TWO FORMS OF DEPENDENCE

New data on the metabolism and pharmacokinetics of marihuana provide a sound rationale as to why two basic clinical forms of dependence appear to exist. When a marihuana cigarette is smoked, THC is converted to two major metabolites, OH-THC and C-THC. THC and OH-THC both have psychoactive effects, and they remain in the plasma at concentrations above about 5 ng/ml to 10 ng/ml for only about two to six hours. During this period they appear to produce a short term characteristic "high" or euphoria. This time period correlates well with the self-administration frequency of Type One marihuana dependence. The C-THC metabolite remains in plasma at concentrations above 5 ng/ml to 10 ng/ml for at least 48 to 72 hours or even longer. Although this metabolite may produce little or no euphoria, it is likely the compound that sustains Type Two dependence. A similar phenomenon also exists with some benzodiazepines, such as diazepam which also has long-lasting metabolites. For example, some withdrawal symptoms and even seizures may not appear for several days following cessation of diazepam dependence. The author has recently observed that withdrawal symptoms following abrupt cessation of marihuana dependence may not appear for several days.

SUMMARY TABLE: TWO FORMS OF MARIHUANA DEPENDENCE

	Frequency of Self-Administration	Likely Dependence metabolite(s)	Usual Referral Route	Patient's Perceived Dependence	Usual Severity of Withdrawal Symptoms	Relapse Rate
Type One	Multiple times each day	THC OH-THC	Voluntary self-referred	Significant	Moderate	High
Type Two	Every 24 to 48 hours	C-THC	Involuntary: Detected by mandatory screening	Minor to moderate	Mild	High

CLINICAL PRESENTATION OF THE MARIHUANA ADDICT

Until about 1982, the author seldom observed marihuana addiction/dependence in Los Angeles. Since that time, however, clinical demand for medical withdrawal treatment has steadily grown. Regardless of whether the patient sought treatment voluntarily or was identified by mandatory urine screening, all patients have essentially the same complaint, "Doctor, I've got a marihuana problem and I can't quit. I need your help."

As with other addictions, the marihuana addict doesn't normally seek medical withdrawal assistance from a physician until he/she has attempted to stop on his/her own, consulted a counselor, minister, friend, or family member, attended self-help groups, or even entered a hospital rehabilitation program and still continued to use marihuana. Unfortunately, there is no specific medical withdrawal treatment for marihuana addiction at this time. However, research is in progress to develop a specific withdrawal treatment.

HOW TO MAKE A PRESUMPTIVE DIAGNOSIS OF MARIHUANA ADDICTION OR DEPENDENCE

Addiction or dependence is assumed to be present if the following are evident:

- Person states that they have used marihuana one or more times per day for thirty or more consecutive days, just prior to evaluation.
- Person states that they cannot stop without medical assistance.
- Person states that they experience withdrawal symptoms, craving, or sickness when they stop use.
- Marihuana metabolite is present in urine or plasma

SECTION V

LABORATORY IDENTIFICATION OF MARIHUANA USE

BACKGROUND FOR LABORATORY IDENTIFICATION

- Modern research has identified, at least to a great extent, how the human body accepts, deactivates, and eliminates drugs. This process is usually called "metabolism" or "pharmacokinetics."
- Laboratory identification for drugs of abuse primarily attempts to assay for the suspected drug in urine or plasma (clear part of blood).
- Urine testing is primarily qualitative and determines what someone used rather than how much was used. Urine tests have some capability of determining approximately when a drug was used.
- Plasma testing can tell the quantitative presence of a drug and give a reasonable estimate as to ***when*** a drug was used. Plasma testing can also give an estimte as to whether ***enough*** drug was taken to ***produce acute*** effects or toxic levels. If the person is tolerant to the drug, a plasma level may have little meaning.
- Quantitative urine testing for marihuana is used primarily to help rule out passive inhalation and determine if marihuana cessation is truly occurring in someone who claims to have ceased use.

BACKGROUND AND HISTORY OF MARIHUANA TESTING

Although urine testing capability for some illegal drugs of abuse occurred in the late 1960's and early 1970's, urine testing for marihuana was not technologically possible until about 1980. Blood (plasma) testing for marihuana is currently changing from research to general status. Due to the newness of the tests, there has been controversy over their interpretation. A large number of recent research studies, however, have clarified interpretation so that urine and plasma testing can now be used with great confidence.

URINE TESTING METHODS AVAILABLE

Five different technological methods are now available for marihuana urine testing. They are summarized below.

TEST	APPROXIMATE SENSITIVITY	GENERAL COST
Enzyme Multiplied Immuno Assay (EMIT)	20 ng/ml	Very Low
Thin Layer Chromatography (TLC)	10-20 ng/ml	Low
Radioimmunassay (RIA)	10-20 ng/ml	Low
Gas Chromatography — Mass Spectrometry (GC/MS)	5-10 ng/ml	High
High Performance (HPLC) Gas Liquid Chromatography	5-10 ng/ml	High

TOXICOLOGY UNITS OF MEASUREMENT

The usual measurement for marihuana metabolites (THC, OH-THC and C-THC) are in nanograms per millimeter. This is usually abbreviated ng/ml.

1 g	=	gram (There are 28 grams in one ounce)	1.0
1 mg	=	milligram (One thousandth of a gram)	0.001
1 ug	=	microgram (One millionth of a gram)	0.000,001
1 ng	=	nanogram (One billionth of a gram)	0.000,000,001
1 pg	=	picogram (One trillionth of a gram)	0.000,000,000,001
1 L	=	liter (approximately one quart)	
ml	=	milliliter (One thousandth of a liter)	

PLASMA TESTING

At this time, plasma testing is very expensive and is done by GC/MS or HPLC. It is quantitative, requires great technological skill and, consequently, is costly. Some commercial laboratories are beginning to offer plasma testing. However, there is little practical advantage of plasma over urine testing for screening asymptomatic persons. The amount of OH-THC and C-THC may not tell either precisely when

someone has used marihuana or how impaired they may be. It should be especially noted that plasma levels over 10 ng/ml, that are not accompanied by acute signs or influence, likely indicate the presence of tolerance and possibly dependence. The best use of plasma testing is to determine if a chronic user is eliminating C-THC from the plasma during withdrawal.

ACCEPTED STANDARDS TO AVOID FALSE POSITIVE URINE TESTS

Unfortunately, some laboratories new to urine testing are not aware of the long-established (at least 15 years!) standard "rule of two." This stan ard calls for testing any positive urine specimen, i.e., urine containing a drug with a second technological method. Only when the drug is detected by a second technologic method, is the urine deemed a true positive.

The one notable exemption to the "rule of two" is when the tested individual admits to recent marihuana use. This situation is frequent in medical and clinical settings. When this is the case, a single method is satisfactory. Other than self-admission, the author recommends the rule of two be followed in the following situations.

1. Pre-employment testing
2. Post-employment testing
3. Screening for covert use
4. Potential litigation

INTENTIONAL FALSIFICATION METHODS

Drug users have numerous techniques to submit a false negative test. Many adulterants may cause urine screening to show falsely negative.

Common Falsification Methods	Adulterants which may cause False Negatives
• Submit toilet or tap water	Salt
• Switch urines	Bleach
• Bring concealed urine in bag, mouth, or in body cavity to testing location	Lemon juice
	Liquid soap
	Blood

URINE TESTING FOR COERCION PURPOSES

There are many instances when the presence of marihuana in urine

may result in a coercise action.

Loss of job
Suspension from job/school
Incarceration

In the early 1980's, the general standard to use a marihuana positive urine test for coercise purposes was to have it confirmed by GC/MS or HPLC after initial detection by EMIT, TLC, or RIA. This standard was primarily established because the less expensive methods, EMIT, TLC and RIA methods were not yet refined. Currently EMIT, TLC and RIA methods are extremely sensitive and specific. This has, for most purposes, eliminated the need for use of GC/MS or HPLC for confirmations. Many experts now believe that when two of these three methods (EMIT, RIA, TLC) are positive, there is actually as much or more assurance that marihauana is in the urine than when detected by GC/MS or HPLC. The reasons for this are that GC/MS and HPLC take extraordinary technical skill that is subject to human error and that the sensitivity is too low (i.e. less than 10 ng/ml).

Despite varying opinions among qualified experts, a given legal or other situation may mandate use of GC/MS or HPLC confirmation. To possibly avoid cost and litigation the author usually recommends that marihuana first be found on two of these three methods (EMIT, TLC, RIA) and that the urine specimen found to be positive be frozen in the event that some legal or other situation demands confirmaton by GC MS or HPLC. Urine specimens can be frozen almost indefinitely without degradation of its marihuana content.

PASSIVE INHALATION

Studies have shown that someone who is extremely close to other persons who smoke marihuana may passively inhale it. Although someone may passively inhale enough to show 10 to 20 ng/ml in the urine for one or two days post-exposure, the author knows of no documented cases which show that passive inhalation can cause as much as 50 ng/ml of marihuana metabolite in urine, unless the subject is exposed to very dense marihuana smoke for many hours.

LENGTH OF TIME MARIHUANA STAYS IN PLASMA AND URINE

A great deal of publicity has been generated as to how long marihuana metabolites may remain in urine It remains detectable in plasma and urine for many days due to the fact that it is fat-soluble. When smoked, marihuana metabolites enter the fat, lodge there, and then leak out over a period of time It is important to point out that it is

only the regular, chronic user or addict that keeps marihuana in urine for more than a few days. The length of time that marihuana metabolites can be detected in plasma is much shorter than in urine because the kidney concentrates drug in the urine 100 to 1000 times that found in plasma. In other words, marihuana can be detected in urine much longer than plasma due to the kidney's ability to concentrate drugs.

APPROXIMATE URINE RETENTION

Approximate Frequency of Use	Approximate Length of Time In Urine*
Once per week	2 to 20 days
Twice per week	5 to 30 days
Daily	15 to 45 days

**Varies as to whether user is a chronic or occasional user and amount used.*

APPROXIMATE PLASMA RETENTION AFTER SMOKING MARIHUANA

Metabolite	Approximate Time In Plasma*
THC	2 - 3 hours
OH-THC	4 - 6 hours
C-THC	3 - 6 days

**Varies as to whether user is a chronic or an occasional user and amount used.*

HAIR AND SALIVA ANALYSIS

Saliva analysis is possible because the smoker leaves THC residues in the mouth while smoking. If found in saliva, it usually means that marihuna has been smoked within the previous one to three hours. However, this test cannot be relied upon for confirmatory diagnosis of marihuana use because the smoker can easily spit or wash the residue out of the oral cavity.

Hair analysis can be done if there is a medical or legal reason to know if someone used a drug approximately 30 days prior to hair sampling. Analysis of hair will not reliably reveal drug use occurring within the past one to two weeks prior to sampling. The major use of hair sampling is in forensic cases, and not appropriate for the usual drug use screening situations.

RELATIONSHIP OF URINE AND PLASMA CONCENTRATIONS WITH IMPAIRMENT OR INFLUENCE

There is no more misunderstood aspect of marihuana identification than the fact that there is no reliable way to correlate plasma or urine concentrations with impairment or influence. Undoubtedly, this confusion stems from the criteria used for determining impairment from alcohol. There is general agreement that a blood (reflected by breath or urine) alcohol concentration of 100 mg/deciliter or .10 mg% indicates some impairment or influence. No such correlation can be made with marihuana since it is fat soluble and released very slowly from the body compared to alcohol. For example, a very low urine concentration may be found in persons severely intoxicated and vice-versa.

The non-correlation of urine and plasma concentrations of abusable drugs with the degree of impairment and influence has recently prompted the National Institute on Drug Abuse to make this statement in the Journal of the American Medical Association: "Testing of drugs or drug metabolites in urine is only of qualitative value in indicating some prior exposure to specified drugs. Inferences regarding the presence or systemic concentration (quantity) of the drug at the time of driving or impairment from drug use are generally unwarranted. The presence of an illicit substance in unne that may indicate prior illegal action can, however, add a dimension to probable cause of observed driving performance."

Despite the lack of correlation between plasma and urine concentration and impairment, the finding of marihuana metabolites in urine or plasma means that marihuana is in body tissues including the brain, eye, nerves and muscles. Although a chronic user or addict may be tolerant and not have physical signs of acute influence, an employer, coach, teacher, or parent must assume that some subtle impairment exists. The author therefore, highly recommends that any individual with marihuana in urine, and particularly plasma, not be allowed to drive, work, play sports, or participate in any activity that could produce harm to the marihuana user or innocent bystanders. Risk type acitivities should not be resumed until repetitive urine tests show no traces of marihuana.

GUIDELINES TO SELECTING A LABORATORY

1. Use only a laboratory that specializes in urine and/or plasma testing.
2. Follow the standard, "Rule of Two."
3. Has procedures to insure integrity and security of samples.
4. Reports results within 72 hours
5. Can freeze specimens for future analysis
6. Communicates well.

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August 7, 1987

Dear Alaskan:

A LINE ON POT

We know a lot more than we used to about what pot does to the lungs. It's becoming common knowledge that smoking pot can do a number on your "windbags."

Part of the job of the scientists is to use the information they have and then put two plus two together. A very important piece of information concerns the smoke made when pot is burned. It contains over 150 different chemicals. One type of chemical, hydrocarbons, are proven to cause cancer. Pot smoke has a lot more hydrocarbons than tobacco smoke.

So add it up. Cigarettes are the leading cause of lung cancer. A key reason for this is the hydrocarbons formed when cigarettes are burned. If marijuana smoke has more of these hydrocarbons than tobacco, do you really need to wait 25 years to be "sure" smoking marijuana can cause lung cancer? Statistics are how we know cigarettes cause cancer. Proof that marijuana causes cancer is only a matter of time.

Even if pot smoke does have more cancer-causing agents than tobacco smoke, is that such a big deal? After all, many cigarette smokers puff through two or three dozen cancer-sticks daily. Not even a heavy burner goes through that much pot. Indeed, hardly anyone smokes a "pack" of joints each day, but think about these ideas:

1. How many cigarette smokers hold the smoke in for ten or twenty seconds after they inhale? Deep and long toking of marijuana allows more time for harmful particles and gases to act on the lung cells.

2. Most post smokers use paper in rolling doobies than you find in cigarettes. Burning paper makes chemicals that irritate the lungs.

3. More marijuana chemicals end up in lung tissues than in many other body parts. They're strongly attracted to lungs, because they flow toward the fat of the lungs like moths to a light bulb.

The lungs have special cells to destroy disease-producing bacteria. For at least six hours after smoking one joint, they don't do their job as well. Swiss researchers exposed over 5,000 samples of lung tissue (from mice, hamsters, and HUMANS) to tobacco and marijuana smoke. Three days a week, a certain number of tissue samples got a "toke." After only 35 weeks, cancerous changes clearly occurred, and the damage was worst in the lung tissues exposed to marijuana. Remember, these are only test cells in a dish, but it's an important clue.

Some studies have not found evidence that smoking pot is especially harmful to the lungs. Most these, however, did not use the kind of detailed tests many doctors feel are needed to detect early marijuana-related lung damage. X-rays have been commonly used to check for lung damage due to marijuana; however, x-rays aren't very reliable for this purpose. Early detection of damage requires more detailed testing.

You know, some people have a really amazing attitude about smoking pot. They don't think it's "real smoking," like smoking cigarettes. Scientists today say--your lungs know no difference!

Taken from MARIJUANA, TIME FOR A CLOSER LOOK, by Curtis L. Janeczek Sandy Spargo

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A LINE ON POT

Dear

Dr. Carlton Turner is often called, "The man who knows more about marijuana than anyone else in the world." He is the Director of the White House Drug Policy Office. He has been the Director of a government-sponsored marijuana reserach project at the University of Mississippi. The following is information from that research project.

Dr. Turner is "up" on the growing of different varieties of cannabis from all corners of the world. He has read over 6,500 scientific papers published on cannabis--and what's more, he and his three staff members summarized each of them. He and his research team published about 100 scientific papers on cannabis. These are the reasons why he has been called, "The man who knows more about marijuana than anyone else in the world."

Dr. Turner and his team identified 421 different chemicals in marijuana, from 18 different chemical classes. For example, there are 50 different types of waxy hydrocarbons--which help make the tar in pot smoke. There are 103 different terpines, most of which, like the tars, are very irritating to the lungs. Twelve fatty acids. Eleven steroids. Twenty nitrogen compounds. There are toxic agents, including carbon monoxide, ammonia, acetone, and benzene. There are also cancer-causing chemicals, including benzathracene and benzoprene. And they are found in pot smoke in amounts which are 50 to 100 percent greater than are found in tobacco smoke.

And when marijuana is smoked, the 421 chemicals turn into over 2,000 chemicals--from one single joint. Furthermore, when these 2,000 chemicals are metabolized--broken down so that the body can get rid of them--many hundreds more chemcials are produced!

There is one chemical in cocaine and one chemical in alcohol.

Pot is very far from being a simple natural weed. Included among the other chemicals are a class of chemicals which exist only in the cannabis plant, and those are the cannabinoids. Dr. Turner and his staff discovered 61 of them. The most famous is Delta 9-THC. Tetrahydrocannabinol, or THC, for short. This one produces the "high."

Only a small percent of the THC in a single joint get through the blood-brain barrier to create the "high," which gives some indication of what a powerful chemical THC is. The blood-brain barrier is the protective system made of capillary walls and cell membranes. It acts as a sieve to prevent certain toxic chemicals in the bloodstream from entering the brain."

A small amount is acting on the brain, and the rest of the THC is acting on the lungs, on sex and reproductive organs, and every cell in the body.

Another thing that few people realize about THC is that it's very jumpy. If you buy a pack of tobacco cigarettes, you can be sure that the next pack of that same brand will be the same. Same flavor and same strength. That can never happen with joints--cannabis cigarettes. This is because the cannabinoids keep changing. They not only change while they're growing in the plant, but there are different THC strengths in different parts of the same plant. What's more, the strengths vary according to the age of the plant and the sex of the plant. There are male and female plants. And, in this case, the males are the weaker of the species--so far as THC goes. Even after a joint is made, TCH strength varies according to the length of time it's stored, the place it's stored in, and the temperature it's stored at.

If pot is so changeable, how did Dr. Turner supply a standard brand for the scientists? The researchers gave their THC a lot of tender loving care. They used a great deal of time, manpower, and special machinery in order to provide researchers with marijuana that has a known amount of THC. Or scientists were given individual cannabinoids. When they got their pot, researchers had to store it in the freezer. Since THC is such a temperamental drug, researchers were asked to submit their samples every few months for re-analysis.

Those 61 chemicals found only in the cannabis plant are fat lovers. They don't dissolve in water, or blood, or urine. Therefore, they're not easily washed out of the body. They seek the fatty organs of the body and settle there. There's one other substance which has as much staying power in the body cells. DDT. It's a useful chemical, but because it clings on in body cells, it was banned.

When the high is gone, the pot is not.

Source: POT SAFARI by Peggy Mann, 1985.

Sandy Spargo
965 Goldbelt
Juneau, AK 99801 586-2392

September 21, 1987

Dear

A LINE ON POT

"The Alaska Peace Officers' Association (APOA) supports recriminalizing marijuana." This position is taken from the Position Statements of the Alaska Peace Officers' Association Concerning Legislative Proposals before the Fifteenth Alaska Legislature, March, 1987.

"Alaska is the only state to have, in effect, legalized small amounts of marijuana--up to four ounces--for personal use. No other state has adopted a similar law. Using small amounts of marijuana legally stimulates trafficking of the drug, which is illegal. The existing statute, in effect, promotes illegal activity.

Possession of any quantity of marijuana is against federal law, while state law permits possession of small amounts. This creates confusion in the minds of the public. This dichotomy of federal law v.s. state law tends to breed disrespect for the law. As the Baltimore Sun editorialized in early 1984, 'Only in Alaska can you sit at home and smoke marijuana, secure in the knowledge that you are breaking federal law with the blessing of the State Supreme Court.'

Alaska's tolerance of marijuana has also inhibited the efforts of the U.S. to obtain agreements by foreign countries to crack down upon illicit drugs in their country. According to the Undersecretary for International Narcotics Affairs, Department of State, in a recent address in Anchorage, several foreign countries have questioned the sincerity of the U.S. regarding suppression of illicit drugs by calling attention to Alaska's legalization of small amounts of marijuana. This is significant, since the U.S. is a signatory nation to two international conventions concerning control of narcotics--the Single Convention on Narcotic Drugs of 1961 and the Psychotropic Substances Act of 1971, which include outlawing marijuana.

APOA considers the contradiction of federal and state law regarding marijuana, the increasingly effective health campaigns against smoking, and the public's proclaimed respect for the law, with state law permitting use, to be sending mixed signals to our youth. Either society condones drug use and smoking or it does not. Our collective position should be clear to our young people.

The Ravin decision leading to legalizing marijuana was based, in part, upon the finding that the state could show no clear and convincing public need to ban marijuana. Since then, more and more information from around the country shows increasing concern about the health aspects of smoking in general and marijuana in particular. The APOA believes that a clear and convincing health issue can now be made to support a ban upon marijuana use.

The APOA knows of no police department that would undertake an intensive enforcement effort against persons possessing small amounts of marijuana, if possession would be recriminalized. Frankly, there are more urgent needs to be addressed. Therefore, we would support a citation, mail-in-bail approach, as is now used for most traffic infractions.

The APOA is more interested in consistency of our laws, clear and concise positions about marijuana for our youth, and other advantages of recriminalization than in a tough and unyielding enforcement program."

The Alaska State Legislature will be looking at House Bill 55 and Senate Bill 32 to recriminalize marijuana next January. The intent of the bills is to make possession of less than 1/2 pound of marijuana a misconduct in the sixth degree. This is a Class B Misdemeanor and is punishable from 0 to 90 days in jail and a maximum fine of $1,000.

Sincerely,

Sandy Spargo
Safe Homes/Juneau
965 Goldbelt
Juneau, Alaska 99801

October 9, 1987

A LINE ON POT

Dear

Dr. D Harvey Powelson (formerly Chief of Psychiatry at Univ. of California Berkeley's Cowell Memorial Hospital reported the following in LISTEN: Journal of Better Living.

"I think marijuana is the most dangerous drug we have to contend with, for a number of reasons.

First, unlike any other drug except DDT, marijuana stays in the body for a very long period of time. It stays in the brain, and it keeps operating long after people are high. This time element is anywhere from six weeks to six months. Biochemically, using tracers has proved that only half of the marijuana leaves your body in a week.

Marijuana just stays there. When marijuana users get high - it usually takes them two or three times, because they have to build up a certain amount in their brain. Once they get high, they take another joint and get a little higher, then the high drops off and they think they are sober again. BUT the marijuana is still active. Then three days later they take another joint and they get high once again. But they are suffering the effects of marijuana ALL THAT TIME.

It could be called a cumulative effect, but what I'm really talking about is the fact that marijuana stays active in the brain long after the user feels high.

(Consequently) many people in this country -- literally millions -- are using marijuana and are stoned. And they may be people you and I are depending on the fly an airplace or drive a bus or perform our surgery, or drive on the highway.

I would say that there is NO EVIDENCE whatsoever that marijuana in any way is good for you. There's very strong evidence, which you can see for yourselves if you look around, that it damages the brain, that it damages your ability to think, it damages your chromosomes, it damages your immunity system -- all of this at a rate of something in the neighborhood of 20 times as rapidly as alcohol. "

Sincerely,

Bobi Trani
Safe Homes/ Parents Against Drugs

November 23, 1987

"A LINE ON POT"

Dear

Juneau was selected as the only city in Alaska to participate in a "Just Say No" Pledge Drive campaign. One student and a parent from Juneau will accompany 50 other participants in Grand Marshall capacity for the National "Just Say No" Walk in May. In conjunction with the "Just Say No" Pledge drive, many other exciting activities and training took place during the week. Bobby Heard, 19 year old teen trainer for "Just Say No" visited Juneau to work with our middle and high school age students to begin to establish "Just Say No" clubs in Alaska. At the conclusion of his visit to Juneau and to Ketchikan, he wrote this letter to our paper and to other members of the Blue Ribbon Commision on Youth. He was very concerned about the attitude our youth have about "their right" to use marijuana. This, once again, is an indicator of what a mixed message our marijuana law is for our youth.

I have submitted Bobby Heard's letter to the Juneau Empire, to you for your information. I was impressed with his insight and his forthright approach in identifying a large problem our youth deal with, and his willingness to do something to address the problem.

Please consider this letter as you begin to establish priorities for the upcoming session. Our youth need your help in sending a clear message that Alaska does not tolerate the use of illicit drugs including marijuana.

Sincerely,

Bobi Trani
Alaskans for Drug Free Youth

State's marijuana law 'just says yes'

Dear Editor:

How very exciting it was to be part of your city's "Just Say No Day." Everyone who participated and was involved should be commended.

Events like yours are very important because they help to focus attention on the massive problem of drug and alcohol abuse. Even though public awareness of drug and alcohol issues is at an all-time high, we must not relax our determination to speak out about substance abuse. The problem of dealing with drug and alcohol abuse must be kept at the forefront of America's agenda.

Even though I left Alaska impressed by your interest in getting involved in preventing drug abuse, I also left concerned. Concerned for the many young people I met who were understandably confused about the stand adults want them to take on the drug issue.

For many years young people have grown up in a "do your own thing," "freedom of choice" environment. According to some experts, it may be this permissive attitude on the part of parents, as perceived by their children, that is responsible for much of drug use among adolescents. It is imperative that parents and communities project a non-use message to their young people; substance abuse will not be accepted.

The most confusing message Alaska is sending its young people is your law which makes possession of marijuana legal for those over 19 years of age. Sure many adults may argue "it's my choice," but what about the young people who also believe it's their choice because they see mom and dad doing it?

In every other state in our country, marijuana is considered a harmful substance and is illegal. How can Alaska ask its young people to "Just Say No" when it's legal for adults to "Just Say Yes"?

Sincerely,
Bobby Heard
Round Rock, Texas

Dear

A LINE ON POT

"He was always an honor student until that time. It took three years for me and my husband to recognize he was using pot. A friend turned him on. All his group of peers used pot. He changed from being loving and open to being withdrawn and self-centered. He was careless and left marijuana papers around, so we found out.... He had real trouble wit[illegible]is memory. He couldn't tell jokes, because he couldn't remember them."

"He got into other drugs: uppers, downers, PCP, Quaaludes. He would steal, at first from his sisters, and he dealt. He got arrested for stealing. He and some friends went to another town and stole tires and brought them home in my car and left them in the driveway. It was as if he couldn't make the connection between stealing and hiding the evidence. The judge ordered him to go to jail for two years or to treatment. He went to a treatment center."--Viola (mother of an ex-user), The Marijuana Question by Helen C. Jones and Paul W. Lovinger.

A 1985 study done by the Justice Department reports, "A higher percentage of today's criminals were under the influence of drugs at the time of their offense than were criminals in the late 1970's. Three-fourths of a representative sample of jail inmates in 1983 admitted using drugs at some time in their lives, and one in four said they were under the influence of one of more drugs at the time of their current offense. Half of the offenders were using marijuana."

Sandy Spargo
Safe Homes/Juneau
965 Goldbelt
Juneau, AK 99801
586-2392 (w)
586-6122 (h)

Dear

A LINE ON POT

Malcolm E. Smith became alarmed when his children were using marijuana. His warnings were answered with the usual, "marijuana is no worse than tobacco or alcohol." He could not give them the facts necessary to convince them otherwise. He was determined to assemble those facts. The Marijuana Danger is the result of endless amounts of time and effort spent in reading, researching, and assembling what he believes is overwhelming evidence that marijuana is not only more dangerous than cigarettes and alcohol, but that it can cause brain damage and adversely affect almost every part of the human body.

— 758 sources as attached

Alcohol damages chromosomes. Marijuana damages chromosomes.

Alcohol damages the immune response system. Marijuana damages the immune reponse system.

Alcohol damages the brain. Marijuana damages the brain.

It takes decades for irreversible brain changes to appear in the heavy drinker. Irreversible brain changes are apparent after 3 years of daily marijuana use.

One person in six who uses alcohol is likely to become addicted. Three in six people are likely to become addicted to marijuana.

One ounce of alcohol completely metabolizes to carbon dioxide and water within 12 hours. One joint takes 30 days to be eliminated from the human body.

Alcohol damages the ability to think. Marijuana damages a person's ability to think 20 times more than alcohol.

The chronic disabling effect becomes apparent after 10 to 20 years or more years of excessive alcohol use. The chronic disabling effect becomes apparent within two or three years of marijuana use.

Hallucinations occur in alcoholics in a far advanced disease stage. The psychotropic effect of marijuana may cause hallucinations in small doses.

It can be predicted with certainty what one ounce of alcohol will do someone. You cannot predict what one joint of marijuana will do to to someone.

Alcohol develops a psychogenic dependency. Young people develop a psychogenic dependency on marijuana more quickly than with alcohol.

" The practice of combining the use of marijuana and alcoholic beverages is becoming more common, and, as such, posses a hazard of more widespread and severe acute reactions resulting from their combined effects," reported the American Medical Assoc. Council on Scientific Affairs, December 6, 1977.

Sandy Spargo
Safe Homes of Juneau
965 Goldbelt, Juneau, AK, 99801/586-2392 (w)

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Dear

A LINE ON POT

The Journal of Respiratory Diseases. November, 1987, has now stated that there is "striking evidence of short- and long-term consequences" of marijuana smoking.

"**Why might marijuana be more harmful than tobacco?** Daily smoking of only a few marijuana joints appears to be comparable with smoking over 20 tobacco cigarettes a day .... One explanation may be that the components of marijuana are more irritating to the lungs than those of tobacco smoke. Comparison of the smoke contents of one joint of marijuana with those of one unfiltered tobacco cigarette of the same weight reveals many similarities, both qualitative and quantitative, as well as a number of differences. While nicotine is present in tobacco but not in marijuana Δ^9-tetrahydrocannabinol (THC)--itself a respiratory irritant--and more than 60 additional cannabinoid compounds are present in marijuana but not in tobacco. In addition, marijuana smoke contains greater than 50% more of the carcinogenic polynuclear aromatic hydrocarbons benzanthracene and benzpyrene than is found in tobacco smoke, indicating the potential for malignant changes in the airways of frequent users.

Another possibility is that more particulates and irritating gases per cigarette are deposited and retained in the lungs of marijuana smokers than in the lungs of tobacco smokers, possibly because of the manner in which each type of cigarette is smoked. To investigatge the latter possibility, we assessed smoking dynamics--the amount of smoke particulates delivered to the respiratory tract and the change in the amount of end-expired carbon monoxide while a single marijuana or tobacco cigarette was smoked.

The results indicate that marijuana smokers took nearly twofold larger puffs, inhaled the smoke into their lungs 40% to 50% more deeply, and retained the smoke in their lungs three to five times longer than did tobacco smokers. Moreover, these differences were associated with a more than three times greater increase in end-expired carbon monoxide and a three to four times greater delivery and respiratory deposition of smoke particulates from a single cigarette of marijuana compared with that of tobacco."

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January 1987

THE EMPEROR SMOKES "POT"

Like the subjects, in Andersen's fable, who lined the streets "oohing" and "ahhing" their naked "Emperor's New Clothes," the American public has incredibly insisted upon disregarding marijuana's presence in every aspect of adolescent and young adult pathology. Unlike those subjects who heeded the observation of the "clear-eyed" child, our child-like citizens have chosen to ignore the warnings of the research scientists and parents who have been shouting that this "harmless" hero of the illicit drugs has been "stark naked" for over 16 years.

The simplest of epidemiologic studies reveal marijuana's central role.

In exact proportion to the unheralded and pandemic increase in marijuana use we have insisted upon ignoring its relationship to:

- the largest proportion of maladjusted veterans ever to return from but 24 months of service (limited to 12 months in Viet Nam) - still in fatigues and "treatment" 20 years after discharge from a war whose 11-year casualty figures approach those of the single Battle of Gettysburg, but for whom we have had to invent a new and wholly improbable psychiatric illness called "post traumatic neurosis" rather than recognize their chronic drug problems.

- a precipitous rise in every category of juvenile and young adult crime (both violent and non-violent).

- a precipitous and progressive increase in truancy and school drop-out.

- a progressive increase in teenage runaways, vagrancy, prostitution, pregnancy, abortion, and venereal disease.

- a progressive and precipitous increase in teenage depression and suicide.

- a progressive and precipitous rise in the psychiatric referral of adolescents and young adults for all known psychiatric diagnoses, as well as the previously unfamiliar consequences of multiple drug abuse.

- A PROGRESSIVE AND PRECIPITOUS FALL IN EVERY MEASURE OF ADOLESCENT AND YOUNG ADULT INTELLECTUAL COMPETENCE, NOT REFLECTED IN ELEMENTARY SCHOOL TEST SCORES.

- A PROGRESSIVE INCREASE IN A HITHERTO UNSEEN AND UNKNOWN "TEEN-AGE" "CHRONIC ORGANIC BRAIN SYNDROME" CALLED "BURN-OUT," WHICH NOW OUTNUMBERS ALL OTHER EXTANT PEDIATRIC, ADOLESCENT, AND YOUNG ADULT DISEASES COMBINED.

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COMMITTEES OF CORRESPONDENCE INC.

Drug Abuse Newsletter

August 1987

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ADDICTION AS A PRIMARY DISEASE

Since the recognition of addiction as a primary disease, a variety of opinions have emerged on the subject. This paper will clarify the primary disease of addiction from the perspective of the parents' movement, and it will hopefully clear the air on the subject. Unfortunately, some prefer for whatever reason to look at addiction as some type of moral issue or character deficit, which it is not.

A disease is a disorder which results in the disruption of normal body function (in this case psychological or physiological function). Most diseases have identifiable signs and symptoms as well as one or more known causes. Many, however, have no known cause.

Heart disease (atherosclerotic coronary artery disease) for example is a prototype disease. It is known that genetics, the environment, personality, and noxious stimuli are factors which may cause heart disease. A person who has a family history but makes an effort at controlling other elements such as diet and smoking may not develop heart disease. On the other hand, a person with no family history but who has a bad diet, smokes, and is under heavy stress may develop the disease. Conscious control of lifestyle early in life can help arrest the disease whether or not there is a genetic predisposition.

Addiction is very similar. It is a chronic, progressive, yet treatable disease with a variety of signs and symptoms. Family history of addiction produces a genetic risk which may increase the risk of subsequent relatives becoming addicted if the right conditions exist.

Even though heavy emphasis is placed on genetic predisposition toward addiction, we should not forget that children at risk were generally raised in impaired families in which addiction existed. The learning of interpersonal skills may become disrupted in such an atmosphere (environmental stress). Other examples of the environment include schools, peer groups and the entertainment media. Any may have positive or negative influences.

Personality has some effect as well. Some individuals are extremely resilient to genetic, environmental, or other risks. Others may fall prey to addiction easily. Evidence exists that fostering early refusal skills while bolstering self image helps to buttress an individual's ability to resist problems.

Last, but certainly not least is the exposure to noxious stimuli (drugs and alcohol). By exposure to mood altering substances alone, addiction may be precipitated. Most addicts intended to originally use recreationally or to self medicate. They all originally believed that they could somehow control their use.

This is the great danger of recreational drug use. Any drug of abuse from cocaine at one end of the spectrum to caffeine at the other is addictive if it is used enough. Furthermore, the evidence is clear that the earlier the exposure to mood altering drugs, the greater the risk of subsequent problems. Thus, no mood altering substance should be used in adolescence.

The symptoms of addiction have been well described elsewhere. In general, a compulsion for mood alteration is the hallmark. As the disease progresses, mood changes, interest in school or work slides, and in general performance suffers. As interpersonal relationships fail, families and friends will bear a great burden. It is generally easy to recognize late addiction, but early addiction may be far more subtle. Early addiction may be manifested as repetitive intoxication despite admonishments to the contrary. Recognizing resistance to maintaining sobriety is the key to early recognition. Excuses and promises of the addict always cloud the issue.

Many attempts have been made to characterize the stages of addiction. I have found the Johnson Institute model very helpful. Although these stages are represented in different ways, the most helpful that I have found are 1) learning the high, 2) seeking the high, 3) early dependency, and 4) late dependency or burnout. So many people only think of addiction as late stage 3

or 4. Actually the behaviors of stage 1 and 2 set up the individual for true dependency. In stage 1 the individual has just become exposed to the experience of getting high (or intoxicated). There may be rapid progression to stage 2 in which the individual actively, knowingly seeks intoxication. In this stage the ability to give up the drug at will may still exist, but it is lost in stage 3. Once true dependency has begun, generally drug rehabilitation and treatment is the only successful approach to treatment. This is definitely the case in stage 4, where the user requires much more vigorous treatment.

Addictionology is the practice of the treatment of drug and alcohol addiction. A wide range of attitudes exists within this field as to whether "responsible drug use" is a real entity. I maintain that those who support the notion of responsible use are short-sighted and do not fully understand the disease of addiction. Some physicians in this field also support the more typical psychiatric orientation that drug use is always secondary to other problems. This is not the case. Certainly drug use may either be the cause of psychiatric problems or be caused by them. Overall however, drug abuse and addiction is a primary disease. If psychiatric problems coexist, the addiction must be treated before there is any hope of controlling the psychiatric elements.

Unfortunately, the disease concept has been abused by many people for a variety of reasons. Some individuals wrongly believe that no matter what stage of addiction the individual is in, he can "get well" if he exerts enough willpower. This attitude has been used as a weapon against the addict to ostracize him. It has been used to label the addict as someone morally weak or unworthy. These attitudes are only counterproductive, and are particularly destructive to an individual who is trying to recover from addiction.

The converse of this is that the addict may hide behind the disease by contending that he cannot be held responsible for his actions "because he is sick." The addict does however have the responsibility for working on and maintaining a recovery program no matter how rocky the road is. A person with heart disease may have even caused his own disease by his lifestyle, but he may be able to control his disease if he controls his lifestyle in a healthy manner.

One of the most destructive misapplications of the disease model has been

to try to justify "responsible drug use." Proponents of responsible use contend that "careful use" in people who have no genetic predisposition toward addiction is relatively safe. The problem is that what may be careful use to one person is abuse to another. Alcohol may be a problem for some people; cocaine or marijuana for others. There is no effective way to predict who will become impaired or addicted. Drug use is like Russian roulette, and the earlier that an individual is exposed to mood altering chemicals, the greater risk of addiction. I have yet to meet an addict who intended to become addicted when he started using drugs or alcohol.

The disease of addiction is most effectively handled through a combined approach of prevention, intervention, and rehabilitation. This is the goal of the parents' movement. We must give our children a set of values and good self esteem; we must teach them how to "say no" and be certain that they do.

We must try to make waters safe by enhancing prevention efforts, decreasing the supply of drugs, and working to rehabilitate individuals so as to not lose them to this disease.

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PANDAA

PARENTS' ASSOCIATION TO NEUTRALIZE DRUG & ALCOHOL ABUSE

ADOLESCENT CHEMICAL USE

This is a special edition of the PANDAA newsletter. It is a guide for parents and professionals to identify adolescent chemical abuse problems. It is for sale in bulk or on a single copy basis. To purchase, use the form on page 11. This guide has been written by parents who have learned about the subject through experience, extensive research, and from their own recovering children and their friends.

WHY DO KIDS DO DRUGS?

Parents must realize that whatever type of home they have, the kids also live in another world - different than what our adolescent world was like. At present, the only way to keep your child from being exposed to the drug culture is to lock him up, without exposure to newspaper, TV, radio, movies, and magazines. Outside influences begin to affect our children at a very young age. TV and movies depict alcohol use as an ingredient for a good time. Drug usage is also portrayed as "cool" and expected behavior. Our kids' role models - TV, movie, and rock stars are open about their drug use, and receive no legal consequences. Rock music lyrics often promote alcohol and drug use. Many professional athletes have been suspended for drug use. The children see widespread alcohol and drug abuse at concerts, outdoor sports events, in school, and in shopping centers. Not only is it socially acceptable in these public places, but there seems to be no consequences from law enforcement personnel. By the time a child is 10 years old he is very saturated with "drink alcohol and do drugs" messages, and the philosophy, "if it feels good do it." It is very easy for a child to rationalize going against values that "old fashioned parents" may have taught.

Alcohol and drugs are easily available to our young people. Many homes have well stocked liquor supplies. Some young adults make extra money by stationing themselves at convenience stores to buy alcohol for underage kids. Some restaurants buy mailing lists of student groups, and mail notices of a special happy hour for students from a specific group or college campus. The breweries have sales representatives on college campuses. On at least the first few encounters, the marijuana is usually given to them free. Marijuana is easier for our kids to buy than it was for our generation to buy cigarettes. They can buy any drug they want at school, shopping centers, convenience store parking lots, etc.

When asked why they started doing alcohol and/or drugs the most frequent answer of the kids was peer pressure. They had ususally refused participation several times before they gave in to peer pressure. Curiosity, love of thrills and danger, desire for acceptance by a group, were other influencing factors. Experimentation continued because it was fun.

> "I started getting high off pot when I was 11, with my best friend. He was 2 years older and I really wanted to be like him. My friend's 16 year old brother did drugs and we would steal his drugs and get high. I did it at first to keep from being called "chicken" or being left out. For almost two years my parents were not fully aware I used drugs. I was sneaky and a good "con" which kept me from getting caught."

Alcohol and drugs were not used to alleviate parental conflicts, low self esteem, etc. until usage was well established. None of them intended to become dependent on alcohol or drugs. If they read literature on drugs they carefully chose reading that favored drug use, and when they observed their drug using friends and role models there were no apparent bad effects from the alcohol or drugs. Indeed, it seemed like these were the people who really knew how to live and had their act together! Some reported that drug education delayed their first encounters and they were very cautious in the beginning. As time went on the horror stories did not materialize or they did not recognize what was happening to themselves.

WHAT DOES "DO DRUGS" MEAN?

When we speak of kids "doing drugs" we are speaking mainly of alcohol and marijuana. As usage continues and tolerance is built up, alcohol and pot often become boring, and they may progress to using uppers, downers, and hallucinogens. Heroin is rarely part of the adolescent scene. Another frequently used term is "partying" or "to party", which means to drink and/or do drugs. For many kids their weekend social life is "partying". Keg parties are held at homes where the parents may or may not be present. Sometimes the parents buy the kegs, with the excuse that at least they aren't doing drugs, or at least they aren't out on the street. Drugs are usually available at these parties. Keg parties are often advertised at school with flyers - even, occasionally, at intermediate level schools.

As usage progresses kids will do drugs under almost any circumstances, and will try anything they can find. Girls have told of raiding medicine cabinets for any labeled or unlabeled pills while babysitting, and of getting the children they sit for high. Many kids admit to getting their pets high. Some tell of getting high with their teachers, school counselors, therapists, policemen, probation officers, at school and on their jobs. Kids will try anything to get a "high", from drinking vanilla or lemon extract to eating nutmeg.

A PERSONAL STORY

Professionally I am associate professor of Chinese at the George Washington University. I have three children. I would like to relate to you our family's experience with drug abuse.

While my son, age 15, and daughter, age 13, were doing drugs, I was unaware for a long time that this was their major problem, even though I myself had smoked quite a bit of marijuana about ten years ago in the early 70's. Indeed, that was part of the problem. I assumed "pot" to be a relatively safe drug, even though, if I could have looked honestly at my own life back then, I would have seen - as I now do - the extent to which my decreasing energy and motivation at the time could be laid at the doorstep of this drug. Luckily, I had weaned myself away from it, and, again, assumed a kid could do the same. I was wrong on this count as well. So even with my own experience, I failed to recognize for a long time what was happening.

What I did see was my son becoming increasingly hostile, volatile in his outbursts of anger - punching big holes right through the wall - and then darkly withdrawn into his cave-like room, which was designed as a shrine to heavy-metal rock groups and the death-like imagery they projected. He was also clearly in great pain and loneliness, although this was covered over for me by the outward behavior.

As for me, I was frightened both for him and of him; and beyond that, furious with him, practically hating him at times. And I was unbearably guilty; I was sure he was doing drugs because I was his adoptive father and he sensed that I rejected him. I was so confused

CONTINUED ON PAGE 11

SIGNS AND SYMPTOMS OF CHEMICAL USE

WARNING SIGNS

When children begin to use alcohol and other drugs few signs are initially noted by parents since many changes are expected during adolescence. Parents rarely find their child intoxicated, "high", or otherwise impaired. Likewise, hard evidence of usage such as finding the actual drugs or alcohol is often a matter of occasional accidental discovery. Parents must rely most often on the subtle signs and symptoms and the inference of drug use which can be drawn from various signs.

Parents may have cause for concern if their child has rebellious attitudes towards parents and other authority figures, changes friends, is very eager for acceptance by friends, uses bad language, is irresponsible toward work and school, strives to develop a "cool" image, or frequents rock concerts. Some changes may start before alcohol or drug use begins as the child becomes attracted to the drug culture.

THE DUAL LIFE

The alcohol or drug-involved child is apt to lead a dual life in the early stages of usage. A clean image is maintained in front of parents, teachers, and straight friends and a totally different image is projected among drug-using friends. Although their drug use may be well hidden, they put an emotional distance between themselves and their parents and other adults. Many are able to maintain a good appearance, good grades, athletic, and other extra-curricular activities for a surprisingly long period of time (years). The ability to lead a dual life also deceives the user into believing he has control of usage.

BEHAVIORAL SIGNS

As he is drawn more to the drug culture attitudes change, and what was once unacceptable (gross, crude, or illegal) behavior is now "cool" and acceptable. Sports, extracurricular activities, and hobbies, may be discarded. Carelessness, laziness, depression, cheating, stealing, lying, conning, vandalism, bad language, rapid emotional ups and downs, poor concentration and memory, falling grades, curfew violations, school and work absences, disrespect for authority, paranoia, interest in witchcraft, and sexual promiscuity point to possible drug use.

As family relationship deteriorates, family activities are shunned, meals are eaten quickly with the child retiring to his room and listening to loud rock music for long periods of time. Eye contact with parents and other authority figures is avoided. Everyone is "on his case." All of his failures are blamed on others.

> "I began to worry about my 14 year old when he became hostile, not just toward me, but to his sister. She had, up to now, been his best friend. I was bewildered by his urge to hurt those who loved him most. This puzzled me and I felt alone and wounded. When he ridiculed his best friend and abused other "friends" verbally I worried even more. Then other strange behavior began. He became insanely jealous of his sister and anyone he thought might get a crumb more of any treat he felt he deserved. He blew up at a moment's notice if he was asked to help around the house. He rarely talked, but when he did he revealed an alarming absence of reality in his thinking, planning a future career as an artist with no thought of education or marketability of his work.
>
> At home he was either arguing, complaining or locked alone in a bedroom, bathroom or basement. His moods swung from apathy to hatred. Hardly ever was there any peaceful ground between."

For some, threats to run away become an effective method to get their way. Many do run away and stay at friends' homes or in the woods. Parents of his friends may be told by the runaway that his parents are abusing him.

The "druggie look" is expressed in a child's flat facial expression, ragged, worn clothes, "bop" walk (walk with a bounce), slouched stance and generally depressed appearance. Girls often use heavy makeup, wear long bangs over the eyes, sexy clothes and jewelry. Both girls and boys strive to appear older. Personality changes can evolve slowly, over the years or occur very rapidly in a matter of months.

PHYSICAL SIGNS

Most physical signs do not occur until alcohol and/or drug use are well under way. Marijuana irritates the whites of the eyes, and the use of Visine or similiar products alleviates irritation and redness. A persistent cough is very common. Other suspicious conditions are a runny nose, nasal sores, a facial puffiness, dilated or constricted pupils, glassy eyes, a skin rash similar to measles, poor muscle coordination, and stains and burns on lips, inside the mouth, finger tips or fingernails. There may be a craving for sweets, excessive or depressed appetite, excessive thrist, bad breath, or a weight gain or loss. Frequent illnesses are common.

Children who "do drugs" are frequently tired because many of the drugs depress the central nervous system. Also, many teenagers are tired because a druggie lifestyle frequently involves sneaking out of the house at night (often through a window) in order to join friends, and returning in the morning before the family awakens. The child catches up on lost sleep in class or at home in the afternoon.

It is important to note that alcohol use alone can manifest many of the above behavioral and physical signs and should be considered just as serious as other drug use.

PARAPHERNALIA

Many drugs require paraphernalia to prepare them for consumption. Some drugs such as PCP and even the insecticide, RAID, are sprayed on substances such as dried parsley leaves and sold in tiny foil packets or baggies. Marijuana is stored and distributed in plastic bags, small jars, or film canisters. Marijuana seeds, about the size of large bird seed, may be found in baggies, pockets, or small containers. The handrolled marijuana joint requires rolling papers and quantities of matches to keep it lighted. The marijuana ash is smaller, more fragile and whiter than tobacco ash.

Marijuana joints (reefers) and other types of drug-treated cigarettes which are smoked down to the butt (roach) are often held by roach clips to avoid burning fingers. These clips resemble the alligator clips found in hardware stores. Fancier ones such as feathered and highly decorated clips can be purchased in many stores and gas stations.

Marijuana, hashish, and other drugs can be smoked in various types of pipes ranging from ordinary tobacco pipes to elaborate smaller ones that can easily fit into a pocket. Small probing tools are used to clean the sticky brown tar residue left from the smoking process. Some drugs can be smoked without pipes by burning them like incense in a partially covered container and inhaling the smoke.

Bongs are especially favored for marijuana smoking and are often shared by a group. A bong is an apparatus that cools, filters, and concentrates the smoke giving the user a better high. It consists of a cylinder 6 to 12 inches high which holds water. A tube leading into the side holds the "bowl" in which the drug is burned. By sucking air at the top of the cylinder, smoke is drawn from the bowl through the water and inhaled. It can also be used to smoke hashish, PCP, quaaludes, and other drugs. Bongs come in many styles and materials, and are often homemade.

Many kids will grow marijuana plants from the seeds they clean from their marijuana.

> "My daughter convinced me that the potted plants growing on her window sill were a school project. Feeling very proud of her new interest in science I helped her keep them watered. Much later I found out I was watering marijuana plants."

"Snorting" is another method of drug use popular among cocaine users. Any powdered or pulverized drug can be snorted. The drug is usually deposited on a mirror and aligned with a razor blade. The "line" is sniffed through a short straw, rolled dollar bill, or tiny spoon.

Items which may indicate intravenous drug use are syringes, eye droppers, spoons for heating and dissolving powders, and cords or belts used for tourniquets. Balloons or paper bags are used for inhalants.

OTHER SIGNS

Much of the alcohol used at first comes from parents' homes. Water is often added to liquor bottles to fool parents. It is well to do a taste test when checking supplies. Soft drink glasses and cans easily disguise alcohol. Girls often hide small bottles of alcohol in their purses.

Medications purchased by the child as innocuous as cough syrup or any over the counter drugs may indicate problems other than coughs or sore throats. These preparations may be used to alter moods when consumed in sufficient quantities. Often they contain alcohol.

Breath sprays mask alcohol use and smoking. Incense, candles, or room deodorizors remove smoking odors from a room.

Popular hiding places for drugs are stereo speakers, trophies, lamp bases, books, albums, stuffed animals, air conditioner vents, parents' and child's out of season clothing, parents' rooms, car trunks, attics, garages, tool sheds and bushes.

Faked or forged ID cards are easily obtained and used to buy alcohol. Bikes, clothes, stereos, etc. may appear or disappear if they are being used for trade in drugs. School yearbook inscriptions often reflect changed values, as do posters, drug culture clothing, jewlery, record albums, and magazines.

Frequent short telephone calls, hanging up when parents answer, prank and late calls are cause for suspicion.

Favorite hang outs include shopping centers, especially stairways, hallways and game rooms; convenience stores and pizza parlors; school smoking lounges; parks and secluded sites.

PUTTING THE CLUES TOGETHER

It is very helpful to write down all the behaviors, events, and physical evidence which have caused concern with either parent. Recall dates as well as you can and continue to keep the list. Such record keeping reduces exaggeration and minimizing, and helps both parents see their child's behavior more realisticly. Bad attitudes, disrespect for authority, and a decline in the family relationship are some of the most tell-tale indicators of substance abuse, and warrant room checks, monitoring of phone calls, spot checks of school attendance, and relating concerns and observations to the parents of the child's friends. Impromptu urine testing for marijuana is of limited value since many factors affect the results of the test. The kids know tricks to bring about negative tests. Determination of which drugs the child is using is unnecessary. The fact that any drug use is causing problems in his life indicates that help is needed. A parent's best guide is probably his or her own "gut feeling" about the child. That "gut feeling" can be confirmed by an evaluation at a drug rehabilitation facility.

REFERENCES: See page 11, Nos. 1-6.

CHEMICAL DEPENDENCY IS A DISEASE

The disease of chemical dependency is established when the user needs mood altering chemicals on a periodic or continuous basis to feel good. The user is unable to control or stop usage, and a psychological and/or physical dependence is developed. Tolerance to the drug also develops, which means that larger doses are needed to produce the original results.

Physical dependency is present when the drug becomes a part of the person's normal body chemistry and unpleasant physical symptoms, such as vomiting, tremors, sweating, muscle cramps, or even convulsions occur when the chemical is abruptly withdrawn. Physical withdrawal symptoms last for 3 to 10 days depending on the drug. Drugs that cause a physical dependence include nicotine, alcohol, narcotics, hypnotic sedatives, and some tranquilizers.

Psychological dependency on any mood altering chemical is much more difficult to overcome than the physical dependence because it lasts for the rest of the user's life. In other words, he is never cured, but is always in either a recovering or active state of the disease. To stay well he can never again use any mood altering chemical.

The cause of this disease is unknown. It is a primary, progressive, and chronic disease which becomes a family disease as it progresses. It progresses faster in women and adolescents. If allowed to progress it can result in death. It is not a symptom of a disease, it is the disease. The undesirable behaviors associated with chemical use are caused by the chemical use rather than the chemical use being caused by other underlying factors such as inadequate parenting, learning disabilities, low self-esteem, etc. No one intends to become chemically dependent when they begin using alcohol or drugs. Most studies show there is no preaddictive or prealcoholic personality. But, once the disease has begun, behavior patterns become very similar in all abusers. Fortunately, these personality changes are reversible if treatment intervenes to arrest progression of this illness. Vernon Johnson, founder of the Johnson Institute, believes all abusers are guilt-ridden people having a very high set of values and morals which appear to be nonexistent because of their destructive and anti-social behavior resulting from their chemical abuse.

The illness is often divided into four stages. The stages are very similar for adults and adolescents but the following description will focus on the adolescent disease in today's drug culture. Chemical dependency can develop in six months in some adolescents, while it usually takes many years for an adult. Adolescents do not often become physically addicted to alcohol but they become psychologically dependent on it. If drugs are involved the progression of the disease tends to be more rapid than when only alcohol is used. Many adolescents begin tobacco use before or along with alcohol and/or marijuana use.

STAGE ONE

The first stage may be referred to as "learning the mood swing." The user learns that the chemical makes him feel good. If only alcohol is involved, this is still classified as social drinking. If other drugs are involved it could be classified as "experimentation". Few unpleasant effects occur. The chemicals involved are probably tobacco, beer, wine, pot, and/or inhalants. They are probably given to and not bought by the user. The child usually refused participation several times, and often did not get intoxicated on the first alcohol encounter or high the first several times he tried pot, because he had not learned how to inhale it. For peer acceptance, he may have faked being high. When he did learn how to use it effectively, very small amounts got him high because no tolerance had been built up. In stage one he drinks and does drugs only when it's convenient and available, mainly on weekend social events. For most there are no observable behavior changes yet, although some kids begin to adopt "druggie" attitudes and behaviors before usage begins. The parents are unaware of any usage unless they accidentally discover evidence or occasionally recognize the child is high or intoxicated. Ususally such a discovery is considered a "normal phase" by the parent.

STAGE TWO

As he enters stage two, he begins to "seek the mood swing." He plans his use of chemicals, buys them, and may use them alone. He begins to feel unpleasant symptoms as his high ends and tolerance increases. New chemicals may be introduced such as hashish, hash oil, "uppers" and "downers". Usage increaes from weekends ("weekend warrior"), to week nights, to week days. The child begins the dual life, gradually progressing to a more obvious druggie dress and life style. Druggie friends are often met away from home.

Unexplainable mood changes begin, including withdrawal, anger, and aggression. Verbal abuse towards parents, profanity, and rebellious attitudes become a constant friction point between parent and child. The child prefers to isolate himself from his family, and spends many hours in his room often with loud musical accompaniment. As drug use and tolerance increase, stealing from parents and siblings begins to pay for drugs. The first signs of the amotivational syndrome appear. That is, there is loss of motivation and drive. Everything is a "hassle." Hobbies and extracurricular activites may be dropped. All of the child's problems are blamed on other people.

As school grades drop, parents may react with strong disciplinary action. The child will bring up his grades, often by cheating or changing grades on his report card. The improvement "cons" the parents into believing the problem is improved or solved.

The child begins to violate his normal moral values. Vandalism, theft, shoplifting, lying, and/or sexual promiscuity is common. As he experiences shame and guilt for these acts, he gets high or is able to wipe out their memory by "blackouts" or selective amnesia.

Drug use increasingly becomes a necessity to feel good rather than a choice. The youngster can no longer control his drug use. Unfortunately, to most parents, school personnel, and counselors the problems are still not distinguishable from normal adolescent growth problems. Chances are slim that the parents can handle the problem alone. The child is already in need of outside help, but it is unlikely that he will receive the right kind of help.

STAGE THREE

The third stage is the dependency stage. Now his life centers on getting high. He may advance to hallucinogins, cocaine, or opium smoking. He is high most of the time. Tolerance increases and attempts to reduce dosage or stop usage fail. Solitary use is frequent. Suicidal thoughts occur. Overdoses and flashbacks begin to occur. Behavior continues to deteriorate, police incidents occur, jobs are lost, and the child may drop out of school. Chronic cough begins. He feels distress when not high. Rationalization of chemical use becomes an art and guilt feelings run high. He cannot see what is happening to himself.

Family life deteriorates. There may be skipping school, sneaking out of bedroom windows during the night, and running away. The child is guilt ridden and self esteem is very low. He thinks he is "different" from his druggie friends. Drugs are no longer fun. It appears to him everyone else is having fun. He becomes careless and maybe obvious with his use and paraphernalia (may be a plea for the help he is unable to ask for). Parents often believe the child is only using drugs occasionally. The family uses rationalizations to deny the problems.

STAGE FOUR

In stage four, chemicals must be used to feel normal. Use is no longer fun. It is compulsive, uncontrollable, and is regular throughout the day. He may be shooting up. Drugs must be used just to function. Physical health deteriorates. Delusions and paranoia can be severe. Euphoria is rarely even experienced from the drugs. Suicidal thoughts are frequent. Overdose, blackouts, and amnesia occur. He is usually well known by the police. The user is often referred to as a burnout or a zombie. If intervention does not occur, death will result from suicide, overdose, an accident, physical illness, or other untoward behavior.

REFERENCES: See page 11, Nos. 1-6

THE FAMILY

As the alcohol or drug using person's behavior deteriorates, each family member experiences anger, shame, guilt, fear, hurt, and loneliness. To relieve the pain of these feelings and to make attempts to cure the abuser, various defensive behaviors develop. These responses may begin before anyone in the family is aware that the problem is actually one of chemical abuse. In the case of the adolescent, usually the parents take on the role of the primary enabler. There are many forms of enabling. The enabler may protect the user by rationalizing his behavior; bailing him out of trouble at school, the job, the law, or even trouble with the other parent; making special allowances that would never be given to the other children; or keeping the problem secret. One enabling parent may become a controller by taking on responsibilities that actually belong to the user such as getting him up on time, taking him to school, blaming others for his problems, or by striking up bargains with the user. The other parent often enables by withdrawing from unpleasant situations, working late at the office, getting deeply involved in community affairs, being a peacemaker between the child and other parent, or blaming the spouse. As each parent takes on different forms of enabling, frequent conflicts arise and often they begin to believe that their declining marriage relationship is the cause of their problems. The user can become very skillful in exploiting this situation to his advantage. The enabling behaviors become just as compulsive as the user's chemical use. The enabler can become just as disturbed as the user.

As one parent comes out of denial and recognizes that the problems are caused by alcohol and/or drugs the other parent may still be in denial. The parent who comes out of denial first is usually the one who spends the most time with the child and handles most of the crises. The second parent may come partially out of denial, but still deny the seriousness of the abuse. Nothing constructive can happen until the second parent comes completely out of denial and the parents are united in their approach. Sometimes denial is broken when that parent is left alone to experience the embarrassment, hurt, or anxiety of each crisis his child creates with the school principal, the police, or in the emergency room. Much help can be gained in this area by attending self help support group meetings such as Al-Anon, Families Anonymous, or Tough Love.

As the conflict between the abuser and his parents continues, the other children in the family adopt various survival behaviors. Some become too good to be true, or "heroes." They overachieve, are very responsible, give the family a good name, but can be bossy, obnoxious, and achieve for attention rather than for healthy motives. Later in life these children are often "workaholics" and enablers to their spouses and their own children.

Another child may become a "scapegoat" and be rebellious, irresponsible, act out, and disrupt class. The reward is negative attention, which takes the spotlight off the user. This child could easily be mistaken for an abuser, and often abuse is in his future.

The apathetic child is often referred to as the "lost child." This child withdraws, shows little emotion, avoids conflict, and develops few social skills. He is sometimes overweight. On the surface the child appears calm and serene, when in reality there is pain, confusion, and denial of the family's problem.

The family clown gets attention by being funny and distracting. (He is often the youngest in the family.) The child is unable to express feelings and despite the humorous behavior there is much pain.

Each family member's defensive behavior becomes compulsive and habitual. As the lifestyle becomes too painful to bear, the person looks for a way out. Hopefully, this will be through a self-help group such as Al-Anon or Ala-Teen or by the family becoming involved in a rehabilitation program. Other forms of escape the person may use are leaving the family or, worst of all, by suicide.

If appropriate help is not enlisted the siblings in the chemically dependent family are more likely to become chemically dependent themselves. They have chemicals available to them, they have not developed good coping mechanisms, and the whole family is involved in unhealthy compulsive behavior patterns. With the proper help the chemically dependent family can become a nurturing family again, but without help, the family situation can only deteriorate.

REFERENCE: See page 11, Nos. 1 - 6.

DOES MY CHILD NEED HELP?

By the time both parents recognize that the problems they have been experiencing are caused by chemical use rather than by other factors, the child has usually been abusing for at least one to three years, and is already chemically dependent, even though his use may be restricted only to alcohol and marijuana. If the parent finds that strict rule enforcement, close surveillance, spending more time with the child, professional counseling, etc. do not solve the problem, it gradually becomes obvious that the parents cannot "fix" their child alone. Outside help is needed from those experienced in the field of chemical dependency.

A child's drug use is not the parents' fault. The main cause is peer pressure. The child made his choice to do drugs. That choice progressed into the disease of chemical dependency. He needs treatment just as a diabetic child needs treatment. Few parents of diabetic children would withhold treatment because their child did not want injections. Untreated diabetes and untreated chemical dependency are fatal. A characteristic of chemically dependent persons is denial of their disease, and so they rarely seek help. In the case of an adolescent, it is the family's responsibility to intervene so recovery can be initiated.

Recovery from chemical dependency is very difficult and takes a long time, just like breaking a nicotine habit. Group therapy seems to be more effective than individual counseling. A good first step for parents is attendance at one of the free self-help groups such as Al-Anon, Families Anonymous, or Tough Love. There the parents will learn how to recognize their own unhealthy reactions to their child's behavior, how to make the child responsible for his actions, and how to use crises created by the child constructively. Often times when the child is no longer able to manipulate his parents he becomes ready to accept treatment. A child who asks for help and is highly motivated may do very well by attending AA every night or enrolling in an outpatient program. These children's programs will be more successful if their parents attend their own self-help group meetings. The less motivated children will probably require very intensive, long term programs. There are many types of treatment programs. It is advisable to meet and talk with parents and kids who have been through the programs that are available.

FREE DIRECTORIES REHAB PROGRAMS

Directory of Community Substance Abuse Programs in Virginia: Secretary for Community Substance Abuse Services, Div. Of Substance Abuse, Dept. of Mental Health and Retardation, PO Box 1797, Richmond, VA. 22214; Call 804-786-1524.

National Directory of Drug Abuse and Alcoholism Treatment Programs. #(ADM) 83-321. NCDAI, PO Box 1908, Rockville, MD. 20850.

CRITERIA TO LOOK FOR IN A PROGRAM

1. It treats drug and alcohol abuse as a disease rather than as a symptom of a disease. It believes the unacceptable behavior is caused by the chemical use rather than by an underlying cause. It makes the user responsible for his own actions.

2. It promotes an alcohol-and-drug-free life style with drug free counselors. Recreational alcohol or drug use is not allowed. Mood altering prescription drugs are not part of the therapy. Out-patient programs often use urine screening to monitor marijuana use, and Antabuse to monitor alcohol use. Antabuse is a medication that makes one very ill when alcohol is ingested. Parents have the right to know results of urine tests, and the side effects of Antabuse.

3. It uses the twelve steps of Alcoholics Anonymous or includes AA meetings as a part of its program. These tools for self-change have a long successful history.

4. It provides daily support in the form of group counseling and/or AA meetings for at least 6 months. Aftercare continues on a less frequent basis, often in the form of AA meetings or self-help meetings.

5. At least some of the counselors should be recovered abusers who can relate by personal experience and read through the "cons" of their clients.

6. It provides counseling and education for the total family including siblings. This may be in the form of Al-Anon and Ala-Teen meetings. The family learns to recognize and to change its undesirable behavior responses it has developed in response to the abuser's unacceptable behavior. It strives to re-establish good family relationships.

7. The client must learn to live free of alcohol and drugs in a drug oriented society. After adequate progress in a structured, controlled, drug free environment the client begins a gradual re-entry into society, learning to remain alcohol and drug free at home, school, job, and during leisure time. Therapy continues during re-entry.

REFERENCES: See page 11, Nos. 1-3.

MARIJUANA

Marijuana (Cannabis sativa) is a plant which contains over 420 chemicals. The effects of most are unknown. In 1964 its principal psychoactive component (intoxicating chemical), delta-9-tetrahydrocannabinol (THC), was identified. The THC content of marijuana has increased dramatically in recent years due to improved plant genetics and cultivation techniques. Seizures made by the U.S. government in 1965 averaged a THC content of 0.1-0.2%, by 1970 the average THC content climbed to 1.0%, and by 1983 the average THC content had climbed to 2-5%. The most potent strain, sinsemilla, averages a THC content of 11-14%, and is grown illegally extensively throughout the U.S. The potency of marijuana has increased from 50 to 100 times since 1960.

Two marijuana derivatives are also widely used. Hashish or "hash" is the pure resin extracted from the flowering top of the marijuana plant dried and compressed into brown or black cakes or balls. The THC content averages 10-20%. Hash oil is a concentrated viscous liquid that varies in color from clear to black. Its average THC content is 30-40%. Pure THC is never sold on the street because it is very unstable and too costly to manufacture. What is sold as THC is actually PCP or some other drug.

Some slang terms for marijuana are grass, Mary Jane, pot, sens, reefer, weed, hemp, and roach. Marijuana looks like dried parsley mixed with stems and seeds. It is usually bought in small plastic baggies, called nickle or dime bags. One ounce of marijuana will make about 40 joints (cigarettes). A joint sells for about a dollar. Joints are hand rolled, smaller than tobacco cigarettes, and twisted on the ends. The end of a joint, a roach, is often held with a "roach clip" and smoked. Marijuana is also smoked in pipes and bongs (described under paraphernalia). Thai sticks are marijuana buds bound onto short sections of bamboo. Hashish is smoked in pipes or bongs. Hash oil is dropped on a cigarette or joint, or smoked in a special opium pipe. Dried marijuana can be eaten but is only one third as potent.

THC is fat soluble and is stored in the fatty tissues of the brain, reproductive organs, liver, kidney, and lungs. "It takes 30 days to eliminate a single dose of THC. ."[14] In comparison, alcohol is water soluble and excreted from the body in six hours. "Carefully conducted studies with known doses of marijuana or THC leave little question that tolerance develops with prolonged use."[15] Marijuana is psychologically addictive. There is evidence that it is also physically addictive, although there are no major physical withdrawal symptoms because of its slow metabolism and excretion.

IMMEDIATE EFFECTS

A single marijuana cigarette induces a "high" within minutes which lasts from 2 to 5 hours and usually does not result in a hangover. It gives an increased sense of well-being, and a dreamy, carefree state of relaxation. The user may experience sensations of floating and a more vivid sense of touch, sight, smell, taste, and sound. There is often a craving for sweets and dryness in the mouth and throat. The eyes may be irritated and red, and have a glassy look. The state of intoxication may not be noticeable to an observer, even an experienced drug user. Marijuana suppresses the nausea resulting from a large alcohol intake so that users are able to consume large (even fatal) quantities of alcohol.

EFFECTS ON DRIVING SKILLS

In a study done in 1974 by Dr. Harry Klonoff, 38 drivers covered a 16 mile route from a university campus to the traffic-heavy downtown area, and back again. They were rated by the system used to examine drivers for licensing. Final figures for the road test showed that those on the low dose (one joint with 1.2% THC) had a 42% decline in driving skills, while the high-dosage drivers (two joints with 1.2% THC) had a 63% decline. Unusual driving behavior included missing traffic lights or stop signs, poor handling of the vehicle in traffic, and unawarenss of pedestrians and stationary vehicles. A 1972 study of driving behavior in a safety-controlled area showed a "marked" decline in driving abilities was still present 5 to 6 hours after smoking, a "definite" effect 8 to 10 hours after smoking, and a lingering effect as long as 24 hours later.

EFFECTS ON THE LUNGS

Marijuana burns at a higher temperature, and its smoke is inhaled deeper and held in the lungs longer than tobacco. Marijuana has 50% more cancer causing materials than tobacco. Benzopyrene, a known cancer causing agent, is 70% more abundant in marijuana smoke than in tobacco smoke. Smoking less than one marijuana joint a day decreases vital lung capacity as much as smoking 16 tobacco cigarettes a day. Marijuana has an irritant effect on the airways, resulting in inflammation and airflow obstruction of the airways. Heavy pot smoking can cause sore throats, bronchitis, sinusitis, pharyngitis, emphysema and other respiratory difficulties in a year or less. Marijuana smoke weakens the defenses of the lung against infection and disease.

EFFECTS ON THE HEART

During the "high", which can last from 2-5 hours, the heart rate increases from the normal 70-80 beats per minute to as much as 130-150 beats per minute. The blood pressure also increases. As a result, the heart muscle requires more oxygen. The marijuana smoke increases the amount of carbon monoxide in the blood, thereby reducing the amount of oxygen delivered to the wanting heart muscle, and weakening its pumping action. Only 10 puffs of a joint reduces the amount of time one can exercise before chest pain occurs by 50%.

EFFECTS ON REPRODUCTIVE SYSTEM

Possible effects on the male include lowered sperm count, enlarged breasts, damaged sperm, and decreased testosterone (male hormone) levels. These effects seem to stop when usage is discontinued. The female may experience irregularities in the menstrual cycle, failure to ovulate, and lower female hormone levels. THC crosses the placental barrier and enters the fetal bloodstream. It also passes into breast milk.

EFFECTS ON THE BRAIN

In a study done on monkeys by Dr. Robert Heath of Tulane University, a heavy smoking group smoked 3 "monkey sized" joints with 2.5 to 3% THC per day, five days a week. A moderate smoking group, smoked one "monkey sized" joint twice a week. A light smoking group received one tenth the dose of the heavy smokers. A fourth group was given an equal dose of THC intravenously to control the variables of smoking effects. A control group was given inactive marijuana to smoke. The heavy, moderate, and intravenous groups showed lasting changes on their brain recordings after only 3 months of usage. The marijuana use was continued for an additional 3 months, and the abnormal changes persisted. The marijuana was discontinued for an 8 month period. Studies were then done on their brains with electron microscopy. The heavy, moderate, and intravenous groups had changes in brain function and in brain structure. Cellular changes were greatest in the areas which control emotion and memory. The findings correlate with the behavioral changes seen in marijuana users.

BEHAVIORAL EFFECTS

Two Philadelphia psychiatrists, Drs. Harold Kolansky and William T. Moore, conducted one of the earliest well-documented studies of the effects of cannabis on the psyche between 1965 and 1970. Only patients who displayed no psychological problems or predisposition to mental illness before marijuana usage began were used. The only drug used by patients was marijuana and/or hashish. They smoked two or more times weekly, usually two or more joints each time. Common symptoms displayed included mental confusion, inability to concentrate, diminished attention span, loss of memory, loss of motivation, lack of goals, and declining academic performance. Irritability and outbursts of aggression were common, especially if the patient was questioned about his personality change, new philosophy, drug use, or if his drug supply was threatened. Control of impulses and judgment was impaired. Most felt a growing sense of isolation from others, a desire to shun social activities, and deep-seated feelings of anxiety and depression. An altered sense of reality, and symptoms of paranoia were observed in many. All of these symptoms began with marijuana use and were reduced or disappeared within 3 to 24 months after marijuana use was stopped.

Dr. Jason Baron states, "Once marijuana no longer relieves the anxieties and conflicts, then a drug with stronger effects is often tried. Of the 6,000 patients treated by our program over the years, at least 90% started their drug usage with marijuana. Do not let marijuana smoking continue in your child, or it may become the first of many drugs he uses during life."[19]

REFERENCES: See page 11, Nos. 1 & 13-20.

MARIJUANA AND EFFECTS ON YOUNG ADULTS

by Harold Voth M.D.

In my experience there is only one certain way to be cured from marijuana smoking. The user must be totally isolated from the drug for a minimum of three months. Only after a period of sustained abstinence will the user become aware of the profound effects the drug has had on him and, at the same time, become free of its addictive effects.

The inability of the user to perceive himself or gain insight into what has happened to him over time is one of the truly pernicious and remarkable aspects of the effects of the drug. Talking rarely works; forthright decisive action by someone willing and able to take responsibility for the fate of the user is necessary. The chronic and heavy, and probably even moderate user, cannot take responsibility for himself.

CONTINUED ON PAGE 6

FROM PAGE 5 - DR. VOTH

How the person or persons exercise their responsibility to the user depends on the age of the user, his life circumstances, the severity of the retrogressive changes and deterioration of the user, and so on. I recommend sparing no effort whatsoever in achieving this objective. Searches are in order, use of police to back up parental authority if necessary, hiring a companion for the user, confinement to the home and hospitalization are all methods that I have recommended and have seen used.

Someone who cares must intervene, totally, consistently and with unrelenting perseverance. Efforts short of an all-out effort generally fail.

In summary, I believe chronic marijuana use affects judgment, motivation, perception, cognition, and will. In addition, the drug causes an overall deterioration of personality; it leads to an estrangement from the mainstream of life; it lowers performance in all areas; and it leads to a social phenomenon in which users bond together into both loose and tightly bound subsocial groups. The effects on the user's family life is frequently devastating.

In my opinion, the influx of marijuana into the United States constitutes a national crisis and should be combatted by the use of any and all methods until the flow of the substance has been completely stopped. It is remarkable that our federal government does not utilize our armed forces to supplement the coast guard and the county and state police to search out and destroy the ships and planes along with the cargo of drugs they carry...such an all-out effort seems entirely justified to me, in light of the incredible harm which is being done to millions of Americans...most of them our youth.

REFERENCE: See pg. 11, No. 7.

ALCOHOL

About 75% of Americans drink alcohol because they believe it helps them relax and is associated with social gatherings and "good times". While most new drinkers do not particularly enjoy the taste of beer, wine, and liquors, they persist until a taste for them is developed over time. Later many people begin to seek the relaxing effects of this drug to "forget" their troubles and to ease the stress of living.

IMMEDIATE EFFECTS

Alcohol is directly absorbed into the bloodstream from the stomach and small intestine, which if full, absorbs it more slowly than if empty. The blood carries alcohol to the brain, where it affects every level of the nervous system. Alcohol is a depressant, although as blood level rises or in small doses it causes a drinker to feel stimulated and confident. The rate of alcohol absorption is affected by a drinker's body weight (women, smaller, and younger people are affected faster than large men), presence of food in the stomach, and dilution of the drink. People who have just learned to use alcohol are more quickly and profoundly affected than "seasoned" drinkers, whose bodies have built up a tolerance to the drug. When the amount of alcohol in an individual's blood is somewhat high he tends to talk loudly and less distinctly, becomes socially uninhibited, or more courageous, and less attentive. An intoxicated person will have difficulty keeping his balance, will have a thwarted memory, and suffer from fluctuating moods. A very high blood alcohol level can cause muscle tremors, stupor, and eventual unconsciousness. A protective response by the body to an overdose of alcohol is vomiting. Death can occur from an alcohol overdose, particularly if tolerance is low, if other drugs or medications have been used, or if any other absorption factors mentioned above are present.

Contrary to popular belief, neither coffee, long walks, nor cold showers will speed the excretion of alcohol from the system. Only time will help a person become sober. Another myth is that beer and wine contain less alcohol than hard liquor. The alcohol content in a 12 oz. can of beer is the same as that of one 5 oz. glass of wine, or 1 1/2 oz. of 80 proof liquor (an average mixed drink).

INTERACTION WITH OTHER DRUGS

Of the 100 most frequently prescribed drugs, more than half contain at least one ingredient known to react adversely with alcohol. The interaction of other drugs with alcohol may be classified as antagonistic, additive, or supra-additive. The effectiveness of both drugs will be diminshed when the interaction is antagonistic. Alcohol inhibits the action of anti-convulsants and some anti-biotics. If the effect is additive, effects that are similar in the two drugs will be intensified. Antihistamines combined with alcohol will produce more sedation than if either drug were taken alone. Alcohol combined with marijuana results in poorer performance driving tests than when either substance is used alone. A supra-additive interaction produces effects more than double - in other words two plus two will not equal four but maybe five or even ten. A blood alcohol level as low as 0.10% combined with barbiturates has caused death. To prevent undesirable interactions, read labels and check with your doctor or pharmacist.

EFFECTS ON ADOLESCENTS

Since the average beginning age of alcohol use is 12.5 yrs. more research is needed on its effects on adolescents. Scientists think it is highly possible that alcohol can cause certain degenerative changes in the brain, especially in the pituitary gland, which governs growth, and the hypothalamus, which is closely associated with emotions and stress. "The younger the age at which an individual starts to ingest alcohol, the greater the chances that he will develop into a chronic alcoholic. For the action of the alcohol is channeled directly toward the adolescent's imbalanced hypothalamus and autonomic nervous system, thereby obstructing his emotional maturation on both psychological and physiological levels. The regular or frequent ingestion of alcohol during adolescence may produce a permanent imbalance of the hypothalamus and a concomitant irreversible malfunctioning of the autonomic nervous system, thereby leading to the development of chronic alcoholism. In brief, the direct action of the alcohol on the hypothalamus produces chronic alcoholism."[11]

EFFECTS ON DRIVING

Alcohol is known to reduce a person's ability to judge distances, speed and angles, as well as one's ability to handle machinery. Because of its uninhibiting effects, alcohol causes a tendency in drivers to take risks and feel overconfident in spite of adverse conditions. It also causes impaired reflexes, forgetfulness and sleepiness. Over 60 deaths every day in this country are due to drunk driving.

CHRONIC EFFECTS ON BODY ORGANS

Continued use of alcohol damages and eventually destroys brain cells, since its action is six times as great on nerve cells as on other cells in the body. From 50% to 70% of alcoholics entering treatment have some central nervous system impairment. Long term alcoholics may develop the Wernicke-Korsakoff syndrome, (the alcohol amnesia syndrome).

Alcohol is directly toxic to the liver and can cause fatty liver, hepatitis and cirrhosis (degeneration). Alcoholism can be associated with pancreatitis, stomach ulcers, and cancers of the mouth, throat, larynx, stomach, intestines, liver, and pancreas. Many authorities feel alcohol abuse is the most common cause of vitamin and mineral deficiencies in adult Americans.

Alcohol has a toxic effect on the heart muscle, causing heart palpatations and difficult breathing. It can lead to heart failure. High blood pressure is common among alcoholics.

Many hormonal imbalances are also caused by alcohol, especially in the reproductive system. It is closely associated with male impotence, infertility, and menstrual disturbances in women. It causes increased insulin secretion, causing diabetic-like symptoms in some people.

In pregnant women, even small amounts of alcohol can pass through the placenta and affect the fetus. Fetal Alcohol Syndrome identifies a characteristic combination of birth defects in infants born to alcoholic mothers. It is the third leading cause of mental retardation in newborns. Alcohol passes into breast milk to the nursing infant.

PHYSICAL DEPENDENCE AND WITHDRAWAL

Physical dependence can develop after 3 to 5 years of very heavy drinking, but more often it requires 10 to 20 years of heavy drinking. Early stages of the withdrawal syndrome may be characterized by nausea, vomiting, irritability, tremors, sweating, and insomnia 6 to 8 hours after heavy drinking has stopped. A more advanced syndrome, delirium tremens (DTs), can include increased blood pressure, heart rate, and temperature; visual, auditory, and tactile hallucinations; severe confusion; heavy tremors; and possible convulsions 2 to 4 days after abrupt withdrawal. Even with proper medical care DTs can be fatal.

CROSS TOLERANCE

A by-product of increased tolerance in heavy drinkers is a cross-tolerance for certain drugs. It occurs only when the person is sober. He may either be less sensitive or more sensitive to the other drug. Alcoholics require higher doses of ether to be anesthetized. Barbiturates or sedatives will have less effect, consequently the sober heavy drinker may take larger doses. Other drugs may require lower doses for the desired effect. Some chemicals may also be more toxic for the alcoholic. Carbon tetrachloride will damage the liver of an alcoholic more than that of a non-alcoholic.

REFERENCES: See page 11, Nos. 1 & 8 - 12.

STIMULANTS

Chemical agents which stimulate the central nervous system are called stimulants. Two of the most prevalent legal stimulants are nicotine, found in tobacco, and caffeine found in coffee, tea, chocolate, and some bottled beverages such as Coca-Cola and Pepsi-Cola. These stimulants relieve fatigue and increase alertness. More potent stimulants which have a high potential for dependency and tolerance are under regulatory control of the Controlled Substance Act. They include cocaine and the amphetamines.

The effects of amphetamines and cocaine are very similar, although the amphetamines are slower and longer acting. Possible effects of stimulants are increased alertness, euphoria, increased energy, a feeling of being powerful and able to master any task, followed by irritability, anxiety, and apprehension. Physical effects include dilated pupils, increased pulse rate, elevated blood pressure, insomnia, loss of appetite, dry mouth, and bad breath. Very high doses can produce tremors of the hands, arms, and legs, hallucinations, paranoia, disorientation, and seizures. If taken by intravenous injection, a sudden "flash" or "rush" usually occurs, followed by a very depressing "crash," which the abuser often counteracts with another dose.

Chronic stimulant users are usually polydrug users. They rely on alcohol and/or other depressant drugs to relieve their tenseness, depression, and insomnia caused by their stimulant use. Chronic users can develop a measles-like rash, weight loss, and probably because of poor nutrition, have trouble with their teeth, gums, nails, and hair. They may begin grinding their teeth, have muscle twitches, exhibit memory loss and paranoia with hallucinations, and have decreased sex drive. Brain damage can occur. When used intravenously over a period of time the user is subject to the complications of unsterile and adulterated injections such as blood infections, AIDS, hepatitis, lung abscesses and endocarditis.

Overdoses may be indicated by dizziness, tremors, an agitated state, headache, flushed skin, chest pains, sweating, vomiting and cramps, high fever, and possible convulsions. Fatalities have been reported among athletes who have been under extreme exertion after using moderate doses of stimulants.

Immediate withdrawal symptoms may last for several days with profound depression, apathy, fatigue, and disturbed sleep for up to 20 hours a day. Anxiety, tenseness, impaired perception and thought processes, and suicidal tendencies may persist for weeks or months.

COCAINE

"An incredible 22 million Americans - one out of every 10 - report that they have used cocaine at least once. And every day, some 5,000 teenagers and adults try it for the first time".[22] It is the fastest growing drug of abuse. In a recent study, the average daily cocaine user spent a weekly average of $637 for cocaine, with a range of $100 to $3,200.[22] It is often called the "Great Addictor".

Cocaine is distributed as a white crystalline powder. In professional medicine it is used as a local anesthetic. Illegally it is used for its euphoric effects. It is usually sniffed or "snorted" through a straw, rolled up dollar bill, or tiny "coke spoon". Because it constricts the blood vessels in the nose, it often results in a stuffy, running nose and nasal irritation, relieved by nasal decongestant sprays. Chronic snorting can lead to erosion and even perforation of the nasal septum. For immediate, more intense, but shorter results it can be injected intravenously or smoked in a free-base form. Using special kits available in paraphernalia stores, the user removes the hydrochloride salt and inert adulterants from the cocaine converting it to free-base, which is suitable for smoking. The conversion process is very dangerous because it uses ether, a highly flammable and explosive substance, which is usually evaporated over a flame. "Freebasing" and IV injection also entail the risk of respiratory failure and death. Depending on the avenue of administration, effects can last several hours but the euphoric high lasts only 15 to 40 minutes followed by a let-down and desire for more of the drug. Chronic cocaine users are sometimes afflicted with tactile hallucinations such as imaginary insects crawling under their skin, often referred to as "coke bugs."

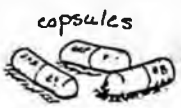
Some slang terms for cocaine are big C, coke, nose candy, snow, white, and snowbirds. Synthetic cocaine composed of a "caine" drug such as lidocaine and glucose is being sold legally as an incense in head shops and through the mail under such names as Toot, Florida Snow, Supercaine, Ultracaine, Base-O-Caine, and Superior Caine. Deaths have been reported from these preparations which are not controlled by the Drug Enforcement Administration.

AMPHETAMINES

Amphetamines are used medically for narcolepsy (uncontrollable desire for sleep), hyperactive behavior in children, and for weight reduction. Vast quantities are produced illegally for the illicit market, especially methamphetamine ("crystal methedrine"), the most potent amphetamine. They are ususally taken orally but can be injected intravenously. Some brand names are Benzedrine, Biphetamine, Desoxyn, and Dexedrine. Look-a-like pills are often sold as amphetamines. Slang terms include speed, uppers, ups, beans, bennies, black beauties, bumblebees, hearts, pep pills, co-pilots, and footballs.

Other stimulants which may be abused are Ritalin and Cylert used medically for hyperactive children, and the appetite suppressants such as Preludin, Didrex, Pre-State, Voranil, Tenuate, Tepanil, Pondimin, Sanorex, Plegine, and Ionamin.

REFERENCES: Page 11, Nos. 1, 21, 22,& 29.



DEPRESSANTS

Substances classified as depressants under the Controlled Substance Act have a high potential for physical and psychological dependency with tolerance developing rapidly. In street language they are "downers" or "downs." Sedatives or sleeping pills and tranquilzers make up this classification. Most of these drugs are taken orally. Therapeutic low doses produce mild sedation and relief of anxiety, irritability, and tension. Higher doses, used by abusers, may relieve anxiety, produce temporary euphoria or the other extreme of mood depression and apathy. They are often used to sooth "jangled nerves" brought on by stimulants, to soften "flashbacks", or to ease a withdrawal from heroin. Intoxicating doses can result in impaired judgement, slurred speech, distorted vision, and often unrealized loss of motor control, making driving dangerous. The user may be quarrelsome and appear intoxicated with no odor of alcohol. Large doses could also induce sleep, stupor, respiratory depression, coma and even death. When mixed with alcohol or other drugs the effects can be very dangerous, sometimes causing death. A moderate overdose resembles alcohol intoxication. A severe overdose causes dilated pupils, cold clammy skin, weak and rapid pulse, either slow or rapid breathing and possible coma. Withdrawal symptoms of depressant addiction are more severe and dangerous than of heroin addiction. Withdrawal should only be attempted in a controlled hospital environment.

SEDATIVES

The following include the more common street drug depressants. Among the barbiturates are Nembutal, Seconal, Amytal, and Tuinal. Some slang terms, often indicating the color of the pills, are barbs, bluebirds, blue devils, red birds, red devils, yellow jackets, and yellows.

Commonly abused non-barbiturate sedatives are Placidyl, Chloral Hydrate, Doriden, Noludar, and Methaqualone (Quaalude). In 1980 Quaaludes followed marijuana as the drug of choice of teenagers. In 1984 this drug was virtually eliminated from the streets when the only legal manufacturer of Quaaludes in the U.S. discontinued their production, and the DEA declared war on illegal importation of the drug.

TRANQUILIZERS

Tranquilizers are the least toxic of the depressants but are highly addictive. Because they are fat soluble, they are eliminated from the body slowly, and withdrawal symptoms do not occur until 7 - 10 days after the drug is discontinued. They are used therapeutically to relieve muscle spasms and anxiety. Since both alcohol and tranquilizers are found in many homes, they are easily abused together by young people. The most common tranquilizers are Valium, Librium, Equanil, Miltown, Serax, Tranxene, and the more potent ones, Thorazine, Mellaril and Halcion. Valium is the most frequently prescribed drug and the most frequently abused drug in drug related emergency room admittances in this country.

REFERENCE: See page 11, No. 29.

LISTEN TO WGTS 91.9 FM

STRAIGHT TALK

RADIO SHOW

TUESDAY EVENINGS - 6:30 TO 7:30

Bill Burns interviews a guest who is experienced in a specific aspect of substance abuse. Call in with your questions about symptoms of drug and alcohol use, rehabilitation programs, parent awareness groups, etc. The program is produced by the Panel on Drug Awareness (PDA), a non-profit media production company.

HALLUCINOGINS

Hallucinogens, often called psychedelics, affect perception, sensation, thinking, and emotions. The user may have difficulty distinguishing between fact and fantasy and may refer to seeing sounds or hearing colors. Other possible effects may include dilated pupils, incoherent speech, lack of coordination, cold, sweaty hands and feet, vomiting, laughing, crying, shivering, goose pimples, irregular breathing, a strong body odor, and suicidal or homocidal tendencies. Chronic use can cause brain damage. The effects may be different in each person with each administration. Persons in hallucinogenic states should be upset as little as possible to keep them from harming themselves or others.

PCP

Phencyclidine or PCP is the most commonly used hallucinogen. Many authorities consider it to be the most dangerous of all drugs including heroin. Because it is so easily and inexpensively produced in bootleg laboratories, it is often sold as another drug, especially LSD. It is sold as a liquid, a white powder (angel dust), crystals, or in pills called "hogs" or PeaCe Pills. PCP can be taken orally or injected but smoking it after being sprayed on cigarettes, parsley or marijuana is the preferred route. The liquid is sometimes dropped in the eye for faster absorption. This can damage the eye. PCP has the odor of ether. One ounce of PCP yields 30-40 dime ($10) bags or foil packets. When sprayed on marijuana it costs about $15 for one fourth of a teaspoon. Some slang terms for PCP include KW, killer weed, green, tac, DOA (dead on arrival) rocket fuel, supergrass, and elephant tranquilizer. PCP sprayed on marijuana is called lovely or loveboat.

Diagnosis of PCP use is frequently missed because the user often looks normal, yet PCP can cause very violent and bizzare behavior, injuring the user or those around him. There are several reasons for this. Physical strength can be greatly increased under the influence of PCP. Police report incidences of users breaking handcuffs and becoming very violent. The drug is an anesthetic and numbs the user so he does not feel physical harm he may do to himself. The drug is also an amnesic so the user may not remember what he did under the influence of the drug. More deaths are caused by the resultant behavior than from the physical effects of the drug. Psychotic behavior may continue for as long as 2 weeks after a single dose. Some adolescents are smoking PCP on a daily basis. When combined with marijuana on a daily basis the user can barely function.

LSD

Lysergic acid or LSD is once again a poplular street drug. It is a difficult and dangerous drug to manufacture. For this reason PCP is often sold as LSD. It is odorless, colorless, and tasteless. Doses of LSD are miniscule - an aspirin sized tablet makes 2 million hits and is worth $600,000. LSD requires very careful handling since it is absorbed through the skin when touched. It is sold in the form of tablets, thin squares of gelatin ("window panes"), and impregnated paper ("blotter acid"). The window panes can be put in the eye under the eyelid for quick absorption or for quick removal of evidence of possession. The blotter acid often looks like stamps which have pictures or Disney type characters (especially attractive to children) on them. It is put on the tongue or licked. Drops of LSD can be frozen in ice cubes or dropped into someone's drink unknown to the recipient. Some slang terms for LSD are acid, green or red dragon, paper acid, white lightening, blue heaven, purple haze, sugar cubes, and blotter acid.

LSD is stored in the fatty tissue of the brain and slowly released back into the bloodstream. This can cause the user to experience "flashbacks", which are the recall of unpleasant effects of the drug weeks or months after the last dose.

MESCALINE

Mescaline is the active ingredient of the peyote cactus and is used as part of the religious rites of some American Indian tribes. It is sold as Peyote buttons which are sliced off the plant and dried to form a hard brown disc. The buttons are chewed and swallowed and have a very foul taste. It is very irritating to the eyes requiring the protection of sunglasses for a week after usage. Synthetic mescaline is rarely found on the streets because of its very high cost. A drug sold as mescaline is usually PCP.

MUSHROOMS

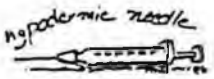
Psilocybin and Psilocyn are derived from certain mushrooms which are brewed in a tea. The taste is very unpleasant. They are chemically related to LSD. Kits are available for growing them through drug culture magazines. Substances sold as mushrooms usually are PCP.

REFERENCES: See page 11, Nos. 1 & 29.

CALL THE ABC

Suspected violations of alcohol control laws may be reported to the Virginia Department of Alcohol Beverage Control (ABC) by calling a toll-free number in service 24 hours a day, 7 days a week. The Department urges citizens to call. Know the name, address, and town where the violation occured.

CALL 1-800-522-3200



NARCOTICS

The term narcotics refers to opium, its derivatives, and synthetic substitutes. Narcotics are physically and psychologically addictive drugs. In professional medicine, they are the most effective pain relievers known. Drug abusers use them for their euphoric effects. Other effects may include drowsiness, stupor, poor coordination, confusion, watery eyes, pinpoint pupils, loss of appetite, slowed breathing and pluse rate, nausea, constipation, and excessive itching. Indications of overdose are deep sleep, stupor, slow shallow breathing, cold clammy skin, limp body, and a relaxed jaw. Coma and/or convulsions can occur. Death may result from respiratory depression. Chronic addiction can lead to malnutrition, neglect of general health, infections from contaminated syringes at sites of injections, blood infection, hepatitis, AIDS, or endocarditis. Physical withdrawal symptoms may include muscle cramps, chills and sweating, and nausea which may last 4 to 10 days after the drug is stopped.

The most commonly abused narcotics are the most addictive ones with tolerance developing rapidly. The intravenous route, "mainlining," is preferred by users. Heroin gives the most intense "high". It is a powder which may range in color from white to dark brown. It may also be snorted, smoked, or injected under the skin, "skin popping." Some slang terms for heroin are big H, boy, brown sugar, snow, stuff, junk, smack, scag, and horse.

Morpnine, Demerol, Methadone, Dilaudid, and Percocan are other narcotics frequently abused. They may be taken orally but injection is preferred by abusers.

Opium may be smoked through a long stemmed pipe. It is also used in antidiarrheal preparations such as paregoric.

Codeine is less addictive and produces less euphoria than the above drugs. It is usually taken orally in preparations combined with Emperin Compound, Aspirin, or Tylenol. Codeine also acts as a cough suppressant and is found in some cough medicines such as Robitussin AC, Cheracol, and Elixir of Terpin Hydrate with Codeine. While Codeine is generally not preferred by narcotics addicts, it should be noted that it is a drug often present in many homes of adolescents who are experimenting with drugs. It should be kept in a locked container.

Darvon and Talwin are pain relievers, not classed as narcotics, but their misuse has caused them to be regulated by the Controlled Substance Act.

Fortunately, narcotics are not frequently abused by adolescents, but as young adults become bored with the other drugs they have been using and their tolerances build up they "graduate" to this classification.

REFERENCES: See page 11, No. 29.

* * * * * COMING IN APRIL * * * * *

PANDAA MOCKTAIL PARTY

DANCE TO THE STARLIGHT ORCHESTRA'S BIG BAND MUSIC OF THE PAST 40 YEARS

AN ALCOHOL FREE DANCE

PARENTS OF TEENS

OFFERS YOU

CONFIDENTIALITY

ANONYMITY

CARE

CALL 237-8121

Parents who have had a child recover from an alcohol and/or drug problem give their volunteer time to help you understand what is happening in your family. They will listen to you. They can relate their own personal experience to you. They understand the hurt, anger, fear, and disruption caused by drug and alcohol problems in the family. They will help and support you.

A parent is on call Monday thru Friday, from 9 a.m. to 5 p.m. to answer your questions, give you support, and mail information to you. Resource lists for those conducting drug awareness meetings are also available. The area code for callers outside the Washington DC area is 703.

DRUG INFORMATION SERVICE

A state-wide toll-free telephone information service provides telephone access to recorded information tapes, 2-3 minutes long, on drug and alcohol related topics. Trained operators are available to supplement the taped messages in the event of emergencies. It is a 24 hour service for push button phones, and a 9 a.m. to 3 p.m., Mon. thru Fri. service for rotary dial phones. Tapes and their No. Virginia code nos. include:

Marijuana
125 - a brief overview
121 - effects - females
126 - effects - males
120 - damage to lungs
127 - increased potency
119 - physical tolerance
128 - emotional impact
124 - body accumulation
117 - Amphetamines
129 - Tranquilizer
130 - Barbiturates
134 - Drug use by youth
135 - Alcohol
118 - Cocaine
133 - Codeine
132 - Heroin
131 - LSD
115 - Opium
114 - Morphine
113 - Methadone
116 - PCP
112 - Smoking

CALL 1-800-552-3784

DID YOU KNOW?

* Virginia law allows a judge to suspend the drivers license for up to one year of any underage person convicted of purchase or possession of alcoholic beverages. This is in addition to a fine for the offense. From Va. Code *4-62, & 4-112(c).

* You can be fined up to $500 and receive up to 6 mos. in jail for drinking or possession of any alcohol on school grounds during school hours or any school activity. From Va. Code *4-78.1.

* You can be fined up to $1,000. and/or be put in jail for up to 1 year if you purchase alcoholic beverages for anyone under 19 years of age. From Va. Code *4-112.1(a).

* If your minor child is abusing driving responsibilities, you can have his license suspended and ask that no duplicate be issued.

INHALANTS

It was once thought that "sniffing" was just a "passing thing" that kids "grow out of." Recent studies show that these youngsters often become our heaviest drug users. As nitrous oxide and butyl nitrite become more and more popular with college students, inhalant use is no longer just "kid stuff."

Inhalants are volatile substances inhaled intentionally for their intoxicating effects. Their effect is immediate because the substance passes directly into the blood stream. Effects usually last for a few minutes, but sometimes can last longer. Because the high is so short, users often inhale repeatedly during each sniffing episode. Inhalants can be classed into three main categories: 1. commercial solvents and aerosol sprays mostly used as cleaning or beauty agents, glues, or as fuels; 2. anesthetics; and 3. the volatile nitrites.

SOLVENTS AND AEROSOL SPRAYS

Some commonly abused items in this group are spray paints, hair sprays, vegetable oil sprays, cold weather car starters, air sanitizers, window cleaners, furniture polishes, insecticides, disinfectants, spray medications, deodorants, gasoline, transmission fluid, glues, paint thinners, nail polish and removers, magic markers, typing correction fluid, and shoe polish. Low doses may produce slight stimualtion, moderate doses cause one to become uninhibited, and high doses can cause loss of consciousness and sometimes death. Especially dangerous is inhaling from a bag. Other effects may be drowsiness, headaches, nausea, vision disturbances, watering of eyes, excess nasal secretions, coughing and salivation, chemical smell on the breath, sores on the nose and mouth, pallor, flushing, and poor muscular control. Long term use can cause damage to the central nervous system, liver, kidneys, blood, and bone marrow.

ANESTHETICS

Nitrous oxide (laughing gas) is used as a general anesthetic, especially in dental offices, and among other uses, as a propellant for whipped cream. For making whipped cream it is either in an aerolized spray can and considered a legitimate food additive, or in a small 8 gram metal cylinder used with a dispensing machine. These cylinders are called "Whippets" and are now sold in head shops and some record stores. Paraphernalia is sold to use with the cylinder, such as a balloon from which the gas is inhaled and a pipe ("Buzz Bomb") which combines with the cylinder. The production of Whippets has tripled in the last few years.

Adverse reactions can include shortness of breath, nausea, variations in heartbeat, and hearing loss. Long term use can cause nerve damage. Death can occur if the gas is inhaled without sufficient oxygen.

VOLATILE NITRITES

The most common nitrites in use are amyl nitrite and butyl nitrite. They are used as a euphoriant and as a sexual stimulant. The high produced lasts only a few seconds to a minute. Consequently users tend to inhale repeatedly during each sniffing episode. The nitrites temporarily dilate the blood vessels, causing the heart to beat harder and faster and fill the blood vessels with blood. Other effects include rapid pulse, headaches, dizziness, flushed face, lowered blood pressure, nausea and vomiting, fainting, and involuntary passing of urine and feces. Increased intraocular pressure with headaches can be a symptom of nitrite use rather than glaucoma. Long term use can cause an impetigo-like rash around the nose and mouth. It is felt that prolonged use may be linked to hepatitis and brain hemorrhage.

Amyl nitrite is a clear yellowish liquid with an ethereal, fruity odor. It was formerly used for treatment of the heart disease, angina pectoris, but has been replaced by other drugs. It is supplied in 0.3 ml. glass containers, enclosed in a gauze jacket of woven absorbent covering which is easily broken and inhaled. The popping sound when broken gives it the street name, "poppers" or "snappers."

Butly nitrite is a liquid which smells like dirty socks or a locker room. A fragrance is added to it and it is legally sold as a "room odorizer" in adult book stores, head shops, and by street vendors. FDA has no control over it. From 4 to 10 million vials of it are sold each year, mainly to older teenagers and young adults. Trade names include Rush, Bolt, Locker Room, Bullet, Jac Aroma, Climax, Loc-A-Roma, Shotgun, Satan's Scent, and many others.

REFERENCES: See page 11, Nos. 22 - 27.

LOOK-ALIKES

A popular addition to the drug scene are the look-alike drugs. Originally they were manufactured to resemble, or look like, prescription stimulants and depressants, with numbers, letters, or markings similar to the drugs they were copying. Because of the passage of "look-alike" laws and certain judgements by the FDA, the manufacturers are also selling pills that no longer look like controlled substances. They are sold in bottles of 100 or 1,000 in stores and through flyers in the mail, often referred to as "legal stimulants", allowing a young seller a very high profit margin. When sold as uppers these pills usually contain caffeine alone or in combination with ephedrine. When sold as downers they usually contain antihistamines.

CAFFEINE: At normal doses, caffeine is a mild stimulant that reduces fatigue and suppresses appetite. In larger amounts, or when there is a sensitivity to caffeine, it may cause restlessness, anxiety and insomnia. The amount of caffeine in look-alikes varies anywhere from 37.1 mg. to 323.8 mg. An average cup of coffee contains 100 mg. of caffeine. Serious side effects have been reported from using more than 600 mg. of caffeine a day.

EPHEDRINE: Medically, ephedrine is often used as a broncho dilator in asthmatic preparations and as a decongestant in prescription and over-the-counter preparations. It is similar to adrenalin. The effects of ephedrine are stimulation of the central nervous system, constriction of the arterioles which causes shrinkage of the mucous membranes and relief of nasal congestion, increased blood pressure and heart rate, dilation of the pupils, dilation of the bronchials, nausea, headache and anxiety.

ANTIHISTAMINES: Antinistamines are used to relieve symptoms of colds and nasal allergies, and to relieve itching caused by allergic reactions. Side effects include drowsiness, dizziness, dryness of the mouth and throat, and disturbed coordination. However insomnia, nervousness, and even convulsions can occur.

Each of the ingredients in look-alikes is dangerous when taken in sufficient quantities. To get a high, kids quickly learn they must ingest several of these pills, or even a handful. By October of 1983 12 deaths had been associated with these drugs due to caffeine intoxication. There is also a danger that a child accustomed to the weak "copy-cat" drug will unknowingly buy the authentic drug, take several pills, and overdose.

REFERENCE: See page 11, No. 30.

* * * * * * * HOTLINES * * * * * * *

PANDAA Parents of Teens (Wash DC Area)
703-237-8121, Mon. - Fri., 9 am to 5 pm
National Federation of Parents
local, 649-7100, or 800-554-KIDS
Pride Drug Information - 1-800-241-9746
National Institute on Drug Abuse
local-443-6500, or 800-638-2045
National Cocaine Hotline - 1-800-COCAINE
Fairfax-Woodburn Center - 573-5679
Family & drug abuse emergencies
Families Anonymous-Richmond-804-771-9109

RESOURCE LIST

NATIONAL FEDERATION OF PARENTS FOR DRUG FREE YOUTH (NFP) Assists in the formation and networking of local parent groups in every state. Member groups less than 15 mos. old are eligible to use NFP's tax exempt status upon completion of proper forms. Membership includes newsletter. NFP offers pamphlets on marijuana, alcohol, and cocaine, at $8.00/100; A Parent Group/Community Task Force Starter Kit & Education Kit/Public Speaking Manual, $5.00 each; Press/Media Guidelines, and Anti-Paraphernalia Kit, $4.00 each; Membership - individual - $10.00, group - $20.00. 1820 Franwall Ave., Suite 15, Silver Spring, Md. 20902, tel. local 649-7100 or 800-544-KIDS (toll free hotline).

VIRGINIA FEDERATION OF PARENTS (VFP) - Assists in formation of groups in Virginia, publishes a newsletter, and co-ordinates legislative goals for Virginia. Membership - individual - $5.00, group - $10.00. P.O. Box 279, Chesterfield, VA 23832, Ph - 804-320-8778.

VIRGINIA COALITION OF PARENTS (VCP) - A statewide parent group oriented toward legislative aspects of substance abuse. P.O. Box 4155, McLean, Va. 22103, tel. 703-455-2230

COMMITTEES OF CORRESPONDENCE, INC. - Newsletter and news flashes sent on urgent issues which need action. A must for group leaders. Excellent resource list available. Membership is $10.00. P.O. Box 232, Topsfield, MA 01983, tel. 617-774-2641.

PRIDE - Newsletter, many publications, and audio-visual aids. Conducts an annual conference and sponsors 1 day conferences for other groups. Drug use survey available. Maintains list of youth groups in U.S. Membership - $8.00. Woodruff Bldg., Volunteer Service Center, Suite 1216, 100 Edgewood Avenue. NE, Atlanta GA 30303, tel. 1-800-241-9746.

FAMILIES IN ACTION - Maintains a drug information center. Publishes Drug Abuse Update Newsletter - $5.00/4 issues, with 16 pages of abstracts of articles on all aspects of drug abuse. Full texts of articles available. 3845 N. Druid Hills Rd., Suite 300, Decatur, Ga. 30033, tel. 404-325-5799.

NATIONAL CLEARINGHOUSE FOR DRUG ABUSE INFORMATION (NIDA) List of free publications available. Parents, Peers, and Pot II, a 100 page book, is excellent for awareness programs. Up to 50 free copies can be ordered. Allow 2-4 weeks for delivery. A must for awareness programs. 5600 Fishers Lane, Parklawn, Md. 20852, tel. 301-443-6500.

NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA) CLEARINGHOUSE - List of free publications available. Will do search on any aspect of alcohol use you request. P.O. Box 2345, Rockville, Md. 20852, tel. 301-468-2600.

AMERICAN COUNCIL ON DRUG EDUCATION - Excellent publications for sale. 6193 Executive Blvd., Rockville, Md. 20852, tel. 301-984-5700.

FREE CATALOGUES - Offer many good self help, AA, and educational publications. Comp Care Publications, 800-328-3330 and Hazelden Educational Services, 800-328-9285.

MARIJUANA UPDATE - Booklet of 4 Reader's Digest articles, $1.25, reasonable quantity discounts. Permission has been granted for anyone to reprint these articles on their own. Reader's Digest Reprint Editor, Pleasantville, N.Y. 10570, 800-431-1726.

ADOLESCENT DRUG & ALCOHOL ABUSE - by Donald I. MacDonald, M.D. A 200 page book written by a pediatrician. Includes: The Epidemic of Adolescent Drug Abuse, Progressive Stages of Drug Involvement, Chemical Dependency, The Drugs, The "Do-Drug Environment, The Susceptible Child, The Parent Revolution, Diagnosis and Intervention, Treatment and Follow-up, Prevention Through Laws and Education, The Role of the Physician. Cost, $15.95. Call 800-621-9262.

GONE WAY DOWN - TEENAGE DRUG ABUSE IS A DISEASE - by Miller Newton, Ph.D. A 72 page book which describes the progression of adolescent chemical dependency. Cost $4.00 includes postage. Send to Joyce Tobias, 4111 Watkins Trail, Annandale, Va. 22003.

COMMUNICATIONS NETWORK HANDBOOK - Free 62 pg. resource on all types of media work for parent groups. Good newsletter information. DHHS Publication #(ADM) 81-981. Office of Communications & Public Affairs, 5600 Fishers Lane, Rockville, Md. 20852.

COURTWATCH MANUAL - 111 page manual explains the court system, criminal justice process, courtwatch activites, and what you can do before and after a criminal is sentenced. Send $2.00 to Washington Legal Foundation, 1612 K St. NW, Wash. DC 20006.

COMMUNITY SERVICES

AL-ANON & ALA-TEEN - 241-2011 (VA) 882-1334 (MD&DC) - Free self-help groups for the parents, spouses, children, and siblings of alcohol abusers who may also be drug abusers.

ALCOHOLICS ANONYMOUS - 241-8195 (VA) 966-9115 (MD&DC) - Free self-help groups for alcohol abusers who may also be drug abusers. Young peoples groups meet every night.

ALCOHOL REHABILITATION, INC. (ARI) - 841-0660 (Arlington) - Private, non-profit, residential treatment facility for chemical dependency for all ages. Ninety day program.

ALEXANDRIA DIVISION OF SUBSTANCE ABUSE SERVICES - 750-5704

ARLINGTON COUNTY ALCOHOL AND DRUG PROGRAM - 528-0884

ARLINGTON HOSPITAL ALCOHOLISM UNIT - 558-6536 - 28 day, inpatient, alcoholism adolescent (13-18) program and an adult program. Includes assessment of alcohol and drug use, use of AA principals, 4 nights a week family program, and 15 weeks aftercare.

CHEMICALLY DEPENDENT ANONYMOUS - 474-0443 (MD) - Self-help group similiar to AA.

DISTRICT OF COLUMBIA SUBSTANCE ABUSE ADMIN. - 727-0443

FAIRFAX COUNTY/FALLS CHURCH COMMUNITY SERVICES BOARD - 281-6420 - County agency whose fees are based on a sliding scale. No service is ever refused for inability to pay. Offers many mental health services. Some are:
Crossroads - 691-2468 - Out patient and small residential drug rehab program for all ages.
Local Alcoholic Services (LAS) - 533-0180 - Outpatient program for alcohol problems.
The New Beginning - 968-7330 - In-house 28 day program for alcoholics.

FAMILIES ANONYMOUS - 620-9353 (Herndon), 460-5839 (Bethesda), 262-4473 (Bowie) Free self-help group for parents of abusers.

HEGIRA HOUSE - 703-343-6332 (Roanoke) - Long term residential program for adolescents and adults. Sliding fee scale. Drug free and uses AA principles. Director recovered addict.

MONTGOMERY COUNTY HEALTH DEPT. DRUG COUNSELING PROGRAM - 565-7729

NARCOTICS ANONYMOUS - 338-7989 (Va.), 459-9355 (Md.), 338-7989 (DC) - A self-help group patterned after the steps of AA.

PRINCE GEORGE'S COUNTY HEALTH DEPT. DIRECTORATE OF ADDICTIONS - 345-2000

RAP, INC. - 462-7500 - (DC) Non-profit, long term, residential program for all ages.

SALVATION ARMY - 642-9270 (VA) - A residential 90 day adult alcohol and drug rehabilitation program based on the steps of AA. Includes AA meetings several times a week. There is no fee, since the clients work 40 hrs. per week at the Salvation Army building.

SECOND GENESIS - 683-4610 (VA) 656-1545 (MD) Non-pofit, long term, residential drug rehab program for all ages. Evaluation and screening, individual, group and family therapy, and vocational services are included. Most individuals are eligible for funding.

STEP ONE SERVICES - 671-6322 (VA) - Private out-patient program. Three counseling sessions per week plus three AA meetings per week. Average length of program is 6 months. Alcohol and drug free status is monitored by use of antabuse and urine screening. Antabuse is a medication which makes one very ill when alcohol is consumed.

STRAIGHT, INC. - 642-1980 (VA) - A not for profit family oriented drug and alcohol rehabilitation program for youth 12-21. The program utilizes the principles of AA and rational therapy combined in a unique group format. Programs are provided for parents and siblings. To attend an open meeting on on Monday or Friday call 48 hours in advance. Assessments done. Out of town clients accepted.

TOUGHLOVE - 569-8915 (Springfield), 522-9038 (Arlington), 361-7633 (Manassas), 670-9075 (Woodbridge), 530-6718 (Beth.), 577-1038 (Lanham), 635-2169 (DC) - A free self-help group for parents experiencing any kind of behavior problems with their child.

NFP SAYS:
COME ON AMERICA! STICK YOUR NECK OUT FOR KIDS AND HELP STOP ADOLESCENT DRUG AND ALCOHOL USE!

FROM PAGE 1 - A PARENT'S STORY

about my own feelings that I did not know at this point whether I did reject him or not. Psychiatrists, family therapists, and drug counselors reinforced my guilt by attributing his drug use to problems in my marriage, problems which were being exacerbated or actually caused by his drug use! This self-doubt, leading to self-hatred for being such a terrible father, was for me the worst aspect of the ordeal. Meanwhile, I was getting about three or more phone calls a week in my office from teachers, counselors, and the principle telling me he had come to school drunk, had been taking pills at school, was missing from class, etc. As I now know, he was in fact using his school as a place to obtain drugs and make contact with "druggie" friends.

Meanwhile, my daughter, in the sixth grade at the time, was following in his footsteps, getting more and more hostile, carving names of rock groups into her hand with razors, wearing tons of make-up, and basically spitting in the face of our family. My marriage was going down the drain along with my kids' lives. Everyone in the home was in tremendous pain. My third kid was withdrawing into himself, and also starting to experiment with drugs to gain the acceptance of his druggie siblings and friends.

Fortunately for us, we found a very rigorous drug rehabilitation program which worked for our family. Our kids have undergone what appears to be a transformation, but is really just the result of good, loving therapy leading to self-awareness. I personally feel better now than ever before in my life - happier with myself, more loving, and stronger than ever before. More has happened than just getting rid of drugs, much more. Each of us has grown with the support, love and help of this program, and I will be grateful from the depths of my heart to it forever.

COURTWATCH

What happens to drug dealers? Join the PANDAA COURTWATCH and find out. We attend trials and sentencings of drug related cases and compile our observations. With our data we are effecting changes in the judicial system and the laws. If you can help once a week or once a month call:

CALL 237-8121

VIRGINIA TEACHER IMMUNITY LAW

*8.01-47. Immunity of school personnel investigating or reporting alcohol or drug use: In addition to any other immunity he may have, any teacher, instructor, principal, school administrator, school coordinator, guidance counselor or any other professional or administrative staff member of any elementary or secondary school, or institution of higher learning who, in good faith with reasonable cause and without malice, acts to report, investigate or cause any investigation to be made into the activities of any student or students or any other person or persons as they relate to alcohol or drug use or abuse in or related to the shcool or institution or in connection with any school or institution activity, shall be immune from all civil liability that might otherwise be incurred or imposed as the result of the making of such a report, investigation or disclosure. Virginia Code 1950, *8:631.1; 1972, c.762; 1977, c.617; 1981.

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Phone - 703-237-8121 - Mon-Fri, 9 am to 5 pm

Editor - Joyce Tobias

This newsletter or parts of it may be reprinted with acknowledgement. Anyone may contribute articles. Articles will be used at the discretion of the editor and will become property of PANDAA , Inc.

PANDAA (Parents Association to Neutralize Drug and Alcohol Abuse, Inc.) was founded at Jefferson High School in Fairfax County, VA in April, 1980 by a group of parents concerned about teenage alcohol and drug abuse. The goals of the group are to combat substance abuse in the home, school, and community and to educate the public about all aspects of substance abuse. PANDAA is incorporated and has tax exempt status. There are no salaried personnel. All donations are tax deductible. Membership is open to any individual upon payment of $5.00 annual dues which includes a subscription to the newsletter. PANDAA is supported solely by dues and donations.

PANDAA publishes an educational 8 page newsletter 5 times a year. Its circulation is 5,000 copies. It is mailed to PANDAA members, federal, state, and local legislators, law enforcement personnel, civic leaders, civic clubs, youth leaders, churches, school counselors and principals, pediatricians, and treatment programs, and it is distributed at awareness meetings, workshops, and conferences.

PANDAA also publishes a 12 page GUIDE TO CHEMICAL USE for parents and professionals which includes why kids do drugs, signs of use, stages of use, effects on the family, treatment, and the drugs of abuse including alcohol. An order form for the GUIDE on page 7.

PANDAA works closely with the County School System strengthening school policies and educating school personnel.

The PARENTS OF TEENS program offers a confidental listening ear telephone service (237-8121) Mon. thru Fri. from 9-5 for parents in need of help and support in identifying an alcohol or drug problem. Materials on drug information, treatment programs, and resource lists for awareness programs may be received by calling this number.

The COURTWATCH committee observes drug cases weekly and is effecting changes in the judicial system. PANDAA also lobbies for legislation regarding substance abuse.

PANDAA does many speaking engegements and assists in the formation of new groups. It is a member of the National Federation of Parents and the Virginia Federation of Parents.

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PANDAA PHILOSOPHIES

Our children have the right to grow up in a drug free environment. Parents have the responsibility to be informed about substance abuse, to communicate to their children a clear and firm "no use" position about alcohol and drug use, to set an example to their children, and to use consistent discipline combined with love and care. A parent's right takes precedence over a child's right to privacy whenever a situation is threatening to the child's health and safety.

PANDAA believes the use and abuse of both legal and illegal drugs has reached epidemic proportions. It has extended into every segment of our communities bringing with it corruption, violence, property loss, family disintegration and disregard for the law. It has become the number one health problem for the 15 to 24 yr. age group, the only age group with a rising death rate.

PANDAA opposes the use of illegal drugs or illegal use of mood altering prescription drugs. PANDAA considers any alcohol use under the legal drinking age abuse. We consider alcohol to be a DRUG which affects emotional and physical development in adolescents, and is capable of producing dangerous changes in behavior and well-being.

The initiation of adolescent alcohol and/or drug use is caused by pro-alcohol and drug media messages, drug using role models, peer pressure, curiosity, availability, acceptance by society, inadequate laws and enforcement of laws. Usage continues because it gives short term pleasure, it becomes a temporary problem solving tool, and society imposes few consequences for abuse. As usage continues it can develop into the disease of chemical dependency which affects the entire family and usually requires treatment. Adolescents can become chemically dependent in 6 months to 1 year while in the adult, dependency usually occurs after 5 to 20 years of usage.

The use of drugs is a clear choice and the user is responsible for any actions committed while under the influence of any drug. Juveniles and adults involved in alcohol and drug related crimes should be evaluated for chemical dependency and where appropriate treatment should be mandated, along with other appropriate consequences. We consider drug trafficking a violent crime which demands serious consequences.

The treatment of chemical dependency has a low success rate. Development of more successful treatment modes is needed. Treatment programs must be free of legal and illegal mood altering drugs including alcohol. They should be accessible, affordable, and acceptable to health insurance plans.

Schools have an obligation to the community and the families they serve to provide an alcohol and drug free learning environment for students. Schools should provide drug education, strictly enforced consequences for violations, substance abuse recognition training for school personnel, help families recognize chemical dependency, and require treatment for readmittance to school when chemical dependency has been diagnosed.

Elected and appointed officials have a responsibility to be informed, enforce the laws as written, and support improved and necessary new laws.

PANDAA GOALS

PANDAA's goal is to eliminate alcohol and drug abuse in our community by:

Offering support and educating families, professionals, and the community about the dangers and legal responsibilities of illegal drug and alcohol use, and prevention and intervention techniques.

Working with school officials, parents, and students for a drug free envitonment at school.

Working within the community to de-emphasize the "do drug" messages, opposing the aggressive commercial promotion of alcohol, and encouraging public and social support for those who choose not to use alcohol or drugs.

Supporting the efforts of law enforcement officials by courtwatching, lobbying, and other civic action activities.

Assisting in the formation and development of groups similar to PANDAA.

LEGISLATIVE GOALS

All persons convicted of a drug felony should have their bonds revoked when found guilty and experience incarceration until sentencing.

All juveniles and adults involved in an alcohol or drug related crime should be evaluated for chemical dependency and mandated to treatment when appropriate as a part of his sentence.

Any juvenile convicted of an alcohol or drug related crime should have his driver's license revoked until his 18th birthday.

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Drug Awareness Information Newsletter

January 1988

57 Conant Street, Room 113 • Danvers, MA 01923 • (617) 774-2641 Connie & Otto Moulton

STORAGE OF MARIJUANA IN THE BODY

George Blernson
322 Holden Wood Road
Concord, Massachusetts 01742

The Lipophilic Property of THC

During World-War II, a wonder insecticide was developed: DDT. It killed the insects, and was completely harmless to man and other vertebrates --- or so we thought. We eventually banned DDT when we realized it was destroying our environment.

The problem is that DDT is strongly fat soluable, and so is absorbed in fat tissue, where it is stored for months. DDT is called "lipophilic", meaning "fat-loving".

Today we have another popular lipophilic chemical: THC, or tetra-hydro-cannabinol. This wonder substance is the psychoactive ingredient in marijuana. Like DDT, THC is also stored in the body for months. It has been found in the milk of mothers who quit smoking marijuana three months before their babies were born.

THC is a very potent drug, but appears to be mild because its high fat soluability makes it act slowly. With this slow action, serious physical trauma from marijuana overdose is rare. On the other hand, being lipophilic makes marijuana very dangerous and insidious when used regularly. This article explains the processes of THC storage in the body resulting from its lipophilic property.

The THC Model

Probably the best data on the storage of THC in the body are provided by pharmaco-kinetic experiments performed on the dog by Garrett and Hunt (Ref. [1]). The concentration of THC in the blood was repeatedly measured over an extended period, following an injection of THC. To achieve high accuracy, radioactive labeled THC was used. Since the level of radiation was quite high, comparable tests cannot be performed on humans. However, this experiment involves basic physiological processes, and so its results should apply approximately to man.

The lipophilic THC molecules are very sticky. Consequently, THC is very difficult to measure quantitatively, because it sticks to the sides of test tubes and other equipment.

Figure 1 shows a model of THC storage in the body, which I derived from the Garrett and Hunt data. The model is implied in their results, but a significant amount of theoretical and computer analysis (Ref. [2]) was required to calculate the model parameters. As a parent, I wanted precise drug information, and so I applied my engineering training to the problem.

As shown in Fig. 1, THC leaves the blood in five different ways: it is metabolized into other chemicals (called "metabolites") as it passes through the liver; and it is stored in four different kinds of "compartments", which act like time-release capsules, feeding the THC back into the blood at different rates. These four storage compartments are different physiological processes, which provide fast, medium, slow, and very-slow storage of THC.

The very-slow storage is due to absorption of THC into the fat tissues of the body, but the three other storage processes have not been identified. Since THC molecules are very sticky, one of the storage processes may be due to sticking of THC molecules to the sides of blood vessels.

The metabolized THC is eventually excreted from the body, but unmetabolized THC is not. A complex array of different metabolites of THC is formed in the body, and there may be several parallel paths, involving different chemical reactions, between THC metabolization and excretion.

The rate of conversion of THC in the blood to metabolites corresponds to a half life of 6.7 minutes. Hence if THC remained in the blood, the THC in the body would drop to half every 6.7 minutes. However, THC is metabolized much more slowly than this, because it is removed from the blood and sequestered in the four compartments.

The numbers in Fig. 1 give the relative rates of THC transfer into, and out of, the storage compartments. These are normalized in terms of the rate at which THC is converted to metabolites (shown as 1.0 in the figure). For example, the arrow leading from the blood to the medium storage compartment (2) has a rate parameter of 2.1. This means that the THC molecules flow into this compartment 2.1 times faster than they are metabolized by the liver.

The rate of THC flow into a compartment is proportional to the amount of THC in the blood. The rate of THC flow from a compartment back into the blood is proportional to the amount of THC in the compartment. For the medium storage compartment (2), the rate parameter 2.1 for flow into the compartment is 10 times the rate parameter 0.21 for flow back into the blood. Therefore, the THC in this compartment eventually reaches a steady level that is 10 times the THC in the blood. At that time, THC flows back into the blood at the same rate that it flows into the compartment.

Figure 2 shows how the THC in the blood varies during the first three hours after an injection. Curve (1) is the response (to 30 minutes) relative to the minute scale, and curve (2) is the response (to 3 hours) relative to the hour scale.

As shown by curve (1), initially THC in the blood decreases very

rapidly. It drops to 50% in one minute, and to 10% in 5 minutes. During this initial transient, 15% of the THC leaving the blood is metabolized, and the other 85% is sequestered in the four storage compartments. The compartments soon begin to feed appreciable amounts of THC back into the blood, and so the rate of THC decay decreases. THC in the blood drops to 5% in 12 minutes, but takes nearly 2 hours to reach 1%.

After 1 day, the process enters the "terminal phase", in which the fast, medium, and slow compartments are nearly at steady-state conditions, and THC in the blood is controlled by the slow return of THC from the very-slow storage compartment (4), which is the body fat. The flow rate from the fat is equal to the THC stored in the fat multiplied by the rate parameter 0.0009. In the terminal phase, this flow rate is equal to the rate at which THC is metabolized, plus the rate at which THC flows back into the fat. Hence, it is equal to (1.0 + 0.55) times the amount of THC in the blood. This indicates that the ratio of THC stored in the fat, to THC in the blood, is equal to

Ratio = (1.00 + 0.55)/0.0009 = 1700

Thus, during the terminal phase, there is 1700 times as much THC in the fat as is carried in the blood.

Since the fat-to-blood rate parameter is 0.0009, the half life corresponding to the release of THC from fat to blood is

Fat-to-Blood Half-Life = (6.7 min)/0.0009 = 5.17 days

Remember that the metabolization half life is 6.7 minutes, which corresponds to a rate parameter of unity. As THC is released from fat to blood, 0.55 nanogram is reabsorbed back into the fat for every 1.0 nanogram that is metabolized. Hence the half life for elimination of THC is 1.55 times greater than this fat-to-blood half life, and so is

Elimination Half-Life = 1.55(5.17 days) = 8.0 days

This shows that it takes 8 days for the THC in the fat to decay to 1/2, 16 days to decay to 1/4, 24 days to 1/8, etc.

Related to the "half-life", there is another useful parameter called the "time constant", defined as 1.44 times the half life. The time constant for elimination of THC from the fat is

Time Constant = 1.44(8.0 days) = 11.5 days

When a person smokes marijuana regularly, the THC contributions from successive marijuana joints accumulate in the fat. The THC stored in the fat reaches a steady level equivalent to the number of marijuana joints smoked during an 11.5-day time constant. For example, a person smoking one joint of marijuana per day carries in his fat a steady THC level equivalent to 11.5 joints of marijuana.

The fraction of the THC entering the body that is absorbed into the fat is approximately equal to

0.55/(1.00 + 0.55) = 0.35

The quantity 0.55 is the rate parameter for flow into the fat, and 1.00 is the rate parameter for metabolization. Thus, 35% of the THC that enters the body is absorbed into the fat.

In the terminal phase, there is 1700 times as much THC in the fat as in the blood, and so the fraction of the THC from one marijuana joint carried in the blood is

$$0.35/1700 = 0.000206 = 0.0206\%$$

If a person smokes one joint per day, the THC accumulated in his fat is equivalent to 11.5 joints. Hence, the steady level of THC in his blood, due to release of THC from the fat, is 11.5 times 0.0206%, which is

$$\text{Steady THC Blood Level} = 11.5(0.0206\%) = 0.24\%$$

This indicates that a person who regularly smokes one marijuana joint per day carries a continual THC level in his blood equal to 0.24% (or about 1/4 of 1%) of the THC absorbed from a single joint. This might seem quite small. However, as we will see, it is enough to produce appreciable sedation --- sedation that occurs continually.

The Blood-Brain Barrier

The brain is isolated from the main blood supply by the blood-brain barrier. This is a protective sieve, made of capillary walls and cell membranes, which helps to protect the brain from toxic substances. The lipophilic THC molecules tend to stick to the blood-brain barrier. Hence this sieve greatly reduces the amount of THC that enters the brain by slowing the flow of THC molecules.

Figure 3 gives data from tests made by Lemburger, et. al. (Ref. [3]), following an injection of THC. The lower plot shows the heart rate, and the upper two plots show results from psychological tests. Each point is the mean value obtained from six subjects.

The heart rate changes very quickly after the THC injection, but the upper plots indicate a lag of about 15 minutes before full psychological symptoms are experienced. This delay is caused by the blood-brain barrier, which slows the flow of sticky THC molecules to the brain. Figure 2 shows that at 15 minutes (point A) the THC in the blood is 4.2% of the injected dose.

The psychological responses in Fig. 3 stay close to maximum until 45 minutes after the injection. At 45 minutes, Fig. 2 shows (point B) a THC blood level of 1.9%. At 2 hours, the psychological measures of "high" and "symptom score" in Fig. 3 are about 50% of the maximum values. At that time, Fig. 2 shows (point C) a THC blood level somewhat less than 1%.

Since the blood-brain barrier slows the transfer of THC to the brain, the THC concentration in the brain blood is much less than in the heart blood during the early part of the transient. However, as time passes, the rate of change of THC in the blood decreases, and so the effect of the blood-brain barrier diminishes. Eventually, equilibrium should exist across the barrier, and the THC concentration in the brain blood should be approximately equal to that in the heart blood.

In the terminal phase, the blood-brain barrier should have essentially no effect on the THC blood concentration in the brain. How much effect this barrier has at 2 hours is not clear. However, let us assume conservatively that the blood-brain barrier is also in equilibrium at that time, so that THC concentration in the brain blood is the same as in the heart blood.

With this assumption, we conclude that a brain-blood THC level of 1% produces 50% of maximum "high". This is only 4 times greater than the steady THC blood level, 1/4 of 1%, in the brain of an individual who smokes one marijuana joint per day. Therefore, this steady THC level should be sufficient to produce appreciable sedation, keeping the daily marijuana smoker in a continually numbed state.

Storage of THC in the Brain

The brain weighs about 3 lbs, and 1/3 of this is fat tissue. Hence, a significant amount of the THC sequestered in the fat is stored directly in the brain. Since the blood-brain barrier strongly limits the flow of THC into the brain, the THC concentration in brain fat is lower than in general body fat. But how much lower?

The slow storage compartment (3) releases THC so slowly it should pass essentially unimpeded through the blood-brain barrier. In Figure 1, the rate parameter for release of THC from compartment (3) is 0.017. This corresponds to a half life of (6.7 min)/0.017, which is 6.6 hours. For this half life, the THC level drops only 10% per hour.

It can be shown that the peak THC level in compartment (3) is 39% of the injected THC. When this THC is released into the blood, 35% of it is stored in the fat. Hence, the THC in the fat that comes from compartment (3) is

$$0.39(35\%) = 14\%$$

The total THC in the fat is 35% of the injected dose. The ratio 14%/35% is equal to 0.40. Hence, 40% of the THC stored in the fat comes from the slow storage compartment, released so slowly it passes unimpeded through the blood-brain barrier.

As THC is released from the fat to the blood, 35% of it is recycled back into the fat. Consequently, 35% of the steady THC level in the fat of a regular marijuana smoker is recycled THC, which enters the fat so slowly it is unimpeded by the blood-brain barrier. Of the remaining 65%, which enters the fat directly, 40% comes from compartment (3), and only 60% arrives at a fast rate. Hence, the fraction of the steady THC level in the fat that enters at a fast rate is

$$0.60(65\%) = 39\%$$

The rest of the steady THC level (61%) enters the fat so slowly it passes unimpeded through the blood-brain barrier.

This analysis shows that the steady THC concentration in brain fat tissue should be at least 61% of that in the general body fat. Therefore, an appreciable amount of THC is stored in the brain of a regular

marijuana smoker.

What is the effect of THC stored in the brain cells? Dr. Robert C. Gilkeson has devoted considerable research to this issue. He explains that the membranes of nerve cells are fat (or "lipid") tissue, and so are sites for storage of THC molecules. The nerve cell membrane is crucially important because: (1) nutrients and waste products for the cell must pass across the cell membrane, and (2) this membrane is the primary source of neural electrical activity. When sticky THC molecules are stored in the nerve cell membrane, they degrade cell nutrition, and suppress electrical activity.

Hence, one would expect that long-term use of marijuana should cause serious brain damage. That this is so was demonstrated by experiments performed on the monkey by Dr. Robert Heath and his collegues at Tulane Medical School (Ref. [4], pp 713-730). Clear and detailed descriptions of this work have been given by Peggy Mann in Refs. [5, 6].

The following experiment was performed several times. For 6 months a monkey smoked the equivalent of 10 to 15 joints of marijuana per week, using monkey-sized joints. After recovering for 6 months, the monkey was sacrificed and its brain cells were examined under the electron microscope. Brain waves were measured from probes imbedded deep in the skull. These signals became severely distorted after 2 months of smoking, and remained distorted 6 months after smoking had stopped.

The brain cells showed severe damage, particularly those in a deep part of the brain called the limbic system, which is the center of motivation. For example, over 30% of the limbic brain cell nuclei had inclusion bodies, which are clots in the nuclei. In normal brains, less than 0.5% of brain cell nuclei have inclusion bodies. The incidence is much higher in old brains, particularly those of senile patients, but even then is much less than was observed in the brains of these young monkeys. When the researchers first observed the enormous brain-cell damage, they were shocked at what they saw.

Historical Evidence

That marijuana is stored in the body, producing continual sedation, is not a new discovery. As explained by historian Franz Lowenthall, Professor of Near Eastern Literature at Yale University (Ref. [4], pp. 739-745), marijuana is an old problem to Arab society. The Arabs have struggled for centuries against the devastating effects of marijuana (or in their words "hashish"). A thirteenth century religious leader, Sheikh Ali al-Hariri, gave the following advice:

> "He has to give it up for forty days, until his body is free from it, and forty more days until he has rested from it after becoming free."

This conclusion by Sheikh al-Hariri, made 700 years ago, is remarkably consistent with our THC model.

What was obvious to Sheikh al-Hariri should also be obvious to people today. Why have we not drawn the same conclusion? Maybe we don't want to know the truth.

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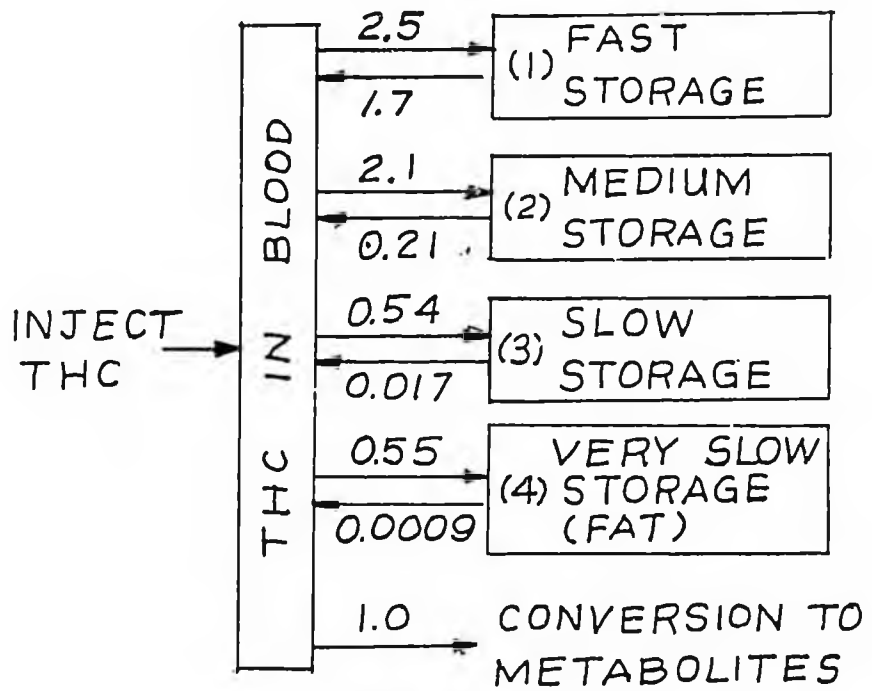

FIGURE 1: MODEL OF THC STORAGE IN THE BODY

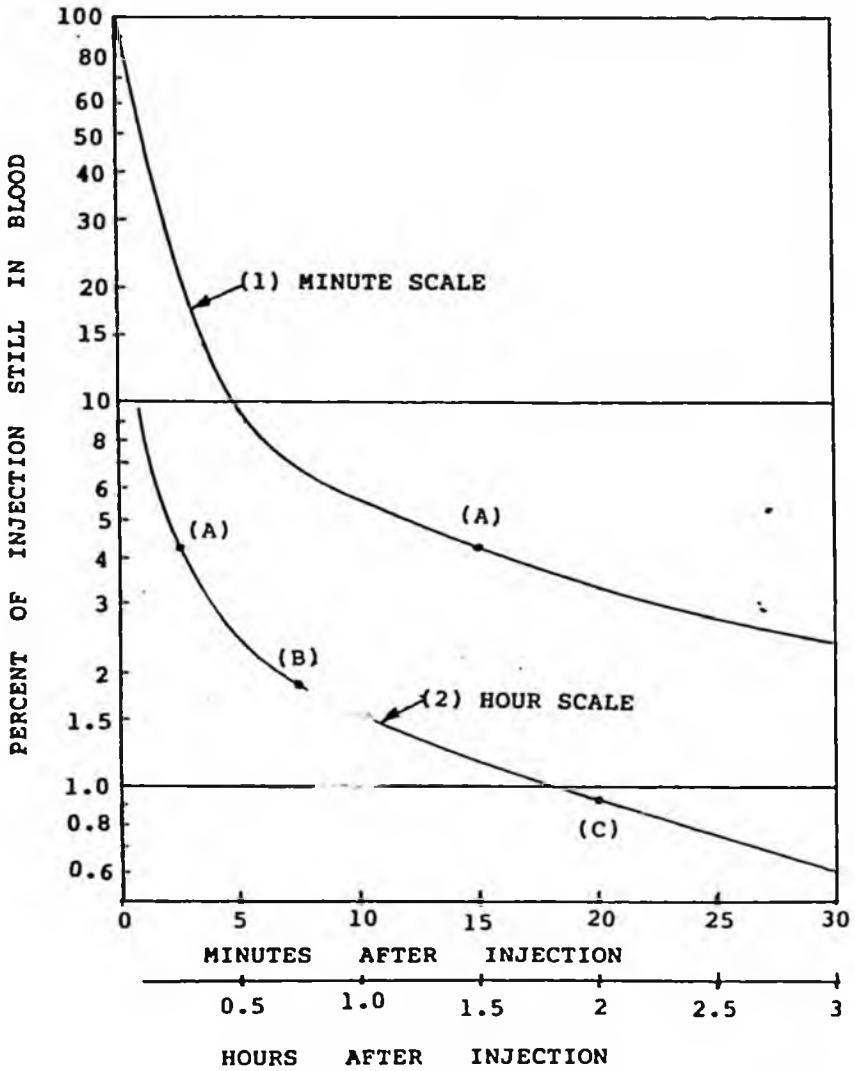

FIGURE 2: VARIATION OF THC BLOOD LEVEL WITH TIME

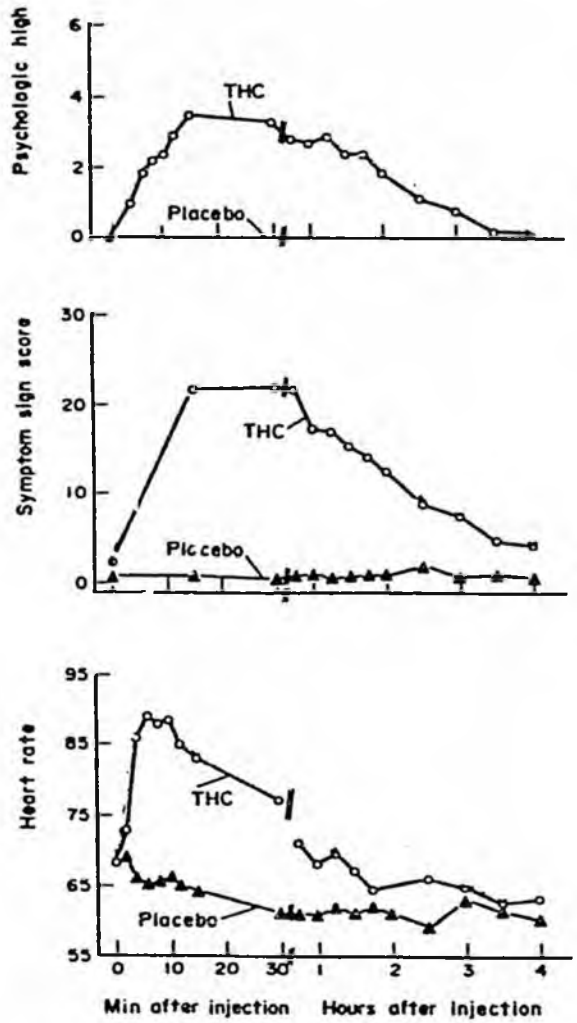

FIGURE 3: EFFECT OF THC INJECTION ON HEART RATE AND PSYCHOLOGICAL RESPONSES

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Drug Awareness Information Newsletter

January 1988

57 Conant Street, Room 113 • Danvers, MA 01923 • (617) 774-2641 Connie & Otto Moulton

SUMMARY OF THE BIOLOGICAL EFFECTS OF MARIJUANA

by George Kornson and Otto Moulton

Marijuana, known scientifically as cannabis sativa and popularly as pot, contains 61 chemicals, called cannabinoids, which are found nowhere else. Its primary psychoactive ingredient is delta-9-tetrahydrocannabinol or delta-9-THC. Three other cannabinoids are known to be psychoactive, but occur in much lower concentration. Many of the cannabinoids probably contribute to the damage of marijuana to the body. However, the evidence against delta-9-THC is sufficient to brand it, by itself, an extremely dangerous drug. Often delta-9-THC is shortened to THC.

Storage of THC in the Body

THC is strongly fat soluble, and so is stored in the fatty tissues of the body for months. The fatty tissues act like time-release capsules, which steadily release THC into the blood, keeping the regular marijuana smoker in continual sedation. The THC molecules are very sticky, and so THC is very difficult to measure quantitatively; it sticks to the sides of test tubes and other equipment. The storage of THC in the body is discussed in detail in Ref. [1].

THC is called lipophilic, meaning "fat-loving". Its fat-storage properties are quite similar to those of the banned insecticide DDT. That lipophilic insecticide was thought to be harmless to vertebrates, until we discovered, to our dismay, that it was accumulating in the bodies of animals, and so was destroying our environment.

The brain is isolated from the main blood supply by the blood-brain barrier, which is a protective sieve of capillary walls and membranes that shields the brain against toxic substances. Lipophilic THC molecules stick to this sieve, and so the flow of THC to the brain is slow.

As THC is absorbed into the blood, most of it leaves very rapidly, to be stored in different physiological processes, which later feed THC back into the blood. As blood passes through the liver, part of the THC is metabolized to form other chemicals called metabolites, which are eventually excreted from the body. Unmetabolized THC is not excreted.

Because of these storage processes, the concentration of THC in the blood drops to a few percent of the initial level by the time the THC

molecules have worked their way through the blood-brain barrier. Hence, only a small amount of the THC entering the body contributes to the "high" sensation. In a light marijuana smoker, the concentration of THC in the brain blood that produces a strong "high" is about 10 micrograms (10 millionths of a gram) distributed throughout the total blood supply of the body.

Thus, THC is an extremely potent drug. It appears to be mild because its high fat solubility makes it slow acting. With this slow action, serious physical trauma from marijuana overdose is rare. On the other hand, being lipophilic makes marijuana very dangerous and insidious when used regularly.

There are four different types of THC storage processes in the body, which feed THC back into the blood at different rates: (1) fast storage, predominating in the first 10 minutes, (2) medium storage, predominating in the first hour, (3) slow storage, predominating in the first 12 hours, and (4) very slow storage, which controls THC blood concentration after one day. Very slow storage is caused by THC absorbed into fatty tissues. About 1/3 of the THC entering the body is absorbed into the fat tissues, which release it with a half life of approximately one week. Hence, it takes one week after marijuana smoking has ceased for THC stored in the fat to drop to 1/2, 2 weeks to drop to 1/4, 3 weeks to 1/8, etc.

All of the marijuana joints smoked over the past month contribute significantly to the THC in the fatty tissues, which is steadily released into the blood. The THC blood concentration from this steady release is low. Nevertheless, for a regular marijuana smoker, it is sufficient to cause sedation, because (1) THC is released so slowly it passes unimpeded through the blood-brain barrier, and (2) THC is extremely potent.

One third of the brain is fat tissue, and so an appreciable amount of THC is stored directly in the brain. Although the blood-brain barrier reduces THC flow to the brain, about half of the THC stored in the fat arrives so slowly it passes unimpeded through the blood-brain barrier. Hence, THC concentration in brain fat tissue should be about half of that in general body fat. (This slowly arriving THC comes partly from THC originally stored in the fat, which is recycled back into the fat, and partly from the slow storage process, described earlier.)

Effect of THC on the Brain

What is the effect of THC stored in brain cells? Dr. Robert Gilkeson [2] explains that the membranes of nerve cells are fat (or "lipid") tissue, and so are sites for storing THC molecules. The nerve cell membrane is crucially important because: (1) nutrients and waste products for the cell must pass across the cell membrane, and (2) this membrane is the primary source of neural electrical activity. When sticky THC molecules are stored in the nerve cell membrane, they degrade cell nutrition, and suppress electrical activity.

Hence, one would expect that long-term use of marijuana should cause serious brain damage. That this is so was demonstrated by experiments performed on the monkey by Dr. Robert Heath of Tulane Medical School, who is world renowned for his research on the brain [3] (pp 713-730). Clear, detailed descriptions of this work are given by Peggy Mann in [4, 5].

The following experiment was performed several times. For 6 months a monkey smoked the equivalent of 2 joints of marijuana per day, 5 days per week, using monkey-sized joints. After recovering for 6 months, the monkey was sacrificed and its brain cells examined under the electron microscope. EEG brain waves were measured from electrodes imbedded in the brain. The EEG waves became severely distorted after 2 months of smoking, and remained severely distorted 6 months after smoking had stopped.

The brain cells showed serious damage, particularly those in a deep part of the brain called the limbic system, which is the center of motivation. For example, over 30% of the limbic brain-cell nuclei had inclusion bodies, which are clots in the nuclei. In normal brains, less than 0.5% of brain-cell nuclei have inclusion bodies. The incidence is much higher in old brains, particularly those of senile patients, but even then is much less than was observed in the brains of these young monkeys. When the researchers first observed the enormous brain-cell damage, they were shocked at what they saw.

Dosage. This research by Heath is often dismissed with the argument that the monkeys were "chain-smoking" marijuana, using huge doses. This is not true. Early in this experiment the smoking apparatus was very inefficient, and little of the THC was absorbed into the monkey's body. This problem was corrected by developing a respirator that forced the monkeys to smoke in a human-like pattern.

With this respirator, a monkey weighing 11 pounds smoked a 0.25-gram joint of marijuana, containing 2.5-3% THC. (A normal marijuana joint is 1 gram, and good street pot today is usually 3.5-4% THC.) This dosage produces the same THC blood concentration, 10 minutes after smoking, as a human smoking a 1-gram joint.

If we scale the monkey's dose by weight, 0.25 gram of marijuana for an 11-pound monkey would be equivalent to 3 grams (or 3 joints) for a 132-pound teenager. However, equivalent drug dosages for different species are not scaled by weight. Extensive studies of drug equivalency have been made for cancer chemotherapy. As shown in [6], for the many drugs evaluated, the maximum tolerable dose for man, per pound of body weight, is approximately 1/3 of that for the monkey. When this factor 1/3 is included, the 0.25-gram monkey-sized joint is equivalent to a 1-gram joint for the 132 pound teenager.

To bury this dosage argument completely, let us ignore this 1/3 factor and assume, very optimistically, that dosage is scaled directly with body weight. Since the monkey smoked 10 times per week, this very optimistic assumption would yield 30 joints per week for the teenager, or 4.3 joints per day. In 1979 the National High-School Senior Survey showed that 10% of U.S. high-school seniors smoked marijuana daily, and the average consumption for the daily marijuana smokers was 3.5 joints per day. This average is very close to the very optimistic 4.3 joints per day corresponding to the monkey experiment, a smoking level that produced serious brain damage after 6 months of smoking.

Clearly, this experiment by Heath is crucially important to our youngsters. Yet, very few have received a reliable account of it in their drug education classes, even though its results were published in 1979. As Peggy Mann reported in the Nov. 1987 Reader's Digest, "We are teaching

our kids to use drugs" in drug education. The misinformation presented in most drug education programs is atrocious.

In 1981 the National Institute on Drug Abuse (NIDA) discontinued funding of this research by Dr. Heath, which is by far the most important research on marijuana ever performed anywhere in the world. This action was preceded in 1980 with the following derogatory evaluation by NIDA of Heath's work [7]:

"A researcher who used electrodes implanted deep within the brains of monkeys, instead of the more conventional scalp recording techniques, has found persistent changes related to chronic use. This same investigator has reported that rhesus monkeys administered marijuana smoke from one joint daily for five days per week for six months show persistent microscopic changes in brain cellular structure following this treatment. While these experiments demonstrate the possibility that more subtle changes in brain functioning or structure may occur as a result of marijuana smoking in animals, the implications of these changes for subsequent human or animal behavior is at present unknown. Other studies, using more conventional EEG techniques to measure brain electrical activity, have found changes temporarily associated with acute use, but no evidence of persistently abnormal EEG findings related to chronic cannabis use."

In EEG (electro-encephalogram) tests on man, the electrodes are almost always placed on the scalp, because it is dangerous to insert them into the brain. Only under extreme conditions, associated with brain surgery, has it been possible to place EEG electrodes inside the human brain. It is well known that EEG scalp records give an extremely limited measure of brain electrical activity. Doctors use the scalp EEG because it is the best that they can get, not because it is "conventional".

With NIDA's unscientific approach to research, is it any wonder that we have a drug epidemic?

The strong brain-wave distortions found by Heath on monkeys were detected only from electrodes implanted within the brain, and were not observed from those placed on the scalp. Hence one would not expect EEG scalp recordings of humans to show strong brain-wave distortion.

On the other hand, psychiatrist Dr. Robert Gilkeson has observed more subtle brain-wave changes from the scalp EEG [8] (p 20). Gilkeson has developed EEG techniques to pinpoint learning disabilities, which he applied to 50 youngsters, ages 13-18, who had used pot at least twice a week for 4 months. They abstained from pot for 2 days preceding the test.

Gilkeson found that all of these EEG records were "markedly immature for age", and had an abnormal amount of slow theta rhythms, "sufficient to be diagnostic of diffuse brain impairment. In the EEG section of academic tasks, none of these youngsters could speed up when challenged. Their brain waves failed to respond to these stimuli in the usual way." These subtle distortions of scalp EEG signals disappeared after the youngsters abstained from pot for 3 months. On the other hand, the severe distortions observed by Heath from deep-brain recordings persisted after 6 months of abstinance.

Effect on the Immune System: Relation to AIDS

In 1973, Dr. Akira Morishima of Columbia University examined, from healthy pot-smoking young men, the chromosomes of T-lymphocytes, which are important cells of the immune system. The men had smoked marijuana for an average of 4 years, and did not take other illegal drugs. For those smoking 2 joints per week, about 1/3 of the T-lymphocyte cells had about half the normal number of chromosomes (46). For the daily marijuana smokers, cell damage was greater, with some cells containing only 5 to 10 chromosomes. This study has been verified by many other researchers. [4] (p 113)

This has strong implications relative to the AIDS epidemic, because T-lymphocytes are a prime target for the AIDS virus. Many people who have been infected with AIDS do not have active symptoms. This study indicates that any use of marijuana may have a serious effect on the development of the disease. AIDS researchers should start correlating marijuana use with the progression of the AIDS symptoms.

Effect on Reproduction

The damage to chromosomes caused by marijuana can produce serious birth defects, which are transmitted through many generations. In experiments by Dr. Susan Dalterio, male mice were given a human equivalency dose of 1 to 3 joints of THC, 3 times per week, for 5 weeks. These mice were mated for a month with normal females. Twenty percent of the females either did not conceive, or had babies that were born dead or died soon after birth.

The resultant sons that matured were not exposed to any drugs and were mated with normal females. About 25% of these female mice did not achieve a normal pregnancy. The resultant grandsons of the THC-dosed mice that matured were not exposed to drugs and were mated with normal females. Many of their offspring showed severe abnormalities, including intestines outside the bodies, and exposed brains and spinal cords. Many of the sons and grandsons showed severe chromosome defects. [8] (p 12)

Effect on the Sex Drive

When mice or monkeys are exposed to marijuana, they have little sex drive: it is difficult to get them to mate. Similar results are observed in humans. A high incidence of impotence has been reported among men in Jamaica who smoked marijuana for 5 years. Dr. Ingrid Lantner, who has discussed marijuana on many radio call-in shows, reports: "Chronic pot smokers often tell me they are impotent, but this doesn't bother them --- since they no longer feel sexual desires." [8] (p 13)

Effect on the Lungs

Marijuana causes serious lung damage, particularly when cigarettes are also smoked. In 1971, studies were performed by Dr. Forrest Tennant on U.S. soldiers in Germany who smoked hashish daily, equivalent to 1-5 joints of marijuana. He found that 1/3 of the cigarette smokers had squamous metaphlasia, a dangerous precancerous condition of the lungs; while 91% of those using hashish plus cigarettes had it. [4] (p 70)

Marijuana as Medicine

Since marijuana contains many different chemicals, marijuana itself is not appropriate for medicine. The only verified medical application of a drug derived from marijuana is the use of THC to combat nausea in cancer patients undergoing chemotherapy. THC is very effective in reducing nausea.

On the other hand, as explained earlier, THC attacks the immune defenses of the body. This is very serious for patients undergoing chemotherapy, because chemotherapy also weakens the immune system, making the patient very susceptable to infectious disease. Obviously, when THC is taken to combat nausea in chemotherapy patients, it must be carefully controlled and used sparingly.

Addiction and Drug Dependence

Marijuana is often claimed to be physically non-addictive because the user does not experience strong physical withdrawal symptoms when he stops smoking it. However, the reason for this is that THC cannot be withdrawn rapidly; the body has its own supply. It takes one week for the THC stored in the fat to drop to 50%, and one month to drop to 5%.

Actually, marijuana probably produces stronger physical drug dependence than any other drug. It generates a "pot personality" and often leads to escalated use of many drugs, because:

(1) As marijuana builds up in the body, it gradually drags the smoker into continual sedation, separating him from reality and forcing him into a dream world of drugs.

(2) As demonstrated by Heath's experiments on the monkey, marijuana weakens the center of motivation of the brain, and in time permanently damages it. Clinical experience has shown that prolonged marijuana smoking destroys normal motivational reflexes, so that the smoker experiences great difficulty living a drug-free existence.

(3) Since marijuana is present in the body all the time, the body rapidly builds up tolerance to it, and the smoker must steadily escalate its use to achieve the same "high". Eventually, the kick from marijuana is not satisfying, and so he reaches for other drugs.

(4) Since marijuana inhibits nausea, people with marijuana stored in their bodies can drink alcohol very heavily without getting sick. Consequently, marijuana has caused an epidemic of alcohol abuse, drunk driving, and death from alcohol overdose. Teenage death from alcohol overdose used to be very rare; without marijuana in the system, the body protects itself by vomiting. [4] (p 51)

Marijuana is often called a "stepping stone" or "gateway drug" because it leads to drugs giving a stronger kick. However, these terms are misleading: they imply that the primary damage of marijuana comes from drugs evolving from its use. Marijuana's dangers are deceptive because its main action is slow and delayed, and so it is difficult for the user to relate cause and effect.

Remember that THC is extremely potent and is stored for months in the body, causing serious damage to the brain, to chromosomes, and to the immune system. THC appears to be mild because it acts slowly. Hence, marijuana is at least as harmful as cocaine and heroin, but is really more dangerous because it is so insidious. In societies where marijuana is readily available, and heroin and cocaine are not, the smoker usually sticks to marijuana, until it destroys him. For example, in Morocco and Jamaica, marijuana-induced insanity is common. [9] (p. 76)

Survey after survey have shown that essentially all users of other illegal drugs started with marijuana, and most continue to use marijuana along with the other drugs. The great reluctance of a heroin addict to stop may be due more to the marijuana he has taken than the heroin.

Many surveys of this sort were available in the early 1970's, when the myth of marijuana's harmlessness was spread across the U.S. For example, the U.S. Commission on Marijuana and Drug Abuse stated in its 1972 report to Congress that "80% of the [San Diego High School] students who had used marijuana weekly or more often had used other illegal drugs, and 50% of this group had used LSD" [10] (p 56). Similarly, Psychology Today (April 1970) found from a survey of its readers that 58% of those who smoked marijuana weekly had taken LSD, while at least 99% of those who drank alcohol but did not use marijuana had not taken LSD. Yet LSD is probably the most harmful psychoactive drug used by man, and its dangers had been well publicized at that time. It produces an hallucinogenic state akin to schizophrenia, and is a common cause of insanity. (Use of LSD and similar hallucinogenic drugs is widespread today: a 1983 survey shows that 21% of young adults have taken them.) [11] (p 364)

These studies were glibly dismissed as being irrelevant. They were buried by using the fallacious argument: "Since marijuana is not addictive, it cannot by itself lead to other drugs; hence these correlations cannot be the result of cause-and-effect relationships."

We hear of statistical studies everywhere we turn. Elections are predicted with remarkable accuracy from them. Our knowledge of the dangers of tobacco is largely the result of statistical evidence. Most of the decisions in modern medicine concerning medical procedures are based strongly on statistical data. Yet, strangely, statistical studies relating marijuana to other drugs, or to crime, suicide, and insanity, are considered to be irrelevant.

Note that the violent crime rate has increased tremendously since the early 1960's, directly paralleling the use of marijuana. It rose from 1.62 per 1000 of population in 1962 to 5.81 in 1980, which is a factor of 3.6. [11] (p 370)

Conclusion

The scientific evidence is more than sufficient to brand marijuana an extremely dangerous drug, yet few youngsters are aware of this. They smoke marijuana because it is there, and they believe it is no more harmful than alcohol. The only way they learn otherwise is to see their classmates being destroyed by it. However, for this mechanism to operate, many young lives must be sacrificed. It is about time that science provided a better learning mechanism.

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NOTES:

References [7] and [10] contain serious misinformation.

References [1] and [2] are available from Committees of Correspondence for $1.00 each prepaid.

References [4], [5], and [9] are available from PRIDE, 100 Edgewood Ave. NE, Suite 1002, Atlanta, GA 30303.

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Marijuana and the Brain

By Robert G. Heath, M.D., D.M. Sci.

Marijuana is used extensively because people like the way it makes them feel. It alters feelings by influencing the brain, perhaps the most fascinating organ of the body. It is the brain that controls or coordinates muscle activity and perception, as well as the vital functions of breathing and circulation. But most unique, the brain is the organ of the mind, integrating behavior through thoughts, emotions, and feelings. While marijuana has been shown to affect all these systems, its mind-altering proclivity is its principal appeal.

BEHAVIORAL EFFECTS OF MARIJUANA SMOKING

Acute Effects

The most consistent and immediate effect of smoking a "good" marijuana joint is a pleasant, relaxed feeling, usually induced after a few puffs. Gradually heightened relaxation is often associated with giddiness and self-preoccupation. The smoker's attentions to his environment diminishes. Indeed, it is the anticipation of these feelings that is the principal motivation for smoking marijuana. While feelings of apprehension and suspiciousness may occur, as well as preoccupation with such sensory stimuli as loud music and flashing lights, these are less consistent symptoms. Typically, the smoker's thinking becomes less precise and more self-centered. The ability to perform tasks is impaired, and inertia proportionate to the strength of the psychoactive ingredients develops. Further, memory mechanisms become altered. These acute effects of smoking usually intensify for 30 minutes to an hour and then gradually subside.

If a person smokes marijuana infrequently - a joint once every ten days or two weeks, - these transient acute effects may be the only changes he experiences although some persons suffer ill effects from only brief exposure. Moreover, an axiom long acknowledged by behaviorists is that pleasure once sampled stimulates repetition. The users of pleasure-inducing drugs corroborate this axiom. According to government surveys, 15 million people in the United States now use marijuana regularly. Moreover, as the pursuit of pleasure has intensified, most smokers have sought increasingly stronger marijuana. And some smokers, still not satisfied, are using other pleasure-inducing drugs as well. In addition to the psychological factors, the drive for stronger pleasure-inducing drugs results from the fact that stimulation of the brain mechanisms for pleasure is, in time, depleting. A cycle is established. Even with frantically increased usage, the desired pleasure continues to be attenuated. Eventually, lasting (chronic) behavioral changes appear.

Chronic Effects

Chronic behavioral changes are those that persist during the intervals between acute effects and, to some extent, even after a person stops smoking marijuana. The intensity of chronic effects and the time it takes them to develop vary considerably, depending on the smoker's constitutional makeup, life stresses, the frequency of smoking, content of the marijuana, and the concomitant use of other psychoactive agents. Intelligent, introspective persons, most of whom were highly aware of their higher intellect, have described the chronic effects of their marijuana smoking thus: First they noticed decreased motivation and enthusiasm in association with reduced ability to absorb, integrate, and effectively use new information. Their anticipation of doing things is less pleasurable. It becomes more of an effort to socialize. And there is a perceptible increase in irritability. Because of marijuana's intoxicating effects, the scholastic performance of the regular user is profoundly impaired. Former marijuana users who are students, teachers, and others engaged in intellectual activities report they are not able to perform at pre-exposure levels months or even years after having stopped smoking. Lasting impairment is more pronounced in those who smoked heavily and for long periods before stopping.

During the 1960's, there were virtually no well documented reports of chronic behavioral impairment as a result of marijuana use in this country. The marijuana of that decade, however, was low in content of delta-9-THC, assays showing the psychoactive ingredient to be in the range of 0.5 to 1.0 percent.

Delta-9-tetrahydrocannabinol (delta-9-THC) is the principal psychoactive ingredient in marijuana. To date, however, 421 separate chemicals have been identified in the cannabis plant. Sixty-one (61) of these substances, the cannabinoids, are unique to Cannabis sativa (Turner et al, 1980).

It was in the early 1970's that reports of profound behavioral changes, seemingly related to heavy marijuana use, particularly in young adults, began to appear in the medical literature. There was abundant evidence of diminished academic performance among users. Further, acute psychotic behavior resembling schizophrenic psychosis was being reported, in addition to disturbances in motivation and impairment of memory. Finally, there were reports of gross brain aberrations. By that time, the delta-9-THC content of marijuana available on the streets had risen to 2.0 to 3.0 percent, and it is still rising. Recently, delta-9-THC content of sinsemilla marijuana grown in California was assayed at 11 to 14 percent.

The past twenty years has seen an increase in behavioral disorders related to chronic use of marijuana that has paralleled the increase in its strength. Although statistics are available, they are not precise, largely because the chronic smoker has often added other drugs to his regimen. Some reports indicate that body fluids of as many as one third of the patients admitted to wards of city mental hospitals show the presence of metabolic breakdown products of marijuana (often combined with other drugs) when toxicological studies are performed. Toxicological studies of persons involved in violent deaths, ranging from accidents to suicides and homicides, are also revealing marijuana use, often associated with use of other drugs. In 1979 in a limited study, we analyzed the body fluids of 55 coroners cases involving violent death (homicide, suicide, traffic fatality) and in 15 of 55 cases, significant levels of marijuana components and/or PCP were demonstrated. In a study done in England toxicology studies were performed on 65 fatal vehicular accidents

randomly selected and in six of the cases (just under 10%), high levels of delta-9-THC were detected (Teale et al, 1977). Only one of the six showed some alcohol in the blood, but it was below the level for intoxication. Regretfully, studies of this type are restricted by lack of instrumentation for detection of the drugs and by legislation prompted by advocates of "human rights."

EFFECTS OF MARIJUANA SMOKING ON BRAIN FUNCTION AND ULTRASTRUCTURE

Ultrastructure refers to cellular anatomy as seen with extremely high magnification of the electron microscope. Despite the increasing number of scientific reports of the deleterious effects of marijuana use, its advocates remain skeptical. They argue that the behavioral changes and associated brain disturbances would have occurred spontaneously in the cases cited, even without marijuana use. Or, they insist, it is other agents (alcohol or other drugs) that are responsible. The rigid controls required to test these arguments cannot be imposed when human subjects are studied. It would be virtually impossible to carry out a study in human subjects in which one could be sure that marijuana (or any other agent one might wish to test) was the only drug the participants would use during the study. Even if an investigator sought volunteer subjects in a controlled environment such as a prison, he could not be certain of a rigid regimen. And, of course, deep brain electrode procedure for obtaining important brain recording could not be used in volunteer-subjects. Finally, informative brain post-mortem studies could not be conducted. Because of legal steps involved in acquiring human post-mortem brains, it would be rare for an investigator to obtain the brain of a marijuana smoker in a sufficiently short time after death to permit its use for ultrastructural studies. Even if one were obtained, findings would be influenced not only by cause of death, but would be questionable due to numerous contributing variables (the subject's general condition before death, history of drug abuse and so forth).

For these reasons, we chose to study marijuana's effects on brain function and ultrastructure in the rhesus monkey, a subhuman primate close to man. Using the monkey, it was possible to impose the rigid scientific controls required to provide answers concerning the drug's effects on the brain. Because of the rhesus monkey's physiological similarities to man, it has been used extensively as the experimental animal of choice to obtain medical information pertinent to human illnesses. It has been used in studies of the RH factor, in the development of polio vaccine, and it has been used widely in studies directed toward understanding vascular and endocrinological disorders in man.

For more than three decades, research in our neuro-science laboratories at Tulane University has been directed toward identification of the brain's neural network for pleasurable and painful emotions as a basis for understanding human behavior and for developing more specific treatments for disordered behavior. Other investigators have likewise conducted studies to demarcate the brain's neural network for pleasure-reward and for pain-punishment. In man, electrical stimulation of certain interconnected deep brain sites has been shown to induce profoundly pleasurable feelings, whereas stimulation to certain other well-demarcated sites has induced profoundly adversive feelings (anger, anxiety, violence); (Heath, and the Tulane University Department of Psychiatry and Neurology, 1954; Heath, 1964; Heath, 1974; Heath, 1975). When given an opportunity a laboratory animal will push a button to stimulate its brain's pleasure system (Olds, 1958; Olds and Milner, 1965) and man will do the same (Heath, 1963). In patients we have shown that the brain's

pleasure system is activated when he is experiencing pleasure or even when he is having pleasurable thought (Heath, Cox, and Lustick, 1974). Similarly, electrical activity in the brain's adversive system is activated during unpleasant situations or in association with anxiety, anger, or fear. In both animals and human subjects, these brain systems have also been localized by administration of drugs which induce profound emotions of pleasure or pain. When marijuana is administered, the acute response is usually a very pleasant feeling. We have therefore used marijuana, as well as other mood-altering drugs, in our comprehensive program to demarcate the brain's neural network for emotion.

It was against this background that we initiated our studies of marijuana in rhesus monkeys - studies that involve sophisticated techniques for monitoring brain function and examining brain ultrastructure. Space limitations permit only a summary description of the studies we have carried out thus far.

Some rhesus monkeys were prepared with electrodes implanted into numerous brain sites identified as a part of the brain's neural network for specific emotions. The electrical recordings obtained from these monkeys, by use of electro-encephalographic machines, would reveal activity deep in the brain, as well as over the surface. Other monkeys were not equipped with electrodes since their brains were destined for electron microscopic studies. A smoking apparatus, fabricated in our laboratories, permitted delivery of smoke to the monkeys in such a way as to simulate man's smoking pattern. The standardized monkey joint we used produced a blood level of delta-9-THC in the animals that approached the level of a person who smoked one marijuana joint.

The significant factor in establishing dosage in the monkey was to determine how much of the agent it actually received. The monkey does not inhale and hold smoke as a man does. In our early studies, before the efficient smoking apparatus was built, we necessarily used large amounts of starting material after discovering that much of the smoke was dissipated in the air when the marijuana was lit. This point was seized upon and exaggerated by marijuana advocates who incorrectly stated that our dosages were much greater than those used by human marijuana smokers (Brecher, 1975). When we obtained blood levels of delta-9-THC in our monkeys, they were no higher per exposure than the blood levels of human smokers. Moreover, the critics chose to ignore the fact that some monkeys in our studies received delta-9-THC intravenously at dose levels that could be carefully controlled.

Active marijuana used in the smoking studies contained 2.5 to 3.0 percent delta-9-THC. To control for nonspecific effects of smoking, we used inactive marijuana, from which all cannabinols (delta-9-THC and delta-8-THC) had been removed, for some of the monkeys. Finally, some monkeys were given delta-9-THC intravenously to control the variables of smoking effects, such as anoxia (lack of oxygen). The monkey smokers of active marijuana were divided into three groups: heavy smokers (three exposures each day, five days per week); moderate smokers (one exposure on each of two days per week); and light smokers (exposed to one-tenth the dose of the heavy smoker). Monkeys exposed to smoke of inactive marijuana were on the same smoking schedule as the heavy smokers of active marijuana (three exposures per day, five days per week).

Acute Recording Effects

Profound changes in brain recordings occurred in those monkeys that smoked active marijuana on the heavy and moderate schedules and those that received delta-9-THC intravenously. Associated with development of a semi-stuporous,

catatonic appearance, recording changes were predominantly at sites identified as being involved in the pleasure circuitry of the brain. They usually persisted for about an hour and a half, subsiding as the monkey's appearance returned to normal. In contrast, monkeys exposed to smoke of inactive marijuana showed no recording or behavioral changes. When the dosage schedule had been in effect for two to three months, persistent recording changes were also noted at brain sites in circuits involved in adversive emotion (irritability, anger, fear) of the heavy and moderate smokers of active marijuana and the monkeys receiving delta-9-THC intravenously. The dose to which the light smokers were exposed was below threshold and had no effect on the monkeys.

Chronic Recording Effects

The monkeys continued on the same exposure schedule for six months (and a few, for eight months). During that period the abnormalities in recordings failed to subside between exposures. We then stopped the smoking schedules and administration of delta-9-THC intravenously enabling the monkeys to "rest" and to be observed for an additional eight months. The recording changes persisted despite withdrawal of the drug. On the other hand, those monkeys that received smoke of inactive marijuana, never developed behavioral or recording changes.

At the end of the eight months' rest period, the monkeys were killed and their brains studied under the electron microscope.

Ultrastructural Changes

For ultrastructural studies, brains of monkeys not prepared with electrodes were also used. The brains of the monkeys exposed to delta-9-THC, whether in the form of heavy or moderate smoking or administered intravenously, showed striking changes at the synapse (the site where one brain cell makes contact with another). It is at the synapse that transmission of a message from one nerve cell to another occurs by release of chemicals at the nerve ending. This is the basis of brain activity. There was widening of the synaptic junction, deposition of a dense material in the cleft, and clumping of the vesicles that contain the chemical transmitters released to carry the impulse across the cleft. Changes were also evident in the rough endoplasmic reticulum, a constituent of the cytoplasm in nerve cells thought to be associated with protein synthesis and possibly the memory process. And finally, there was deposition of proteinaceous substances (called inclusion bodies) in the nuclei of brain cells. These changes, all significant, have been associated with brain damage from other causes. Brains of other monkeys in the study (those exposed to smoke of inactive marijuana and those not exposed - serving as further control of the study) showed no ultrastructural changes.

Comment

The findings reported here indicate that exposure to delta-9-THC, the psychoactive ingredient of marijuana, at doses commensurate with those used by human marijuana smokers, produces permanent changes in brain function and structure of monkeys, a subhuman primate close to man (Heath, et al, 1980).

Some aspects of these studies have been conducted at other research centers. At the University of Toronto, where brain studies have been carried out in rats exposed to active marijuana similar recording changes have been reported (Fehr, Kalant, and LeBlanc, 1976). Data from the University of British Columbia, where investigators have conducted ultrastructural studies on brains of rats exposed to marijuana, likewise support our findings in monkeys (McGeer and Jakubovic, 1979).

Granted, there is some risk in extrapolating data from one species to another. But the consistencies between our monkey findings and the clinical observations and subjective reports of human marijuana smokers cannot be denied. The functional and ultrastructural changes in the monkeys were at brain sites where neural activity has been shown to correlate with emotional behavior. Changes seen in heavy users of marijuana, ranging from mild apathy to the "burned out" syndrome, suggest the same brain sites of human smokers are being affected similarly.

This subject cannot be dismissed without brief consideration of broader complications that can occur when a person seeks to alter his neural network for pleasure-pain by use of drugs. The drug-user is a component of our society.

The fate of cultures in which drug use has been extensive substantiates the consequences of inducing pleasure dissociated from utility and survival. In our own culture, in which use of drugs is ever-increasing, the pattern is rapidly emerging. When the pleasure a person gains from taking a drug replaces reward for a job well done, we have shoddy workmanship. When puffs from a joint replace the pleasure of a swim on a warm afternoon or a good tennis game, we have apathy and physical deterioration. When the anxiety before an examination is eliminated by the instant pleasure of a drug, the student does not prepare and fails the examination. When ingestion of a chemical substitute replaces the satisfaction of solving a problem, being creative, or helping another person, what are the implications for the future of our society--or even our survival as a nation?

* * *

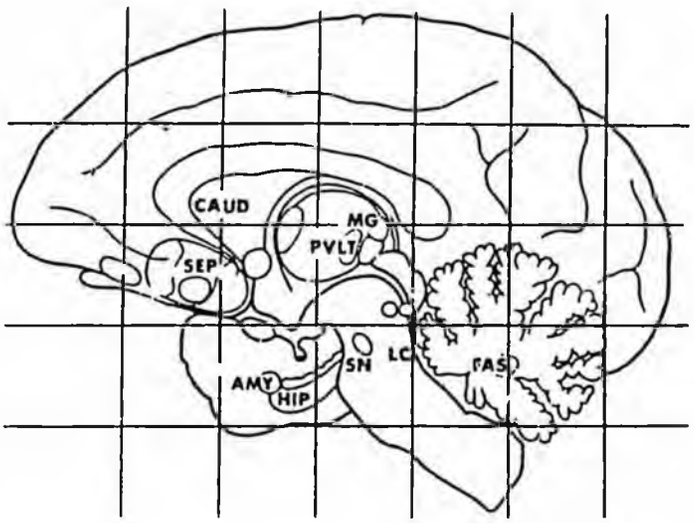

Figure 1. Cross-section of rhesus monkey brain showing cell populations involved in emotion and behavior. HIP-hippocampus; AMY-medial amygdala; SEP-septal region (A-anterior, P-posterior); CAU-caudate nucleus; PVLT-posterior ventrolateral thalamus; LC-locus ceruleus; SN-substantia nigra; FAS-fastigial nucleus of cerebellum.

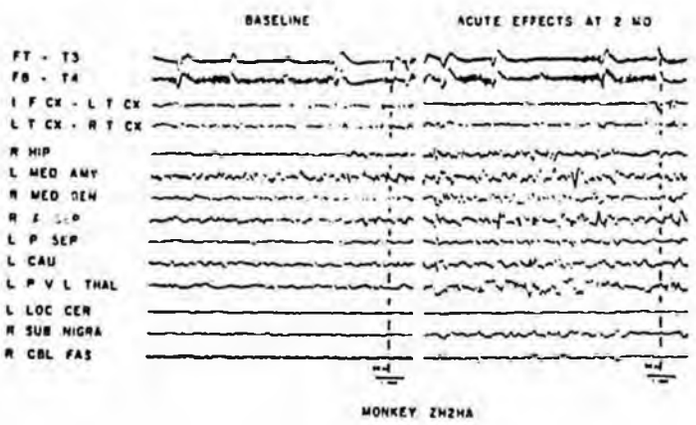

Figure 2. Bipolar electrodes implanted at the brain sites shown in Figure 1 record the electrical activity of these nerve cell groups before any smoking (baseline) and with exposure to smoke of active marihuana (acute effects). Letters and numbers refer to various regions of the brain.

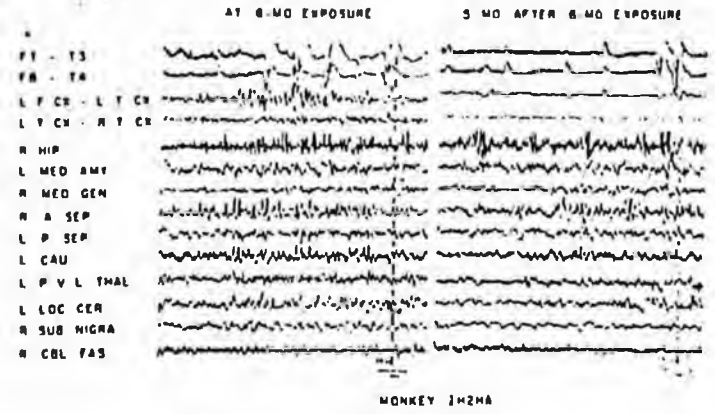

Figure 3. Electrical activity of nerve cell groups after six months of exposure and in the post-smoking follow-up period.

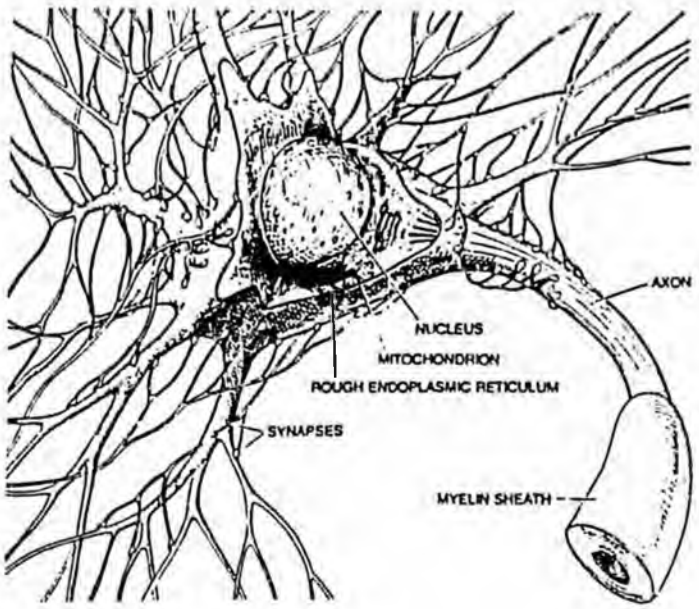

Figure 4. Typical brain nerve cell receiving input from neighboring cells (via synaptic connections) and sending output through axon which synapses onto other cells. (Drawing with permission from *Scientific American*, September, 1979.)

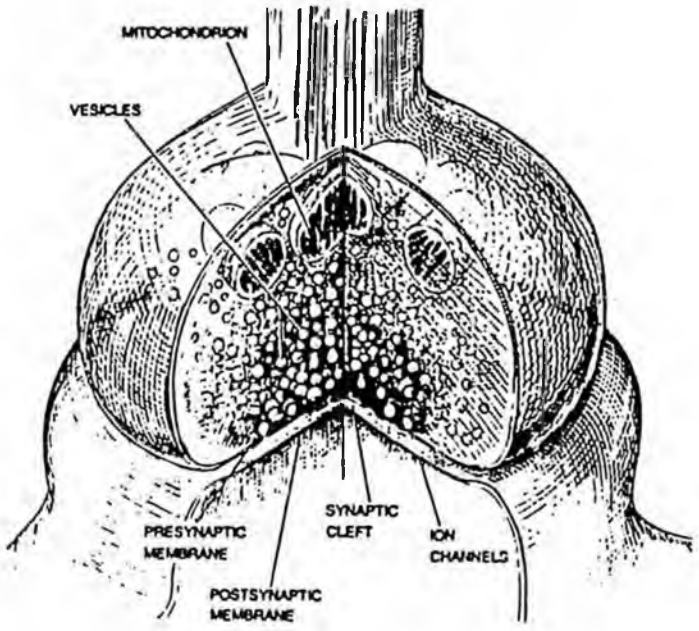

Figure 5. Detailed view of synapse which passes information from one nerve to another. An electrical signal in upper cell causes chemical (neurotransmitter) to be released by vesicles into cleft. This chemical is recognized on postsynaptic membrane of lower cell, resulting in new electrical signal in that cell. (Drawing with permission from *Scientific American*, September, 1979.)

Figure 6. Electron microscopic pictures of synaptic tissue in monkey. *Left:* Normal synaptic junction. *Right:* similar tissue in heavy-smoking monkey (x 20,000). Magnified inset views (x 60,000) show changed structure of synaptic cleft more clearly. (With permission from Biological Psychiatry.)

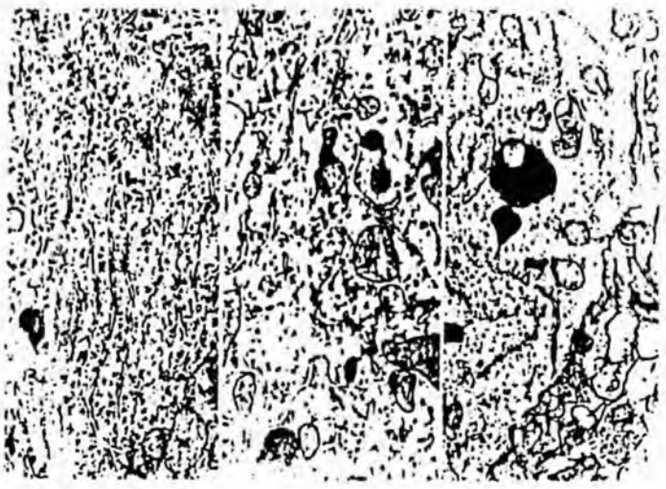

Figure 7. Electron microscopic pictures of rough endoplasmic reticulum (involved in protein synthesis) within cell body of monkey brain. *Left:* Normal. *Center:* from monkey that received delta-9-THC intravenously. *Right:* From heavy smoking monkey (x 6,000). (With permission from Biological Psychiatry.)

Figure 8. Electron microscopic pictures of inclusions within cell nuclei of heavy smoking and intravenously injected monkeys (x 15,000). (With permission from Biological Psychiatry.)

* * *

ABOUT THE AUTHOR

A native of Pittsburgh, Robert G. Heath, M.D., D.M. Sci., is a graduate of the University of Pittsburgh School of Medicine. He trained in psychiatry at the Pennsylvania Hospital in Philadelphia and in neurology at the Neurological Institute in New York City. Dr. Heath is also a graduate of The Psychoanalytic Clinic of the Columbia University College of Physicians and Surgeons and he is a recipient of Columbia University's Doctor of Medical Science degree. He is Board-certified in both psychiatry and neurology.

In 1949, Dr. Heath became the first Chairman of the Tulane University Department of Psychiatry and Neurology in New Orleans, a post he filled until his retirement in June 1980. Nearly 400 psychiatrists and neurologists were trained in the Department under Dr. Heath's leadership, including many prominent medical educators.

Dr. Heath is acknowledged as a pioneer in the study of schizophrenia as a biologically-caused disorder. In 1949 he and his research team began charting the pathways of emotional expression in the brain, work that led to the therapeutic use of a brain pacemaker in patients with severe chronic behavioral disorders that failed to respond to conventional treatments. Of major concern to Dr. Heath since the early 1970's has been his research on the detrimental effects of marijuana on the brain.

Dr. Heath is the author of 360 scientific papers and the principal author and editor of three books. He has been elected to a number of honorary societies and is the recipient of numerous international, national, and regional awards. A Professor of Psychiatry and Neurology on the Tulane faculty, he is continuing his research concerned with the brain and behavior.

Dr. Heath serves as Chairman of the Scientific Advisory Board of the American Council on Marijuana.

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Drug Awareness Information Newsletter

October 1987

57 Conant Street, Room 113 ~ Danvers, MA 01923 • (617) 774-2641 Connie & Otto Moulton

MARIJUANA: TOXIC TO CELLS

Synopsis of the Videotape *Marijuana: Myths and Misconceptions*

ROBERT C. GILKESON, M.D.

Until Americans change their wholly erroneous perception that marijuana is the "least harmful" of all "illicit drugs" it will continue as the drug with the gravest national consequences.

ALL DRUGS ALTER BRAIN CELL FUNCTION

Every drug that alters your mood, your feelings, your coordination, your thinking, or your behavior has altered the cells in your brain and disrupted their normal chemical function. Before using a drug of any kind, one should know what chemicals it contains, which cells in your brain and body they most affect, and exactly how these cells are altered.

CELL MEMBRANES

Each cell in your body is surrounded by a delicate membrane which allows the cell to perform its specific work and protects it from the toxic waste products floating by in the circulation. Cell life depends on the unobstructed passage of nutrient and waste chemicals in and out of this membrane. This membrane is composed of an intricate pattern of lipid (fat) and protein molecules. The pattern is determined by the cell type, the function it performs, and its specific needs.

MEMBRANE TRANSPORT

Nothing is more essential to the healthy cell than the proper function of its membrane. Each of the chemicals which provide the ENERGY to keep the cell alive must be selected from the circulation and brought through the membrane. All of the special products which the cell produces and the waste products from that work must pass out of the cell through the membrane. This constant movement of chemicals in and out of the membrane occurs through submicroscopic channels between the lipids or the complex actions of the protein molecules specifically assigned to them.

MARIJUANA: AND ITS TOXIC CHEMICALS

Marijuana contains 421 bioactive chemical molecules; 61 of these are called cannabinoids. The cannabinoid which causes the acute marijuana high is delta-9 THC, but all of the cannabinoid molecules in street pot are extremely soluble in lipid molecules, and disrupt cell function. Every cell membrane in the body is composed of an intricate arrangement of lipid and protein molecules essential to cell function.

The purpose of all of these messages is to keep track of all of the other cells in the body, to keep them functioning properly, and to keep them alive. "Internal" messages deeper in the brain relate the needs of the cells within the body. "External" messages from the eyes, ears, nose and skin provide information about the environment outside and the problems that must be solved to satisfy those needs.

Neurons from all the areas of the brain must accurately pass their information from one to another until they reach the frontal lobes of the brain where they must be kept going over time so they can be correctly analyzed and the most intelligent plan can be formulated to initiate and direct the complex sequential actions necessary to meet the needs of all of the cells in your body and for your optimal survival.

NEURON "FIRING"
Each time a message is passed from one neuron to another, precise amounts of sodium, calcium, chlorides, and complex messenger chemicals (neurotransmitters) must enter or leave through the proper membrane channels in 0.4 to 1.0 milliseconds. To be accurate each message must be transmitted in exactly the right amplitude and frequency. Because of their chemical complexity, their constant activity, and the speed at which they operate, neurons are affected more than any other cells in the body by substances which alter or block cell membranes or change the speed or amplitude of their firing.

THE BRAIN'S ENERGY CENTER: (The RAS)
That area of the brain which controls and directs the amount of energy going to and coming from each of the other brain centers is called the Reticular Activating System - The RAS. Because it alters the energy going to and coming from each area, the RAS coordinates the interaction of all the other brain centers. The RAS must make more connections (synapses) than any other center and must be constantly in operation. It controls our waking, sleeping, and alertness - our very level or consciousness. Because it turns on (increases) or it turns off (decreases) the chemical messages between areas of the brain, it regulates the intensity of messages between the centers for memory, the center for feelings, and the centers for analyzing all the messages from inside and outside of the body. Most importantly, it determines the level of the activity and the number of connections that can be made in our frontal lobes which analyze all incoming messages from our environment and formulate the most intelligent plans in the right sequence of movements and behaviors necessary for our optimal survival over time. Since this determines the level of complexity of our thought and behavior, it determines our intelligence.

Whenever the energy of the RAS is decreased or depleted by depressant drugs such as marijuana, the energy of the entire brain is decreased. But that area most affected by this loss in energy is the rich and multisynaptic frontal lobe where we analyze the significance of all sensory images, and plan and program our most intelligent responses.

The most complex thoughts and the most sensitive feelings, demand the most complex circuitry and depend on the number of synapses which can be activated. Decreasing the energy flowing in the neuronal circuits reduces the number of those circuits which can be activated, and reduces the degree, the intensity, and the alacrity of those that are left.

Cannabinoids are not interested in the IQ of the user, only the lipids in his cell membranes. No matter who - or how intelligent before he began - even the occasional smoker has less energy to activate the cells and circuits of his brain.

CANNABINOIDS BLOCK MEMBRANE TRANSPORT

The cannabinoids are found in an oily resin which coats the buds and youngest leaves of the marijuana plant nearest the sun. This oily coating blocks water and water-soluble substances from escaping (evaporating) from inside the leaves, helping to conserve water through periods of drought. But if this same resin were scraped from the leaves and applied to the roots, it would prevent their absorption of water from the ground and then be TOXIC to the plant itself.

Unfortunately, when the cannabinoids are inhaled in smoke or eaten, they are immediately attracted to and become embedded in the lipids in every cell membrane in the body, and increasingly interfere with membrane transport very much as they did in nature.

MARIJUANA ACCUMULATES IN CELL MEMBRANES

Since these cannabinoids are of no chemical use to the cell and are hidden from the circulation, they are not easily broken down or eliminated, and they remain embedded in the lipids of every cell membrane of the body for months at a time.

After smoking only one 3% THC marijuana joint, 40-50% of the THC remains in your cell membranes for four to eight days; 10-20% is still there at thirty days; and 1% to traces can be found from forty-eight days to 4.6 months.

"OCCASIONAL" MARIJUANA USE CAUSES CHRONIC CELLULAR IMPAIRMENT AND CRIPPLES RATHER THAN KILLS

Smoking marijuana more than once every four months (faster than your cells can eliminate the cannabinoids from the last ingestion) leads to the accumulation and eventual saturation of the cell membranes.

Since saturation limits further acute toxicity, cannabinoids chronically CRIPPLE rather than KILL.

As they increase, however, they progressively interfere with membrane transport, and increasingly rob it of nutrients. This leads to an obligatory loss of cell ENERGY and insidiously retards the growth and maturation of every cellular system. Cells with less energy can do less work.

Saturated membranes may not lose their cannabinoid molecules for many months after stopping smoking.

CANNABINOIDS CONCENTRATED IN MOST VITAL ORGANS

Cannabinoids become concentrated in the lungs, liver, kidneys, adrenal glands, ovaries, testicles, bone marrow, and the center of brain activation. Studies of all the systems these organs maintain have repeatedly shown their disruption by marijuana.

BRAIN CELLS FAR THE MOST VULNERABLE

The brain cannot feel pain. The brain is the only organ or body part not equipped with pain fibers or sensation. While it hurts to pull a single hair from the scalp, massive areas of brain tissue can be slowly or rapidly injured or destroyed without any warning or awareness. You "feel no pain" from the drugs that damage the brain.

The most important, the most specialized, the most complex and the most fragile cells of the body are the 100 billion cells of the brain. These cells, called neurons, make 100 trillion connections or synapses where chemical messages are passed from one neuron to another.

Marijuana not only reduces the richness and sensitivity of our feelings, it not only impairs our ability to analyze the world around us, but it diminishes in sequence our most complex and highest order brain functions which are all related to our ability to generate and activate the neuronal circuits which allow us to foresee or preview future, we are less able to plan and carry out the most intelligent actions and behaviors necessary to achieve and assure our most optimal future survival.

The first, the most common, and certainly the most discouraging symptom of the chronic marijuana smoker, is his apparent and increasing disinterest in the necessary behaviors he must pursue now, to assure his most optimal gratification for his future life. Without the energy to direct his own future, he is forced to go with the flow, and hope he has the energy left to take care of whatever lies ahead after it has happened to him.

SUMMARY

In summary, the cannabinoid molecules in marijuana become embedded in cell membranes throughout the body, blocking the channels through which critical chemicals must pass, particularly calcium, in order to keep each cell functioning properly. As more and more cannabinoids saturate the membrane, the cell is progressively robbed of important nutrients and slowly loses its ENERGY. When this interruption of membrane transport occurs in brain cells, the loss of energy affects the centers of the brain that regulate our highest levels of thought, feeling, memory, behavior, and our ability to envision and make the most appropriate plans to meet the future.

Most simply: every marijuana smoker is dumber than before he began, and he remains that way not only for the months it takes until all of the cannabinoids are gone, but however long it takes after that for his injured cells to recover if they still have the capacity to do so, and the longer impaired the greater the residual loss.

INVALID RESEARCH

Any sincere research investigation that does not reflect the obligatory loss of cell ENERGY from the presence of cannabinoids embedded in cell membranes must be simply and immediately rejected as scientifically invalid. While often intentional, any study not reflecting this loss, is by very definition inadequate in its understanding of basic concepts, or inaccurate and inadequate in design, instrumentation, or scientific methodology.

Immediate review of each of the poorly controlled and frighteningly subjective behavioral studies which fail to demonstrate marijuana's insidious toxicity reveals that in every case the primary investigators must be embarrassed that they ignored the most basic chemical property of the cannabinoids: their lipid solubility and their months'-long membrane storage.

HUMAN BEHAVIORAL STUDIES THE LEAST SCIENTIFICALLY ACCURATE

Unable to introduce toxic substances to naive research subjects (non-marijuana users), investigators were forced to use chronic marijuana smokers whose membranes were saturated before their "studies" began, and remained so throughout the entire study.

Since they then failed to allow sufficient time (months) for subjects to eliminate embedded cannabinoids before their studies began, and repeated the same error in measurements taken only days or weeks after ingestion was concluded, observations or conclusions comparing the acute and the chronic effects of marijuana, in these studies are wholly inaccurate, scientifically naive, and invariably invalid. Particularly invalid are observations about withdrawal, addictive properties, and observations of baseline behavior, since they have been made with the presence of cannabinoids still saturating the membranes.

INVALID BEHAVIORAL STUDIES THE MOST WIDELY PUBLICIZED

It has become a national tragedy for a scientifically ignorant public - particularly its developing adolescents - that such simplistic and basic errors in scientific methodology were not only unrecognized but incredibly repeatedly published by such influential bodies as the National Institute for Drug Abuse. That they were not immediately rejected only reveals and substantiates this body's disturbing but repeated scientific naivete in a matter so vital to public trust and public health.

THE NATIONAL INSTITUTE OF DRUG ABUSE CONTRIBUTES TO CONFUSION

Even more upsetting, is to realize that despite their immediately invalid design such research studies were not only published, but repeatedly funded by NIDA at enormous expense to its victims.

PUBLIC TRAGICALLY MISLED BY THE MEDIA

Ironically "adopting" a century old intoxicant as their symbol, marijuana was transformed and promoted as a fervently partisan political rather than scientific issue. As a result, the more invalid the study, the more avidly it was selected and the more widely it was publicized by a scientifically ignorant and adolescently biased public media.

THE MEDIA ALARMINGLY NAIVE

With inexcusable professional negligence, this same media has persisted in dubbing as "expert" any they interview and have pursued and quoted more vested lawyers, drug "industry" lobbyists, and "users", than qualified scientific investigators.

SCIENTIFIC FACT SACRIFICED FOR ENTERTAINMENT

Choosing to stage controversial "debate" with wholly unqualified "witnesses", rather than investigating readily-available facts, the media has intentionally ignored, purposely distorted, and naively contested, the over 8,500 published scientific papers which have overwhelmingly condemned marijuana for its insidious, long-lasting, often subtle but obligatory cell energy depletion.

ABOUT THE AUTHOR

Robert C. Gilkeson, M.D., teacher, pediatrician, adolescent neuropsychiatrist, and brain researcher, has the unique ability to make clear to non-scientists and scientists alike how the chemicals in drugs disrupt the normal functions of human cells. Dr. Gilkeson has lectured extensively throughout the United States on drugs, the neurophysiology of learning, and normal adolescent development. His audiences have included the National Association of Independent Schools, The Independent School Association of Central States, The Headmasters' Association, The United States Senate and State Senate Hearings, The Department of Justice, national parent organizations, and countless schools and medical groups.

FOR MORE DETAILED INFORMATION ON THIS SUBJECT, WE RECOMMEND PURCHASE OF THE VIDEOTAPE - MARIJUANA: MYTHS AND MISCONCEPTIONS which is a 90-minute VHS presentation which reviews the latest findings in drug and brain research, taking the viewer step-by-step from the chemicals in drugs - alcohol, cocaine, amphetamines, LSD, and heroin - to their alteration of brain cells to the result of those brain-cell changes on personality, learning and performance.

This videotape is not just a drug program - it provides the basis for an extended drug curriculum. The price is $400.00 which includes a 24-page teaching guide. Discounts are available for three or more tapes. Demonstration tapes are available. For more information write or call: Committees of Correspondence, 57 Conant St., Room 113, Danvers, MA 01923, 617/774-2641. Checks may be made out to The Center for Drug Education and Brain Research and mailed to Committees of Correspondence.

Alaskans for Drug-Free Youth has this video. Call Sandy Spargo at 586-6122 (evenings).

GLOSSARY OF SPECIALIZED TERMS

MARIJUANA CHEMICAL COMPONENTS AND THEIR PROPERTIES

CANNABIS - Cannabis, or more technically Cannabis Sativa, is a leafy plant whose leaves, flowers, stems, and seeds are dried and crushed to form the street drug, marijuana.

CANNABINOIDS - Chemical components found exclusively in marijuana.

DELTA-9-THC (TETRAHYDROCANNABINOL) - A fat-soluble cannabinoid most responsible for the nervous system changes associated with being "high."

SINSEMILLA - Seedless variety of high-potency marijuana.

FAT-SOLUBLE - Capable of being stored in the lipid (or fatty) cell tissue.

SATURATION - The point at which cells' storage capacity for a substance (such as THC) has been reached.

BRAIN AREAS

HIPPOCAMPUS - An area of the midbrain beneath the cortex, essential to memory formation. It is part of the limbic system closely intertwined with the feeling center.

FEELING CENTERS - Part of the limbic system in the midbrain area giving sensations of pleasure, pain, fear, surprise, sexual arousal, depression, anger.

RETICULAR ACTIVATING SYSTEM (RAS) - the energy controller of the cortex. Consciousness cannot be maintained without its activity. It is the major target of drugs. This center controls facilitation and inhibition. It activates or suppresses the feeling and memory centers.

SENSORY CORTEX - It contains the receptors for vision, hearing, touch, and the ability to localize oneself and other objects in depth and space.

FRONTAL LOBE - Contains the motor area, a premotor (programing) area, and the prefrontal lobe (analysis).

PREFRONTAL AREA - The very forwardmost part of the brain and the last to mature. Richest associative area with all parts of the cortex and the midbrain. It contains the reverberating circuits which hold images in place over time so they can be analyzed. It is your analyzer and programmer.

MOTOR AREA - Stimulates muscles of limbs and body.

CELL COMPONENTS AND CELL PROCESSES

CELL MEMBRANE - The coating or protective covering surrounding every cell, composed of tightly packed fat (lipid) molecules, interspersed with special proteins. This membrane controls all the chemicals which enter and leave the cell.

MEMBRANE CHANNELS - Passageways or tunnels through the protein molecules in the cell membrane, which can be opened and closed by the cell to let the chemicals in or out of the membrane.

NEURONS - The cells in the brain and spinal cord capable of passing messages to each other in milliseconds.

DENDRITES - The receiving end of a neuron, resembling branches of a tree.

CELL BODY - The metabolic center of a neuron, where the nucleus resides.

AXON - The sending trunk of a neuron that releases the chemical messenger at its end.

SENSORY NEURONS - Neurons equipped with special receptors which respond to light, sound, touch, pressure, heat, chemicals, pain, taste.

MOTOR NEURONS - Contract muscles, move body parts constrict blood vessels and excite glandular secretions.

MESSENGER NEURONS - Relay messages between sensory and motor neurons.

NEUROTRANSMITTER - The messenger chemical made by neurons and released by their axons to stimulate other neurons, muscles, glands.

RESTING MEMBRANE POTENTIAL - The difference in "charge" between the positive outside surface of the neuron membrane and the inside surface.

DEPOLARIZATION - The rapid flow of positive sodium ions into the cell when the sodium channels are opened.

REPOLARIZATION - Restoring the membrane "charge" by pumping all sodium ions out of the cell.

MITOCHONDRIA - Submicroscopic membrane-coated sacs containing chemicals which burn fat, carbohydrates and proteins to produce cell's energy.

Your brain is a precious resource; it is your computer!
The brain generates all human behavior, both peaceful and violent.
It stores all human experience - social, cultural and educational.
It is the source of energy, motivation, organization and pleasure.
All drugs taken into the body go to the brain in the blood and cause a chemical imbalance.
DO NOT TAMPER WITH YOUR BRAIN!

COMMITTEES OF CORRESPONDENCE. INC.
57 Conant Street, Room 113, Danvers, MA 01923

MATERIAL LIST

THE COMMITTEES OF CORRESPONDENCE is a non-profit agency which publishes a quarterly Drug Abuse Newsletter, written on a specific subject relating to drug-abuse issues. Extra mailings are sent when urgent issues need letter-writing attention. We are affiliated with the National Federation of Parents for Drug-Free Youth and PRIDE. An important part of our work has been the detection and exposure of drug-culture proponents who have undeservedly been "legitimized" in various sectors of our society. Our information is carefully researched and documented. A "New Membership Package" (included in our $15 subscription fee) contains the following:

NEWSLETTERS

School Policy Guidelines - Discipline for Drug Offences
*Biological Effects of Marijuana
Courtwatch - Citizen's Guide to Judicial Accountability
*Cocaine - The Great Addicter
Sky High - Who's in Control?
Drug Abuse in Industry - What Does It Cost & What Can Be Done
*Beware ---- Incorrect Information
*Evaluating Resource Material on Mind-Altering Drugs with Reading List
How To Mobilize Your Community for JUST SAY NO MARCHES
Dealing With Smoking Areas in School - How to Eliminate Them
The Experimental Use of Cocaine in Man: Is It Acceptable?
Drug Testing in the Workplace by Dan Haigh
Addiction as a Primary Disease by Eric A. Voth, MD
Marijuana: Toxic to Cells by Robert C. Gilkeson, MD
The Magistrate/Adolescent Intervention Program

ARTICLES

Drug Prevention Curriculum and Resource Review Guidelines (NFP)
Marijuana: The Myth of Harmlessness Goes Up In Smoke by Peggy Mann
Marijuana: The Effects on the Unborn by Dr. Susan Dalterio
Marijuana: The Effects on the Brain by Dr. Robert Heath
Speeches on Drug Abuse by Otto Moulton
Some Unsettling Thoughts About Settling In With Pot by Richard Hawley
*Drug Prevention - The Role of the Schools by Malcolm Lawrence
A Parents Guide to Teenage Parties
Drug-Free Community Plan by Deerfield Citizens for Drug Awareness
A Man of Our Time: Dr. Gabriel Nahas
PRIDE Position Paper: A Drug Policy of Our Times
The Media as Drug Promoters by David Martin
*Making Sure Kids Get the Right Message by Atty. Gen. Roy Zimmerman, PA
Drugs, Drinking and Adolescents by Dr. Ian Macdonald
Don't Drink Before You're 21 by William N. Plymat, Sr.
Alcohol --- is a Drug, Too! by Straight, Inc.

PAMPHLETS

*Cocaine - The Great Addicter
*What Parents Must Learn About Marijuana
*Marijuana: More Harmful Than You Think
*A Straight Pitch About Marijuana
*Helping Young People Kick the Sniffing Habit
*How to Form a Just Say No Club
*Crack
*Peer Pressure - It's OK to Say NO
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Drug Abuse Newsletter

March 1984
Issue #16

BIOLOGICAL EFFECTS OF MARIJUANA

WHAT IS MARIJUANA

Marijuana is neither a plant nor a single substance. It is a crude drug obtained from the dried leaves and flowering tops of the plant species Cannabis sativa.

There are three types of Cannabis plants:

the drug type
the fiber type
the intermediate type

Marijuana is most often smoked in cigarette form, but may also be ingested in cookies, tea, etc. Marijuana smoke is composed of several hundred chemicals, many of them toxic. Its potency varies from weak to extremely powerful.

To understand marijuana, you need to know two things about it:

1. Its chemical components.
2. The solubility of these chemicals.

CHEMICAL COMPONENTS

There are over 421 chemicals in marijuana. This number increases to over 2,000 when it is smoked.

More than 61 of these 421 chemicals are called cannabinoids and are found in no other plant.

All cannabinoids tested to date are biologically active. This means that each cannabinoid will alter some normal function of a living organism. These alterations may not be visible since they occur at the cellular level, but they can be documented in research laboratories.

One of these cannabinoids is delta-9-tetra-hydrocannabinol. This is the psychoactive cannabinoid that causes the familiar marijuana "high" or state of intoxication. "THC" stands for the several chemicals in the tetrahydrocannabinol class. It is the chemical that has been researched the most.

The potency of marijuana is determined by the amount of THC it contains. The higher the THC content, the more intoxicating and **harmful** it becomes. The marijuana grown today is up to 10 times more potent than that used prior to 1970.

All cannabinoids have one important factor in common: They react on all types of living cells by interfering with the cells' ability to manufacture pivotal molecules.

Pivotal molecules contain substances required for the proper division of cells, which is necessary for the continuation of our body functions. These substances you have heard of many times - DNA, RNA and proteins. DNA is the basic chemical contained in the core of all cells and it carries the genetic code for heredity.

SOLUBILITY

The major chemical components (all cannabinoids) of marijuana are fat soluble. This means that they do not mix with water, but they do mix with fat.

The body is rich in fat and fat-like material (collectively called lipids). The brain, lungs, and sex organs are especially loaded with lipids.

Every cell in the body is covered by a fatty membrane, which makes the fat volume of these membranes alone very huge. In essence, the body can figuratively hold a keg-full of THC or fat-soluble chemicals.

Once the THC from marijuana is in the storage sites, it is released ever so slowly into the blood stream. THC is similar to DDT in the way that it accumulates in fat tissue.

THC possesses a high order of reactivity. THC molecules are very busy, and they are up to no good seeping through the fatty membrane wall of the cell and into its core; creating havoc with the chemical process of cell division.

Creating a slowdown or interference of production of DNA, RNA and protein replacement within the cell causes the following to happen:

1. Cellular activity decreases.
2. This decrease in activity can eventually become a stoppage.
3. This stoppage can result in cell death.

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When this happens, every function in the body is depressed:

- Energy level
- Thinking
- Sperm count
- Testosterone production
- Ovulation
- Even the sense of time

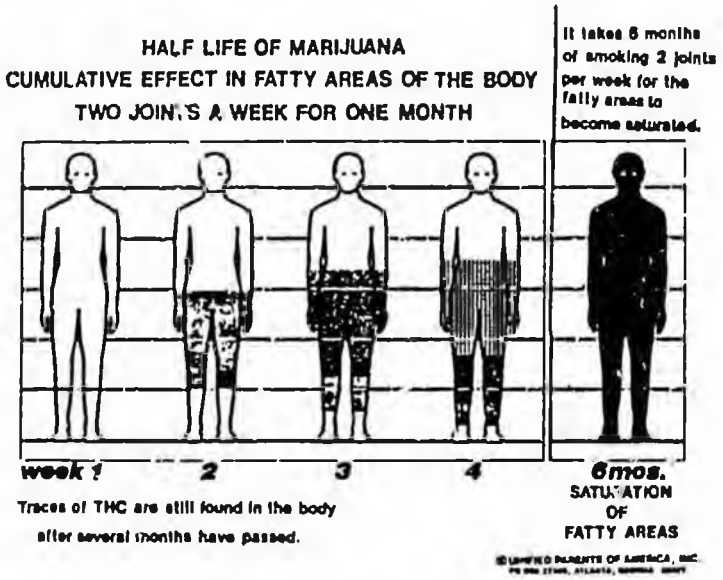
How much damage can THC do to the various systems of the body? That depends on how long and how much of the THC is present within the cells. The body can not get rid of marijuana's chief chemicals easily - trapped as they are in the lipid stores of the body - so the damage continues, slowly but surely!

RETENTION OF CHEMICALS

The marijuana "high" is rather short-lived, and the detectable effects during this time are significant, but there is more to it than that. When a single marijuana cigarette is smoked, THC and other cannabinoids have an average half-life of about 72 hours in the human body. Half-life is the time it takes the body to break down and/or get rid of one half of the drug taken into the body.

It takes 21 days to excrete THC and fat-soluble chemicals from a single marijuana cigarette. Stored in the cells of the liver, lungs, brain, spleen, lymphoid tissues and sex organs, half of the THC leaves these cells in the first three days. The remaining half is released into the bloodstream ever so slowly over the next 18 days. At the end of this time less than 1% remains in the body. This is as a result of smoking only one marijuana cigarette.

However, if one is a regular marijuana smoker (i.e. smoking 2 joints per week for six months), the fatty areas of the body become completely saturated with fat-soluble chemicals. Traces of THC are still found in the body after several months have passed.



CELLULAR DAMAGE - - THE EFFECTS ON THE IMMUNE SYSTEM

Cellular damage from marijuana use is a proven fact, and long-term users of this crude drug display an impairment of their cellular control immunity.

The immune system is a complex system of defense involving the white blood cells which specialize in fighting infections and destroying substances foreign to the body such as cancer cells and tissue transplants.

The immune system can be weakened by drugs, nutritional deficiencies, and by intense emotional stress.

In studies done at Columbia University, scientists studied the immunity response of 51 marijuana smokers, 16 to 35 years of age, who had smoked an average of three marijuana cigarettes a week for four years and who had used no other drugs except tobacco and alcoholic beverages. They compared these studies to a group of control subjects who did not use marijuana but did use tobacco and alcoholic beverages. (Science, Vol. 183, 419-420, 1974). The results of the immunity response of the marijuana smokers was 40% less than that of the non-marijuana smokers.

Something to think about.... Could there be any connection with the lowered immune system of marijuana smokers to the new disease of Acquired Immune Deficieny Syndrome (AIDS)?

How is it that the weekly consumption of only three to four marijuana cigarettes containing 15 to 20 mg. of THC may induce such cellular damage? It is because THC hangs around in the fat tissues for long periods of time. Most other drugs are water soluble and are flushed out of the body in a short period of time. This is not the case with marijuana.

CELLULAR DAMAGE - - THC EFFECTS ON REPRODUCTIVE CELLS

Available evidence indicates that cannabinoids exert significant negative effects on all phases of reproduction in males and females because they are stored in the sex organs and in the brain.

EFFECTS ON MALE REPRODUCTION.

Researchers at Columbia University have proven that moderate to heavy marijuana smokers have a decrease in sperm count and mobility and produce an abundance of abnormally formed sperm.

Cannabinoids disrupt the development of germ cells in the testes and disrupts the hypothalamus gland in the brain which controls this production.

Since men constantly produce millions of sperm, conditions will probably return to normal when pot smoking is stopped.

EFFECTS ON FEMALE REPRODUCTION:

This information is from studies done by Ethel Sassenrath, Ph. D., UC at Davis.

However, the effect marijuana smoking has on women may be lasting. An infant girl is born with her lifetime supply of eggs. If these are damaged, there is NO replacement!

A female using marijuana will notice a change in the menstrual cycle due to the effect of THC on the hypothalamus gland in the brain which programs the release of hormones from the pituitary gland.

The use of marijuana before conception and during pregnancy has been associated with a high incidence of fetal

oxic effect and neonatal deaths.

Infants born to marijuana-smoking mothers had a reduced birth weight (by one pound) and a smaller head circumference.

There is a subtle difference in their behavior - they seem less attentive in playing and less loving and caring to people.

Dr. Gabriel Nahas states: "These findings indicate that the pot smoker may not only be damaging his own mind and body, but may be playing genetic roulette with his or her unborn children. It is most urgent that we learn to what extent frequent use of marijuana will impair the genetic equilibrium of a person's sex cells. The hereditary fate of future generations may rest upon this research."

Dr. Carlton Turner states: "There is no other drug like marijuana, used or abused by man, that has the staying power and broad cellular actions on the body."

What can be more harmful than interference with the life processes?

What are we doing to future generations?

Is self-pleasure worth the possible harm that can be done to our children yet to be born?

CANNABINOIDS AS POSSIBLE THERAPEUTIC AGENTS

Research areas where individual cannabinoids are being studied are:

a) Reduction of nausea associated with chemotherapy treatments. (There are other medications that do the same thing with no harmful side effects and do not lower the immune system.)

b) Reduction of intraocular pressure associated with glaucoma. (There are at least five other medications that work well without harmful side effects. Refer to Committees of Correspondence Newsletter #6.)

REPORTING RESEARCH FINDINGS

Drug educators, practicing physicians and the media have a major obligation to translate the marijuana research literature into a form readily understandable and correct to the general public.

ONE THING MUST BE UNDERSTOOD —

Marijuana is **NOT** THC . . . and THC is **NOT** marijuana

The media often uses the word marijuana when they should use the word THC and vice versa. This is not correct and is misleading.

Incorrect wording gives people the impression that marijuana smoking is a cure for cancer and glaucoma.

CONCLUSION

There are over 8,500 scientific research papers on the health hazards associated with marijuana use. None give it a clean bill of health. (MARIJUANA: AN ANNOTATED BIBLIOGRAPHY), Vol. I, II and 1980 supplement; MacMillan Publishing Company.

It has been proven beyond a shadow of a doubt that marijuana effects **EVERY CELL IN THE BODY.** (MARIJUANA: BIOLOGICAL EFFECTS), Dr. Gabriel Nahas; Pergamon Press

With the information that we have now, why is anyone looking for something good about marijuana? The detrimental effects far outweigh any possible good that might be found.

The usual order of testing products is that they have to be proven safe **before** they are prescribed for use.

Once these basic concepts are understood about marijuana, it should be easy to conclude that there are no redeeming factors in using marijuana.

A MOST SERIOUS PROBLEM - YOU CAN CHANGE IT.

The information on marijuana in all the new family medical guides is outdated and not correct. Write to the authors, point out this fact and ask them to correct the situation.

* * *

A few expressions that are disturbing:

"Recreational use of drugs"...

The word "recreation" means to do something healthy for one's mind and body. -- What is healthy about marijuana?

The terms "soft" or "hard" used to describe a drug. Very often the term "soft" is used to describe marijuana. Anything that is so harmful to the body can not possibly be considered gentle and soft.

* * *

BOOKS TO READ FOR MORE INFORMATION:

Available from Committees of Correspondence prepaid.

BITTER GRASS & POT IN A NUTSHELL
by Dr. Roy Hart ($4.50)

POT SAFARI & MARIJUANA: THE MYTH OF HARMLESSNESS GOES UP IN SMOKE
by Peggy Mann ($6.95 & $1)

THE MARIJUANA CONTROVERSY
by Dr. Carlton Turner ($3)

SENSUAL DRUGS
by Dr. Harden & Helen Jones ($10.95)

KEEP OFF THE GRASS
by Dr. Gabriel Nahas ($4.25)

Mary Jane and the Sex Cells

by Gabriel G. Nahas, M.D., Ph.D.

Seldom in the course of centuries has a plant ever created a controversy as great as has **Cannabis sativa**, better known under the name of marihuana, Indian hemp, or hashish.

Eight centuries ago Moslem scholars from Cairo and Bagdad debated the pros and cons of this magic herb which allows man to dream while still awake. Their discussions had the same alacrity as those of today's American intellectuals. It appears now that this controversy, at least from a medical standpoint, has been partially answered.

One of the greatest uncertainties concerning marihuana, was the lack of evidence of cellular damage related to its use. It was known long ago that marihuana produced marked changes in thinking and behavior. This was brilliantly described by the French physician Moreau, 130 years ago, in his book "Hashish and Mental Illness." He observed that heavy long-term users of marihuana displayed a slowly progressive mental and physical deterioration, but these symptoms were non-specific, vague and had never been directly associated with cellular damage.

Cellular damage from marihuana has now been observed. Long-term marihuana users display an impairment of their cellular controlled immunity. This immunity is a function of T-lymphocytes (white blood cells) which specialize in fighting virus infections and destroying substances foreign to the body, such as cancer cells or tissue transplants.

My colleagues, Dr. J. P. Armand, Dr. N. Suciu-Foca and Dr. A Morishima, of the College of Physicians and Surgeons of Columbia University, and I studied 51 marihuana smokers, 16 to 35 years of age who had smoked an average of 3 joints of marihuana a week for 4 years. (Science Vol. 183, 419-420, 1974) These subjects had used no other drugs, except tobacco and alcoholic beverages.

We sampled blood from the veins of these volunteers and isolated their lymphocytes. The cells were tested with special substances which normally cause them to divide and grow.

The fact that marihuana products are stored in the sex organs, raises the possibility that marihuana might adversely affect the sex cells of men and women.

Such a test, the blast transformation test, measures the strength, or response, of the immunity system of the body.

We compared the immunity response of marihuana smokers with that of control subjects who did not use the weed, but smoked tobacco and drank alcoholic beverages. The immunity response of the marihuana smokers was 40% less than that of the nonsmokers. Furthermore, their immunological response was similar to that of patients with cancer, or kidney transplants (treated with immunosuppressant medicines).

The mechanism of this decrease in the division of lymphocytes was determined in another series of experiments. We were able to show that these lymphocytes from marihuana smokers could not increase the DNA production required for their proper division. DNA (desoxyribonucleic acid) is the basic chemical contained in the core of all cells. It carries the genetic code for heredity.

Similar observations were made on lymphocytes taken from subjects who did not smoke marihuana, but which were exposed in the laboratory to the drug. These cells were incubated in a test tube with very minute amounts of THC (THC is the active ingredient responsible for the effects of marihuana). They presented the same impairment in division and DNA production as those taken from marihuana smokers.

Our results confirmed those of Dr. Stehchver, from the University of Utah Medical School, who observed an increase in chromosome breakage in the lymphocytes of marihuana smokers.

Other scientists have made similar observations on other cells. Dr. Leuchtenberger, from the University of Lausanne, showed that lung cell cultures exposed to marihuana smoke did not grow properly and presented an abnormal DNA production. Dr. Zimmerman, at the University of Toronto, reported that the growth of tetrahymena, a microorganism, was diminished by miniscule amounts of THC which interfered with DNA synthesis.

How is it that the weekly consumption of only 3 to 4 marihuana cigarettes containing 15 to 20 mg. of THC may induce such celluar damage? The answer may lie in the fact that the active ingredients of marihuana, THC, are insoluble in water and are stored in fat tissue. The excretion from the human body of a single dose of marihuana requires more than one week's time. People who smoke marihuana more than once a week will store its by-products in the liver, lungs, brain, spleen, lymphoid tissues and sex organs (testes and ovaries).

The fact that marihuana products are stored in the sex organs, together with the known cellular alterations related to marihuana, raises the possibility that marihuana might adversely affect the sex cells of men and women.

It is most urgent that we learn to what extent frequent use of marihuana will impair the genetic equilibrium of a person's sex cells. The hereditary fate of future generations may rest upon this research.

DID YOU KNOW? Since men constantly produce millions of sperm, the formation of sperm probably returns to normal when pot smoking is stopped, but the effect on women could be lasting. A female is born with about 400,000 eggs. If they are injured, there is no way to repair the damage. It has been proven that THC accumulates in the ovaries as well as other organs.

Gabriel G. Nahas, M.D., Ph.D., who was decorated by the French and British governments for his work in the French underground during World War II, is now Professor of Anesthesiology at Columbia University College of Physicians and Surgeons in New York City.

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Cannabis 1988
Old Drug, New Dangers
The Potency Question

TOD H. MIKURIYA, M.D.* & MICHAEL R. ALDRICH, PH.D.**

The story of the new, allegedly stronger and more dangerous marijuana was rebirthed in January 1986 by the late Sidney Cohen, M.D., Professor of Psychiatry at UCLA: ''. . . material ten or more times potent than the product smoked ten years ago is being used, and the intoxicated state is more intense and lasts longer." In addition, Cohen (1986) asserted that ''the amount of THC [tetrahydrocannabinol] in confiscated street samples averaged 4.1 percent THC during 1984. The sinsemilla varieties were about 7 percent with some samples reaching 14 percent. . . . all marijuana research to date has been done on 1 or 2 percent THC material and we may be underestimating present day smoking practices."

The average potency of marijuana samples seized by the Drug Enforcement Administration (DEA) increased from 0.5 percent THC in 1974 to 3.5 percent in 1985-1986, with sinsemilla (seedless marijuana) at 6.5 to 12 percent, announced Dr. Richard Hawks of NIDA later that year (Kerr 1986: 1). ''Parents who experimented in their youth are not aware that the potency is much higher," added Donald M. Delzer, Chairman of the National Federation of Parents for Drug Free Youth (Kerr 1986: 18).

''Now perceived as a hard drug, marijuana has increased 1,400 percent in potency since 1970," proclaimed the flyer of a national conference on marijuana (Henry Ohlhoff Outpatient Programs 1986). Drug abuse treatment professionals soon elaborated on the outcry. Tennant (1986) asserted that the drug of the 1970's contained one to three percent THC, while that of the 1980's contained five to 15 percent. Furthermore, the brain registers the difference exponentially, so the difference between one percent and 10 percent THC was not nine percent, but more like 900 percent (Garcia 1986: 3). Smith (1987) stated that Cohen ''taught us that marijuana was a lot more dangerous than we originally thought, particularly with the use of more potent preparations by young people." Inaba (1987) added that ''this new, stronger marijuana has a more disruptive effect on brain chemistry and body physiology than we had imagined previously," and mentioned heretofore undescribed side effects among athletes: ''Baseball players who get beaned a lot admit to smoking marijuana. It impairs their ability to follow the ball."

In a column for drug abuse counselors, Meyers (1987) advised ''supportive therapy" for the effects of the ''new" marijuana, which were described as ''depersonalization, disorientation, derealization, changes in perception, and alterations in body image . . . acute brain syndromes with temporary clouding of mental processes . . . a change of time sense---where minutes seem like hours---slowed thinking, and feared perception of brain damage." Schick Shadel Health Services drug abuse treatment clinics (Unsigned 1987) now advertise that ''marijuana has increased THC content from one percent THC in 1975 to six to fourteen percent THC in 1985 due to hybridization techniques. . . .

For those who have become addicted to marijuana, whether it was years ago, or recently, treatment is necessary---even more critical today."

Despite the respectability of these authorities, none of these alarming claims are new, and neither is the potency issue. There are several claims intertwined: (1) that the marijuana available today is much stronger than that available previously, particularly since the early 1970's; (2) that the effects of this so-called new marijuana are different from effects known earlier; and (3) that all previous marijuana research has been done with weak material and is therefore irrelevant. Before leaping on the bandwagon, one should examine the validity of these assertions.

HISTORICAL PERSPECTIVE

Extremely potent marijuana has been described for 150 years by Western scientists and (with the possible exception of the bean-ball syndrome) so have the effects of the new marijuana. There has been a great deal of research on high-potency cannabis in many countries.

In the paper that introduced cannabis to Western medicine, O'Shaughnessy (1839) discussed the widespread social and medical uses of ganja (sinsemilla) in India and noted symptoms of ''delirium which the incautious use of the Hemp preparations often occasions, especially among young men first commencing the practice." Cannabis tinctures soon appeared in Europe and America (Robertson 1847; Savory 1843) and Fitz Hugh Ludlow (1857) described florid psychedelic trips after their oral ingestion, including all the symptoms mentioned by Meyers (1987). The Ohio State Medical Society (McMeens 1860) reviewed some 15 years of clinical experience with the drug and acknowledged

the intense but physiologically benign mental effects caused by high doses or idiosyncratic sensitivity.

Wood (1869) reported the subjective effects of a tincture made from North American marijuana, experiencing a distortion in time sense, convulsions and memory loss, but no adverse aftereffects. He reported considerable success with it in the treatment of severe neuralgia. However, 15 years later Wood and Smith (1884) commented on the variable potency of cannabis and outlined appropriate treatment for overdoses in medical practice.

Early investigators (McMeens 1860; Bell 1857) attributed this variability to ''defective pharmaceutic processes" employed in foreign countries, and recommended that extracts prepared at home would be preferable. However, extreme variations in locally manufactured preparations were soon recognized in the Dispensatory of the United States (Wood & Bache 1868: 379-382). A practical bioassay technique was gradually perfected starting from the systematic observations of Hare (1887), followed by Evans (1894) and Marshall (1898), to compensate for batch-to-batch potency variations.

Pragmatically, the solution to the overdose/potency problem in both the United States (Wood & Bache 1868: 382) and England was to titrate the dose. In London, a patient who signed a letter to the editors of Lancet, W.W. (1890) reported a typical case: W.W. had inadvertently been given an overdose of cannabis for treatment of neuralgia by his doctor and had suffered perceptual distortion, agitation, mood swings, and fear of death. Sir J. Russell Reynolds, M.D., F.R.S., physician to Queen Victoria's household, responded with a recommendation based on 30 years of experience with the drug (Reynolds 1890), stating ''that Indian hemp, when pure and

administered carefully, is one of the most valuable medicines we possess. . . . a minimum dose should be given to begin with, and . . . the dose should be very gradually and cautiously increased."

During the nineteenth century, social and scientific research on marijuana, as well as tinctures, were conducted with much stronger material than is available on the illicit market today. For example, the Indian Hemp Drugs Commission of 1893-1894 investigated the social, religious and medical uses of bhang (marijuana), ganja (sinsemilla) and charas (hashish). The potencies of varieties from different parts of the subcontinent were evaluated by government chemists and botanists (Evans 1894; Hooper 1894), using the ''acknowledged superiority" of Bengal ganja as the standard. The Commission found that the moderate use of even highly potent marijuana caused no significant physical, mental or moral damage (Kaplan 1969; Mikuriya 1968).

In the 1890's, at the peak of medical interest in the drug, British chemists (Wood, Spivey & Easterfield 1899) isolated an impure active principle, cannabinol, using a ''red oil" distilled from Indian cannabis as a starting point, which was considered to be the active ingredient until the 1930's (Work, Bergel & Todd 1939; Cahn 1931). In 1909, Marshall demonstrated that oxidation during storage was the primary cause of the drug's variable potency. With this advance the pharmaceutical industry shifted its attention to the production of standard extracts that could be used to assay medicinal compounds (Colson 1920). Because it had long been known that ganja and charas produced the most reliable extracts (Wallich 1883; Robertson 1847), in practical terms this meant the European and American producers had to learn how to grow ganja.

Sinsemilla cultivation by the Indian technique of culling male plants from the fields before female plants could set seeds---the very process to which recent researchers attribute the potency of the new marijuana---was exhaustively described by the British government in India (Kaplan 1969: 59-84; Prain 1893; Kerr 1877). In an effort to promote Bengali ganja, the British Raj imposed an export duty on inferior Bombay ganja at the turn of the century, and pharmacognosists in Europe and the U.S. began learning sinsemilla cultivation (Mair 1900).

Holmes (1900) discussed the potencies of Calcutta and Bombay ganja and recommended that the former be used for pharmaceutical preparations, either by home cultivation of ganja according to the Bengal methods he outlined (Holmes 1902a) or by extracting it immediately in Bengal and shipping it in tightly closed containers (Holmes 1902b). Comparing the potency of cannabis from Uganda, France and India, Holmes (1905) urged that only Indian sinsemilla preparations be admitted to the British Pharmacopoeia.

Likewise, Whinery (1909) and Hooper (1908) described ganja cultivation and manufacture, pointing out that cannabis grown in North America by the Indian methods could be as fully potent as Indian hemp. The National Standard Dispensatory of 1909, which included medicines from the pharmacopoeias of the U.S., Britain and Germany, gave the details of sinsemilla cultivation and featured a drawing of a perfect Calcutta ganja flower top (see Figure 1) as an example to be emulated by Western cultivators (Hare, Caspari & Rusby 1909: 374).

In the U.S., Hamilton and his colleagues (Hamilton 1918; Hamilton 1915; Hamilton, Lescohier & Perkins 1913; Houghton & Hamilton 1908) demonstrated that if care was exercised in cultivating and processing

the plant for extraction, American-grown ganja and its extracts were as reliable as those from India and would not deteriorate significantly if stored properly. Information on cultivation of extremely potent seedless marijuana was thus widely disseminated to Western pharmaceutical producers during the first two decades of the twentieth century.

The U.S. government ignored these sensimilla cultivation techniques at the first federal marijuana farm established in 1904 on the Potomac Flats (where the Pentagon now sits) in Washington, D.C. (Silver 1979: 262-263), and as a result the 10-foot marijuana plants grown there and elsewhere in America proved to be much less potent than good samples of Indian hemp (Eckler & Miller 1912). However, private pharmaceutical firms were more successful. The Eli Lilly and Parke-Davis companies ran a cooperative venture at Parkedale (Parke-Davis's farm near Rochester, Michigan) from 1913 until 1938 to develop cannabis extracts for medical use, at first from Cannabis indica, but later standardized on a highly potent strain they developed that they called Cannabis Americana (Wheeler 1968). Pharmaceutical companies were marketing cannabis extracts that were uniformly effective at 10 mg dose levels (Parke-Davis & Company 1930: 82) 11 years before its official removal from medicinal availability.

In 1941, cannabis was removed from the United States Pharmacopoeia (USP) at the behest of the Federal Bureau of Narcotics, which suddenly claimed that marijuana had no medical uses (Mikuriya 1973: xx). Yet even the removal of cannabis from the USP did not end scientific and social research on highly potent forms of cannabis, ranging from the red-dirt marijuana of the Midwest to the red oil of the laboratories. Adams, Pease and Clark (1940) described improved procedures for preparing purified red oil from Minnesota wild hemp,

and comparison of the potencies of Minnesota marijuana and red oil was of significant interest to Loewe, pharmacological director of the LaGuardia Committee (Mayor's Committee on Marihuana 1944: 186ff). Red oil concentrates were used along with marijuana in the LaGuardia Committee's experiments on prisoners, under Loewe's personal direction (Mayor's Committee on Marihuana 1944: 32); for a subjective account see Mezzrow and Wolfe (1946: 317ff). In the 1940's, Adams and Loewe in the U.S. and Todd in England isolated other cannabinoids, including THC, which Adams (1940) postulated as the active principle.

Such isolates were the mainstay of marijuana research during the 1940's and 1950's. A potent marijuana oil created as a truth drug for interrogation purposes by the Office of Strategic Services during World War II (Lee & Shlain 1985: 3-5) was the forerunner of later clandestine experiments conducted by the CIA and the Department of Defense at the Edgewood Arsenal in Maryland from the 1950's to the 1970's (Mikuriya 1973: xxii). Experiments with the designer drug synhexyl, a potent analog of delta3-THC, were conducted from the 1940's (Adams et al. 1941) until the mid-1970's (Lemberger 1976; Pars & Razdan 1976), but were abandoned before its potential was fully explored.

In the 1960's, the identification of pure delta9-THC as the active principle in cannabis (Gaoni & Mechoulam 1964) made it possible to assay the relative potencies of cannabinoids directly in human subjects (Isbell et al. 1967). Although Weil, Zinberg and Nelsen (1968) demonstrated the safety of human marijuana research, much of the U.S. research of the 1970's was conducted with low-potency marijuana because the government would not approve human research with

high-potency strains. Indeed, in one early study (Jones & Stone 1970), a THC concentrate was removed from Mexican marijuana and then redistributed back into the bulk marijuana to return its potency to 0.9 percent THC. Outside the U.S., these strictures did not apply: The fact that cannabidiol interferes with the effects of delta9-THC was discovered in Brazil, using both purified cannabinoids on humans (Karniol et al. 1974).

The 1960's and 1970's saw a worldwide flowering of cannabis research, including its social, psychological, chemical, botanical and legal aspects as well as covering an enormous range of potencies and dosages. Major botanical work involved potency questions: observing phenotypes at the University of Mississippi (Fetterman et al. 1971) and in Canada (Small 1979); establishing a lectotype for Cannabis sativa L. (Stearn 1974); distinguishing C. sativa from C. indica and C. ruderalis (Schultes et al. 1974); and cultivation techniques for increased THC production (Clarke 1981; Frank & Rosenthal 1978).

Thus the claim by Cohen (1986) that "all marijuana research to date has been done on 1 or 2 percent THC material" is not accurate for the 1970's or for any other decade going back to 1839. It ignores much of the laboratory research in the U.S. that was summarized by Cohen himself (Cohen & Stillman 1976), Hollister (1986) and the National Academy of Sciences (1982), and all of the social research on high-potency marijuana in Jamaica (Rubin & Comitas 1975; Bowman & Pihl 1973), Costa Rica (Carter & Doughty 1976), Greece (Fink et al. 1976) and Africa (DuToit 1980). It is difficult to think of any country in which the claim is true.

RECENT ESTIMATES OF POTENCY

Since the advent of quantitative analysis technology, there has been sporadic reportage of the percentage of delta9-THC and other cannabinoids in natural and semisynthetic cannabis products. Notwithstanding the psychophysical effects of other cannabinoids, the amount of THC present in a marijuana sample is believed to determine the drug's potency (National Commission on Marihuana and Drug Abuse 1972: 50), and potency is usually expressed in percent THC by weight. The results of quantitative analyses performed on street samples of marijuana have been published since the late 1960's. These results are generally higher than the alleged 0.5 percent THC content of marijuana cited for the early 1970's.

Lerner and Zeffert (1968) described the development of quantitative analysis for the determination of THC content, and noted much variation among samples of marijuana, hashish, and red oil (still being used experimentally in the 1960's). The THC content of confiscated Mexican marijuana was 0.8 to 1.4 percent, hashish averaged eight percent and red oil 31 percent in 1968.

Quantitative analyses of street samples of marijuana and hashish conducted by Canadian laboratories in 1971 for the Commission of Inquiry into the Non-Medical Use of Drugs (1972: 28-29) showed a range of 0.02 to 3.46 percent THC (median=0.93%) for marijuana, with hashish ranging from 1.0 to 14.3 percent THC (median=4.82%). Samples seized in police raids were less potent: marijuana was 0.05 to 1.65 percent THC (median=0.21%), while hashish was 0.0 to 8.6 percent THC (median=1.3%). The reported difference between confiscated police seizures and street samples submitted to laboratories for analysis may be due to the voluntary samples being submitted precisely because of their extraordinary potency, or that storage conditions in police evidence lockers are hardly optimal for potency stability.

This has a bearing on the potency question because the low potency cited by both Cohen (1986) and Hawks (see Kerr 1986) referred to samples confiscated by the DEA. It has been known since the early days of its isolation (Wollner et al. 1942) that THC oxidizes to cannabinol rapidly in samples stored at room temperature (24oC). Lerner (1963) reported that the concentration of THC in marijuana decreased at a rate of three to five percent under normal room conditions, and Razdan (1970) reported a rate of 10 percent per month. The influence of temperature, light and age on potency was addressed by Starks (1977: 13-15). The low-baseline percentage of THC reported for the early 1970's may be due to this deterioration in confiscated, stored samples. In any case, the low baseline makes the difference in the THC content of later-reported samples appear much greater than it may have been in actuality, assuming that the marijuana smoked by consumers was fresher than stored police seizures.

For a short while in the early 1970's, PharmChem Laboratories in Palo Alto, California, tested and reported the percent of the THC content in anonymously submitted marijuana samples. For 1973, PharmChem reported an average THC content of 1.62 percent in marijuana, compared with hashish at 4.6 percent and hash oil (a refined extract of hashish) at 13.5 percent (Ratcliffe 1974).

In 1974, the DEA published guidelines that no longer allowed laboratories to provide quantitative results directly to the sample donors. This, in effect, restricted public access to analysis information to whatever government officials wished to reveal. However, nonspecific summaries of THC percentage ranges were allowed to be published (Unsigned 1974).

The results of an independent examination of gas-liquid chromatographs of street samples of marijuana from California that

were submitted to PharmChem during 1973 and 1974 are shown in Table I.
Seeded varieties ranged in THC from an average of 2.2 percent (Mexican) to 4.9 percent (Panama Red), while sinsemilla averaged 2.8
percent for Big Sur ''Holy Weed" to above six percent for Thai Sticks
and Hawaiian ''Maui Wowie." This would appear to be a much more
representative sample of the types of marijuana available in California in 1973-1974 than the half-percent grade cited by Cohen
(1986) and Hawks (see Kerr 1986), or the one to three percent grade
cited by Tennant (1986).

A retrospective summary of street-drug analysis trends from 1969
through 1975 published by PharmChem (Perry 1977) confirms the fact
that quite potent forms of cannabis were available on the illicit U.S.
market by 1975: ''Early quantitative work showed a range of 1.0-2.5
percent THC for average marijuana. In 1975, the range was 1.0-2.5
percent; samples in the range of 5.0-10.0 percent were not uncommon,
and some contained as much as 14.0 percent THC. . . . Hash oil
(concentrated from hash, usually amber or red in color) and grass oil
(from marijuana, dark green or black in color) . . . vary greatly in
potency, some samples [containing] up to 40 percent THC." Abundant
information on the comparative potencies of cannabis grown in the U.S.
and other countries in the mid-1970's was summarized by Starks (1977:
41-87).

In the spring of another election year, 1980, Cohen and DuPont
launched a similar campaign, stating that confiscated marijuana in
1975 contained only 0.4 percent THC, while in 1979 the average was
four percent, a 10-fold increase (Brody 1980: C1). This data conflicts
directly with that published by PharmChem for 1975 street samples
(Perry 1977) and that shown in Table I. Perhaps one should be thankful

that, according to these estimates, marijuana potency dropped from four percent THC in 1979 to 3.5 percent THC in 1986 (Kerr 1986).

The most recent comparison of cannabis potencies was compiled from published sources from 1972 through 1981 by the National Academy of Sciences (1982: 16), and is summarized in Table II. It again demonstrates the great range of products available legally (i.e., NIDA samples) and illegally during that decade, and may in fact underestimate some potencies. For example, the 2.8 percent THC content cited for Jamaican ganja (Marshman, Popham & Yawney 1976) is slightly lower than the mean 2.96 percent THC material studied by Rubin and Comitas in 1970 through 1972 (Unsigned 1973), and significantly lower than the four to eight percent THC Jamaican ganja cited by the National Commission on Marihuana and Drug Abuse (1972: 50).

The government ''research harvests" in Table II (Rosenkrantz 1981) are considerably less potent than the sinsemilla samples that averaged three to 11 percent THC (Turner 1981, 1980). Perhaps this is because cultivators at the government marijuana farm at the University of Mississippi, like their predecessors in 1904, never learned proper sinsemilla cultivation (Turner et al. 1979), while illicit cultivators in California and Hawaii were making it standard for the industry (Frank & Rosenthal 1978: 258-259). If so, this alone could explain the wide discrepancies between the potency of marijuana reported by government sources and that actually being grown in the U.S. during the 1970's and 1980's.

SELF-ADJUSTMENT OF DOSE

An important consideration in regard to the potency issue is autotitration, the adjustment of dose by the individual user to obtain

optimal effects and avoid unpleasant ones. As noted above, cautious titration of dose was standard practice when cannabis preparations were used in medicine. Smoking marijuana, customary in present social use of the drug, requires knowledge of when to stop in order to avoid symptoms of overdose. The smoked route gives rapid feedback to the user with regard to levels of effect because the drug goes directly to the brain from the lungs, unimpeded by the gut or the liver.

Researchers for the Mayor's Committee on Marihuana (1944: 13) were among the first to notice that experienced marijuana smokers in the ''tea-pads" of Harlem routinely practiced autotitration. The confirmed user, they noted, ''appears to be quite conscious of the quantity he requires to reach the effect called 'high.' Once the desired effect is obtained he cannot be persuaded to consume more. He knows when he has had enough . . . and is ever-conscious of preventing himself from becoming 'too high.'" Similarly the Commission of Inquiry into the Non-Medical Use of Drugs (1972: 48) observed that ''great variations in potency are usually accommodated by the experienced user through a 'titration' of dose (intake is reduced or stopped when the smoker reaches the preferred level of intoxication)." For U.S. users, the National Commission on Marihuana and Drug Abuse (1972: 166) commented: ''. . . whatever the potency of the drug used, individuals tend to smoke only the amount necessary to achieve the desired effect."

SUMMARY AND CONCLUSIONS

Observation of the real world of social marijuana use, where autotitration is the norm, renders the scare tactics of the new marijuana proponents not only inaccurate but irrelevant. There is much

published evidence about the availability of highly potent varieties of cannabis from the nineteenth century through the present day. The effects attributed to the new marijuana are the same ones debated for centuries in many different cultures. The assertion that ''all marijuana research to date has been done on 1 or 2 percent THC material" (Cohen 1968) ignores several thousand years of human experience with the drug. The old medical cannabis extracts were stronger than most of the forms now available, though the potency of illicit hash oils by the mid-1970's was approaching the level of medicinal preparations available before their removal from the USP.

While it may be true that sinsemilla is more widely available than 10 or 15 years ago, its potency has not changed significantly from the 2.4 to 9.5 percent THC materials available in 1973-1974 (see Table I), or the five to 14 percent sinsemilla of 1975 (Perry 1977). The range of potencies available then (marijuana at 0.1% to 7.8% THC, averaging 2.0% to 5.0% THC by 1975) was approximately the same as that reported now. With such a range, the evidence simply cannot support the argument by Cohen (1986) that marijuana is ''ten or more times more potent than the product smoked ten years ago." And to say that marijuana potency has increased 1,400 percent since any date in history is patent nonsense.

It is not legitimate to imply that average low potencies represent the full range of potencies available in reality. Neither is it valid to cite the low end of the range then as a baseline to compare with the high end of the range now. The claimed baseline for THC content in the early 1970's would appear to be too low, probably because confiscated, stored police samples were utilized; and this low

baseline makes the claimed difference in potency appear to be greater
than it has been in reality.

In sum, the new marijuana is not new and neither is the hyperbole
surrounding this issue. The implications of the new disinformation
campaign are serious. Many people, particularly the experienced users
of the 1960's and their children, will once again shrug off the
warnings of drug experts and not heed more reasonable admonishments
about more dangerous drugs. This is not only abusive to those who look
to science, the medical profession, and government for intelligent
leadership, but will sully the reputations of drug educators who
wittingly cry wolf, and will inevitably diminish the credibility of
drug abuse treatment professionals who pass on such flawed reports.

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\F0\cCOMPREHENSIVE RATIONAL
\cDRUG ABUSE CONTROL
\c- A PROPOSAL\f1

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\f0Summary\f1

A compelling need exists for a COMPREHENSIVE, rational, realistic, and equitable change in laws pertaining to psychoactive substances in order to achieve any substantive control. The current crazy-quilt of traditions and selective contradictory application of laws are based upon denial, hypocrisy, and competing special interest groups' priorities and needs, which harm society in general. The specific proposals for reform are:

1. Remove exemptions from product liability laws for alcohol and tobacco products.

2. Share liability for medical and casualty losses from alcohol and tobacco products.

3. Repeal all "sin" or excise taxes that cause inherent conflicts of interest within the government.

4. End price supports for tobacco and deregulate tobacco farming.

5. Set up drug users cooperatives run by consumers, medical societies, and pharmacies.

6. Legalize marijuana with free cultivation for personal use by adults.

7. No testing of body fluids, brain waves or muscle movement patterns without probable cause or due process guarantees. Those ordering the test subject to drug testing themselves.

\f0Introduction

\f1Despite continuing valiant efforts by enforcement and corrections sectors, a growing awareness exists that the government's war on drugs is being lost. Control by criminalization as a social policy has failed, and casualties of secondary crime only evidence surface manifestations of the harm to society. A massive and uncontrolled underground economy is fueled by a market of eager consumers in whom a powerful pharmacologic reflex has been carefully cultivated by advertising from an early age.

Outspent and outmaneuvered by organized and entrepreneurial criminal elements, the least competent overpopulate jails, prisons, court dockets, and probation case loads. Resources are diverted from protecting the public from other serious crime.

Alcohol and Tobacco

\f0Tobacco\f1

The Southeastern colonies' economy was founded upon and still depends greatly upon tobacco. Principal American founders ran large plantations that cultivated the drug. North America was (and still is) the largest grower and producer of smoked addictive psychoactive substances for ourselves and the world. Well-financed, powerful political forces effectively represent the tobacco industry and successfully resist efforts to curb print advertising and other marketing efforts inducing people to take on a tobacco habit.

Local, state, and federal governments are hopelessly addicted to revenues from tobacco excise or sin taxes that, in addition to supporting the revenue collectors, contribute to general fund revenues.

\f0Alcohol\f1

The famed repressiveness of the puritans did not extend to the alcohol use. The colonial days were awash with fermented and distilled spirits. (Beer,

ale, stout, and naturally fermented wine with less than 12 percent alcohol vs. rum, whiskey, brandy, vodka or gin with over 40 percent.) Rum punches, toddies, and ciders were consumed starting in the morning as "eye openers" for men, women, and children. That good old time religion meant getting together with your neighbors to share rum punch and enthusiastic exhortations against Satan.

The Temperance movement grew from reactions to the excesses in 19th century England, where ubiquitous London gin shops guaranteed "Drunk for one pence, dead drunk for two with straw to sleep on." Both were imported into Colonial America. Temperance discouraged intemperate use of distilled spirits and favored the moderate use of fermented spirits.

With the industrial revolution in the first half of the 1800's, the incompatibility of widespread daily intoxication and drunkenness with efficient factory operations was recognized.

\f0America Polarizes;
A War Against Alcohol is Won and Lost\f0
The Temperance Movement Becomes the Prohibitionist Party

\f1In 1869 the Temperance movement hardened into the Prohibitionist movement, which demanded total alcoholic abstinence. Zealotry flourished. The Drys overcame the Wets state by state over the next fifty years. In 1919 the Prohibitionist party and their sympathizers finally realized their divinely inspired moralistic goal of the national prohibition of alcohol.

Even the most virulent anti-drug extremist admits that prohibition failed disastrously. It established and capitalized organized antiestablishment crime, whose ranks were filled by recently immigrated minorities. Public confidence in law enforcement was shaken by widespread graft and corruption. The grand American social experiment of legislated morality ended after 14

years in the depths of the great Depression as part of a general repudiation of the previous administration's policies.

The pendulum has swung the other way. Emboldened by a privileged freedom, the alcohol industry aggressively hawks its wares, appealing to insecurity and needs for social acceptance. Enmeshed in a symbiotic relationship with government hopelessly dependent upon excise revenues and political contributions, the alcoholic beverage industry controls the government rather than vice-versa. A form of attitudinal blackmail still remains from the colonial days: Men who cannot handle their liquor are still regarded as weak or suspect as to their manliness. Legislatures and other representative bodies are still governed by this pathologic pharmacologic machismo. Alcohol excise or sin taxes are regarded as the least unacceptable to levies of guilt tithes for the users and producers.

\f0Fiscal Institutionalized Denial:
\f0Alcoholism Treatment Programs: Last to be Funded and First to be Cut.

\f1While billions of excise and sales taxes collected from users invariably find their way into the general fund, monies for the treatment of alcoholism and related illnesses remain the lowest priority at all levels of government. In times of financial crisis, these services are the first to go. The compartmentalization and disjointedness of public opinion and the resultant public policy is nowhere more evident.

It would be appropriate to study the comparative public revenues from sales with expenditures for treatment of alcohol and tobacco related diseases, trauma, and property costs. My global impression is that the costs far outstrip the revenues. It would be useful to develop a social policy that

minimizes overall costs to society. The earmarking of excise and sales revenues to pay these costs would improve levels of awareness of the connection of these drugs' use with the adverse consequences of abuse. Sadly, institutions continue to reflect a fragmented, flawed, and fictionalized perception of reality preventing meaningful solutions to substantial self-imposed biosocial problems.

\f0Shared Liability:
Partial Remedy for Alcohol and Tobacco Abuse
\f1

A precedent for drug liability was set by the 1964 settlement of the thalidomide case. The manufacturer of this minor tranquilizer paid huge sums of money for birth defects caused by mothers taking the drug in the first pregnancy trimester. But how is it that the manufacturers of alcohol and tobacco, whose effects are far more toxic and much more widely used, have been able to evade responsibility for the well-known adverse effects? The endemic and blatant denial that alcohol and tobacco are indeed drugs. While medicine and science regard these psychoactive substances as drugs, the body of common usage expressed in the laws defines alcohol and tobacco as things other than drugs. The same patterns of denial seen in individual abusers of these substances is recapitulated collectively in public opinion and articulated through institutions, customs, and laws.

This flawed collective perception distorts resulting public policy, causing it to resemble "Through the Looking Glass" rather than a logical, thoughtful product of an enlightened society dedicated to decency and reason. How else can one rationalize attempting to discourage smoking while subsidizing the growth of tobacco?

The proposed salient change is based on the premise that alcohol and tobacco are dangerous drugs. Groups profiting from producing, processing, and

trafficking should bear partial responsibility for adverse reactions through failure to adequately inform the user. Users, however, bear ultimate responsibility for the invocation of adverse or untoward reactions from alcohol and tobacco. Government programs are largely ineffectual or often worsen drug problems.

\f0I. Repeal Product Liability Exemptions for Alcohol and Tobacco\f0 With Temporary Shared Liability for Restitution
\f1

In order to end generations of victimization by these industries that continue to evade their share of social responsibility and prey on human frailty, fairness calls for a period of restitution to equalize liability. Because of a history of deceptive advertising that has systematically omitted cautionaries or warnings about adverse effects, it would not be unfair for them to bear the responsibilities for a share of the medical and casualty losses caused by their products...say 49 percent through an industry assigned risk pool. The individual should still be liable for the majority of the responsibility for his or her conduct and pay 51 percent of the medical and casualty costs.

\f0"Sunset" Period of Industry Restitution\f1

The restitution period should continue for a length of time required to attain a public truly informed of the use of these drugs - perhaps for an equal number of years from the implementation of this policy going back to date of prohibition's repeal.

\f0Self-restraint in Advertising.\f1

Resulting advertising practices would become appropriately cautious and prudent since corporate counsel would carefully screen advertising campaigns to minimize liability exposure.

\f0II. Abolish Excise or "Sin" Taxes\f1

Sumptuary or excise taxes constitute a breach of the separation between church and state. Separation is violated by the extraction of a payment for using a disapproved substance. Detoxification from dependence on revenues derived from excise taxes would remedy an inherent governmental conflict of interests.

\f0III. Illicit Drug Control

Historical\f1

The passage of the Harrison Narcotics act of 1914 nationally defined drug dependence problems as MORAL DEFECT that call for retribution or deterrence; not mental or physical diseases that require medical intervention. Since then, police, courts, and prisons have been utilized in attempts to prevent nonmedical drug use with retributive methods. Despite vigorous and continuing efforts at great expense over the years to enforce these laws, there has been minimal impact on illicit drug trafficking. Noxious side-effects of this criminalization include increased primary and secondary crime motivated by high illicit profit margins, diversion of police services corruption, crowded prisons, and more red tape for the health professions. Ineffectual, self-serving, expensive government agencies rationalize their continuing existence as they claim to protect us from the drug abuse menace.

Most recently, the dramatic escalation of the use of urine drug screens to ever widening populations in the workplace and on the highway afford the use of police and administrative penalties. WRONGDRUG has become the moral jihad of the decade. Despite protestations of medical interventions, and lip service to the disease of drug abuse, the overbearing presence and use of the enforcement/corrections resources prevails. Fueled by martial rhetoric the War Against Drugs inflames the passions of middle America to ferret out the sources of "trouble in River City".

Assisted by the defacto assumption that this is proper behavior for public and workplace authority, growing numbers of citizens face random urine testing by reason of circumstance, not probable cause. Vulnerability to this intrusion is not equal, but a function of status.

\f0Semantic Abuse\f1

The term "controlled substances" is a euphemism like "intelligence" as in CIA or "security" as in weapons for a foreign country. Illicit drug traffickers continue to operate beyond society's control. These drugs should more properly be called \f2uncontrolled substances. \f1Unconstrained by budget, protocol, or interagency bickering only the least competent or unlucky illicit traffickers get caught, leaving the rest to enjoy untaxed profit margins at least ten times that of the same drugs sold through legitimate channels.

The following scheme would effectively eviscerate the illicit market by making the drugs available to the public on a non-prescriptive, medically controlled basis. By definition, a smaller population of drug criminals thus created would be much more effectively and economically targeted by enforcement agencies. Drugs would come in off the streets back into the pharmacies where they belong.

More importantly, currently illicit drugs would cease to have the appeal of "forbidden fruit", losing the allure of life in the fast lane and an oppositional way of defining adolescent independence. The demographic alteration would revert to an older population like those in the pre-criminalization before 1914, with the motive of palliating disease and discomfort rather than anger and thrills.

\f0 Voluntary Drug Users Cooperative\f1

The demonstration project proposes a voluntary, non-prescription controlled substances dispensing program supported by its consumers and supervised by the local medical society, pharmacy society, users, and the public.

All revenues derived from transactions are earmarked for support of program which include:

1. Dispensing
2. Administration
3. User Education
4. Treatment of Adverse Reactions
5. User Health Survey
6. Research

\f0Method\f1

Users would be eligible to enter the program at the age of majority and would be required to:

1. Undergo screening medical tests.
2. Demonstrate informed consent by passing written tests on:
   a. Mental and physical effects of specific drugs.
   b. Program rules and procedure.
   c. Personal responsibilities and liability.
3. Sign an agreement to abide by the program terms.

\f0Administrative\f1

To avoid user exploitation and provide competent guidance, the county medical society, county pharmacy society, and consumers would constitute the board of directors for this non-profit organization. It supervises a credit card type invoicing system to dispense drugs through co-operating pharmacies. This "Drug Control Agency" responds to cases of misuse (e.g. admission to hospital or emergency room visit for overdose, public intoxication, complaint of spouse, etc.) by referral to public and private community health resources or enforcement/corrections agencies, as warranted by the nature of the infraction. DCA also provides user health advisories

and updates new user test questions and education manuals. DCA coordinates
voluntary periodic health surveys and participates in research.

\f0Dispensing\f1

Controlled substances will be dispensed utilizing an embossed identification
card presented to the participating pharmacy. The pharmacy imprints a
special multi-part form sent to the bank as with ordinary VISA or MasterCard
transactions. The participating banks submit monthly drug statements
dispensed to the DCA office with accounts flagged that show unusual activity
(significant increase in number of transactions or size of order).

The DCA office first contacts the user by mail and requests him/her to
contact a designated drug abuse specialist to attempt to resolve exceptional
drug use patterns or drug related problem. If the incident is either
unresolvable or of a serious nature, such as driving under the influence or
furnishing drugs to anyone else, the case is turned over to the Department
of Motor Vehicles or the District Attorney's office.

If the user fails to respond to the mailed notice, his or her identification
card number is placed on a list of suspended users. The pharmacy informs the
user at the next transaction that dispensing the requested drugs must be in
exchange for surrendering and destroying the identification card or the
drugs are denied and the user is told to contact the drug abuse specialist.

Users may be put on probationary status or temporarily or permanently
suspended from the program. Entry dose level would be determined at final
intake interview by a drug abuse specialist and depend upon the
participant's drug history. If no data is available then a therapeutic dose
is given based upon weight or body surface area. This entry dose level then

becomes the standard against which exceptional or unusual drug use activity is defined.

\f0Financing\f1

The program would be self-supporting through fees collected from the users' transactions at a rate agreed upon by the board of directors, meeting the costs of the program providers at a reasonable consumer price. Costs would be contained by utilizing existing community facilities and proven bank and pharmaceutical transaction recordskeeping methods.

\f0. Marijuana - Legalize Growth and Use by Adults for Personal Use. Commercially Produced and Subject to Drug Product Liability Laws \f1

Current efforts to suppress cannabis cultivation or trafficking have not only failed but adversely affect enforcement, court, and corrections resources by adding to their overload. Still, marijuana crime provides a source of temptation for selective enforcement and corruption. Cannabis prohibition has created a giant underground economy with grossly inflated user costs not subject to taxation or regulation for consumer protection. Cannabis sold in crude or purified form should conform to standards and definitions in pharmaceutical preparation methods used prior to the removal of cannabis from the U.S. Pharmacopeia in 1941.

Recent efforts by the Drug Enforcement Agency to use Paraquat and other toxic herbicides to eradicate cannabis show gross irrational recklessness. Poisoning users in order to protect them from using the weed is a most dangerous and unconscionable intervention by government.

Attempting to utilize the deterrent value of having the word sent out that the cannabis crops are being poisoned, espoused by proponents within the enforcement community, harms the public since they rely on the cooperation

of the public for their effectiveness. A policy of disinformation would diminish trust for these public institutions through damaged credibility with consequent adverse effects on the delivery of enforcement services.

\f0No testing of body fluids, brain waves or muscle electrical activity without probable cause and due process.\f1

Recent technological advances have made it possible to detect the presence of most psychoactive substances with varying degrees of reliability. While it is undoubtably desirable to protect the public safety and health from impaired intoxicated behavior, safeguards must be guaranteed lest the abuses resulting from misapplication outweigh the benefits.

The drug testing industry has been notably seclusive about sources of error and observed error rates. Monitoring of laboratories by state and federal health agencies reveal significant levels of inaccuracy over the years. The recent increased levels of testing not only increase the actual numbers of false readings but the rate as well. All specimens must not only be confirmed and verified by other tests, but the sample itself retained indefinitely for possible retrospective analysis.

Recently a device was patented that alleges to identify specific drug intoxication states by monitoring brain waves and eye muscle movements. The Veritas 100 is touted to be a fairer estimate of current mental state rather than measuring drug breakdown products for what was happening hours before. Analytic methods of these complex waveforms have yet to be confirmed and margins of error and artefact remain to be defined.

The requiring of a citizen to undergo drug testing without the showing of compelling need, probable cause, and due process safeguards is far more

insidious and toxic a doctrine than any drug side effect. It poisons the very assumptions of the framers of the constitution of the sanctity and worth of the individual.

The suspension of the fourth amendment of freedom from illegal search and seizure and the fifth amendment protecting against self-incrimination are hardly trivial social costs. The attempts to implement programs that harm the individual will not only fail to deter the undesired behavior but will diminish the mutual respect and trust required for government to govern and degrade the quality of life in general.

THM Berkeley, California 8-7-86

15-year study links marijuana use to schizophrenia

NEW YORK (AP) — A 15-year study of more than 45,000 Swedish soldiers suggests that heavy marijuana users are six times more likely than non-users to develop schizophrenia.

The authors of the study said the statistical association between schizophrenia and marijuana, or cannabis, does not necessarily mean that the drug causes schizophrenia.

"Cannabis consumption might, on the contrary, be caused by an emerging schizophrenia," the researchers said in their report, to be published Thursday in The Lancet, a British medical journal.

American researchers asked about the report were not familiar with it, but Dr. Charles Schulz, chief of pharmacology research for the schizophrenia branch at the National Institute of Mental Health, said the findings did not surprise him.

"Many psychiatric clinicians have noted over the years that a patient's illness starts with marijuana use or overuse," Schulz said.

Marijuana might cause latent schizophrenia to become apparent, he said. Researchers have also noted that the hallucinogenic drug LSD can trigger persistent mental illness, Schulz said.

Furthermore, there is a chemical link that might explain why marijuana and schizophrenia would be related, Schulz said.

Schizophrenia is thought by some to be related to a disorder in the brain's production or use of dopamine, one of the many so-called neurotransmitters that brain cells use to communicate with one another.

In schizophrenics, there is evidence that the dopamine system is hyperactive, Schulz said. And, he said, "there have been basic studies demonstrating that marijuana stimulates the neurotransmitter dopamine."

The Swedish study — conducted by Sven Andreasson of the Karolinska Institute and Ulf Rydberg of Karolinska Hospital in Stockholm and their colleagues — cites numerous previous studies that have found that marijuana aggravates schizophrenia or triggers psychotic episodes.

In the Swedish study, 45,570 soldiers were given questionnaires at the time of their induction into the country's compulsory military service. They were asked about drug use, among other things. They were also given psychiatric evaluations.

Sweden maintains a national registry of psychiatric care provided to its citizens, and that was used to follow the conditions of the soldiers for 15 years.

The researchers found 197 cases of schizophrenia among 41,280 members of the group who reported no marijuana use. In contrast, 21 cases of schizophrenia were found in the 752 soldiers who reported heavy marijuana use.

From those figures, the researchers calculated that the heavy marijuana users had six times as great a risk of schizophrenia as the non-users.

Marijuana robs your body cells of energy

By ROBERT GILKESON, M.D.

No chemical can alter your mood, your feelings, your coordination or your behavior unless it has altered the cells in your brain and disrupted their normal chemical function.

Before using a drug of any kind, one should know what chemicals it contains, which cells in your brain it most affects, and what brain cell chemistry it changes.

The wall -- or the membrane -- that surrounds every cell is composed of fat (lipid) molecules and complex protein molecules. These molecules form an intricate membrane around each cell arranged in patterns specific to each cell type, according to its functions and its specific needs.

All the chemicals providing the ENERGY necessary to keep each cell alive must somehow pass through this membrane into the cell, and the waste products from its metabolism must exit through these membrane molecules back into the circulation.

This constant movement of chemicals in and out of the membrane occurs through submicroscopic channels between the lipid or the protein molecules specifically assigned for them.

MARIJUANA contains 421 bioactive chemical molecules. Sixty-one are called cannabinoids, which are extremely soluble in fat, or lipid, molecules. When inhaled or ingested, these cannabinoids become absorbed by, and remain imbedded in, the lips in the membrane of every cell in the body. Since they are of no chemical use to the cell and are hidden from the water-soluble enzymes outside the cell membrane, the cannabinoids are not broken down, but remain imbedded there for months at a time.

Whenever you smoke marijuana at a rate faster than the cannbinoid molecules can be eliminated, they ACCUMULATE in the membrane, leaving it in a chronic state of saturation. As they accumulate one after the other in the membrane, they increasingly prevent the passage of those chemicals which must enter and leave the cell. Progressively robbed of such nutrients, cells become starved and slowly lose their energy.

AFTER ONE JOINT: 40-50% of the THC remains in the membranes for four to eight days; 10-20% remains for 30-48%; 1% to traces remain in the membranes for 4-6 months.

Saturated membranes may not lose the cannabinoids for nine months or more. Smoking marijuana faster than your cells can eliminate the cannabinoids leads to their saturation of the cell membrane. As they accumulate, cannabinoids interfere more and more with cell's metabolism, decrease its energy and growth, and retard the development of every cellular system. Marijuana is concentrated in lungs, liver, kidneys, adrenal glands, ovaries, testicles, bone marrow and the brain.

The most important, the most specialized, the most complex, and the most fragile cells in the body are the 100 billion cells of the human brain, called NEURONS. These cells make 100 trillion connections or synapses along which chemical messages are passed.

The purpose of these messages is to keep track of all the other cells in the body, to keep them functioning properly, and to keep them alive. Internal messages relate the needs of the cells in the body. External messages tell us everything going on in the "outside world." The brain "reads" these messages, analyzes them, then plans and initiates the correct movements, the glandular secretions, and the other functions to meet those needs.

To pass accurate messages, sodium, potassium, calcium, chlorides and the complex messenger chemcals called neurotransmitters must all go in and out through their membrane channels in the correct amounts, in 0.4-1.0 thousandth of a second.

Because of their chemical complexity, their constant activity, and the speed at which they must operate, substances which block membranes affect neurons more than any other cells in the body.

The center of the brain coordinating the interaction of all the other brain centers and controlling the amount of brain energy is called the Reticular Activating System or the RAS. Since it makes the most connections and is always in operation, it is the most saturated and affected of all the centers. This center controls how alert we are and the level of our "consciousness." When the energy of the RAS is decreased, the energy of the entire cortex is lowered.

This activating system turns ON and increases, or turns OFF and decreases, the chemical messages between areas of the brain that regulate the very level and complexity of human thought and behavior. It regulates the intensity of messages between the centers for memory, the center for feelings, and the center for analyzing all the messages from inside and outside the body. This information in turn triggers necessary motor behavior or glandular activity.

The less energy flowing in the neuronal circuits, the less rich and sensitive our feelings will become and the less clear our imagination, plans and ideas will be.

More simply, the less energy available to run our brains, the more stupid we become.

DR. ROBERT GILKESON is a former teacher and pediatrician and now has a national reputation as a child and adolexcent neuropsychiatrist.

abuse much more often in

MARIJUANA: IT'S A SERIOUS HEALTH PROBLEM.

Marijuana contains over 400 known chemicals, and 61 of those are known as cannabinoids which affect the central nervous system. The primary psychoactive or mind-altering ingredient is called delta-9-tetrahydrocannabinol, or THC. Researchers have clearly shown that marijuana interferes with immediate memory and intellectual performance. And it can impair concentration and reading comprehension. Preliminary research has shown that the extended use of marijuana can produce severe anxiety, apprehension and fear of others.

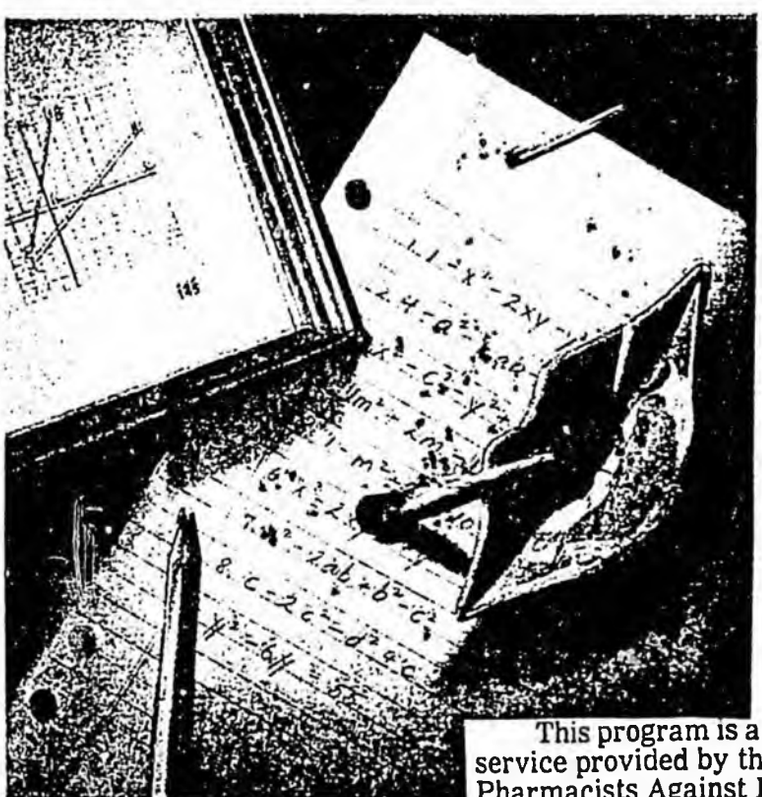
And marijuana not only has an adverse effect on the brain, it also affects the heart and lungs. Further, marijuana has a higher concentration of known cancer-causing agents than tobacco.

Studies have shown that males who use marijuana daily have a lower sperm count than those who don't. And it can reduce the body's production of testosterone – the hormone that makes men, men.

Finally, pregnant women who use marijuana are exposing their unborn children to unnecessary risks.

The source of marijuana ("grass," "pot," "weed") is cannabis sativa, a plant grown all over the world. The crumbled leaves and flowering tops of the plant are usually smoked in hand-rolled cigarettes (called "joints") or in pipes. It can also be eaten (although it takes more to produce the same effect).

Did you know that the National Institute on Drug Abuse has reported that in 1975 the average confiscated sample of marijuana contained 0.4 percent THC; in 1979, the average THC content was about 4 percent – that's 10 times stronger. Thereby increasing the physical and mental effects and the possibility of health problems for the user.



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School of Pharmacy
University, MS 38677
(601) 232-5324

September 14, 1987

Det. John McIntosh
Ketchikan Police Dept.
361 Main St.
Ketchikan, Alaska 99901

Dear Det. McIntosh:

Attached is an analysis report of the marijuana sample #87-3673 you sent to our laboratory on June 19, 1987.

The material has a profile typical of drug-type Cannabis - high Δ^9-THC (4.38) coupled with little or no CBD content. The average Δ^9-THC for whole plant material is approximately 2.5%, well below the THC percentage of this plant.

If you have any questions or if we can be of service to you again, please let me know.

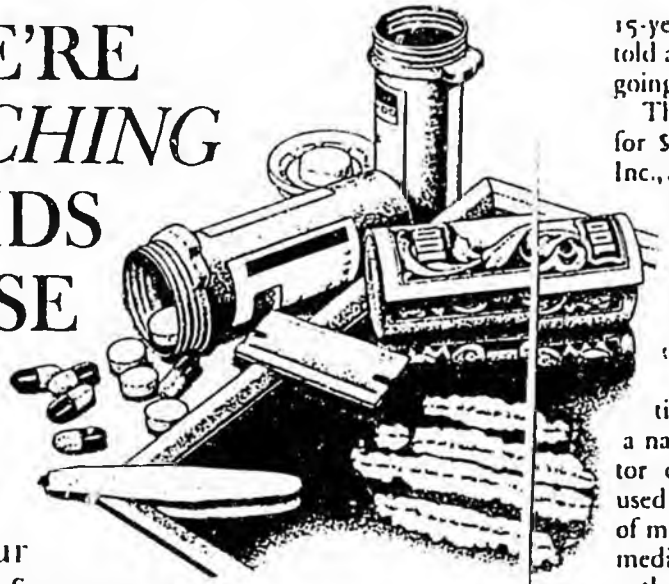
Sincerely

Carol T. Abel
Laboratory Supervisor
NIDA Marijuana Project

CTA/kkl

Enclosure

"WE'RE *TEACHING* OUR KIDS TO USE DRUGS"



The drug-education courses offered in our nation's schools too often carry this incredible message: If you do drugs "responsibly," it's okay. It's *not* okay. And it's time we told our kids the truth

By Peggy Mann

Sophomores in the health class of a Lancaster, Pa., high school were totally absorbed as a smooth-voiced narrator for the filmstrip *Marijuana Update: Its Use and Abuse* extolled the medicinal qualities of the plant, tracing its use back to the Late Stone Age. "Throughout history," he stressed, "man has been a drug user. For at least 5000 years cannabis has supplied one of his favorite intoxicants." Then he described pot's pleasurable effects: "the euphoric feeling of relaxation, contentment, inner satisfaction; the sensations of floating beyond reality."

The 55-minute cassette contained only 105 seconds on pot's possible ill effects, and it claimed that "the role of cannabis in causing them has not yet been confirmed." The final 19 minutes of the film were devoted to promoting legalization of marijuana, echoing the platform of the "pro-pot" National Organization for the Reform of Marijuana Laws (NORML).

"Obviously," said one indignant 15-year-old, "everything I've been told about pot is wrong. Now I *am* going to try it."

This filmstrip currently is sold for $179 by Guidance Associates, Inc., a large and respected producer of audio-visual materials for schools. *Marijuana Update*, released in 1975, has *never* been updated to reflect current knowledge about the dangers of pot.

During a recent presentation to a group of sixth graders, a nationally known health educator declared, "Any drug can be used in a positive manner." Typical of many mis-educators, he lumped medications and illegal drugs together; for example, he listed aspirin on the blackboard as "might be a narcotic or a barbiturate," followed by "angel dust (PCP) is an analgesic" (a pain reliever). Not surprisingly, when he asked "How many of you are drug users?" all the sixth graders raised their hands.

His further instruction included these phrases: "Heroin can be used in a bad way or a good way. It is the person who is misusing the drug—the drug itself is not bad."

National Tragedy. These are not isolated cases. Far *more* isolated are reports of schools that are doing an effective job in the drug-education area. Says Congressman Charles Rangel (D., N.Y.), chairman of the House Select Committee on Narcotics Abuse and Control, "We have a national tragedy on our hands in drug education."

In August 1986, Sen. Paula Hawkins (R., Fla.), then chairman of the Senate Subcommittee on Children, Family, Drugs and Alcoholism, held hearings on the impact of drug education. Hawkins cited the book *Chocolate to Morphine*, published by Houghton Mifflin in 1983 and co-written by Andrew Weil, longtime advisory-board member of NORML. The book's first sentence indicates it is written for teen-agers. But, Hawkins noted, "The publisher says it is also quite popular with school counselors and professionals." She then read from several paragraphs:

"Question your parents about the drugs they use. If you can convince them that your drug use is responsible, you may be able to allay their anxiety. Drugs are fascinating because they can change our awareness. Occasional snorting of cocaine in social situations is probably not harmful."

"With drug use running rampant," Hawkins asked, "why are our children being exposed to such garbage?"

Why, indeed, since the kids themselves are demanding facts. In 1977 and every two years since, the National Gallup Youth Survey has asked youngsters ages 13 through 17 to name "the biggest problem facing people your age." Each year drug abuse has been No. 1. Another eye-opening survey, this one of 500,000 children in grades 4 through 12, was published by *Weekly Reader* last spring. When

asked to circle "the *one* thing you think is most important for schools to do to fight drugs," the top answer was: "Teach us the facts."

Instead, what *are* we teaching kids? Most programs focus on three main messages:

1. "Responsible use." Children are taught they should use drugs "responsibly," the implication being that experimental or occasional use is not harmful. Yet the annual National High School Senior Survey has shown since 1975 that one-third of occasional pot smokers become daily users at some point in their lives, and, of seniors who currently smoke pot at all, about half use one or more additional illegal drugs. (Virtually no non-pot smokers are regular users of any other illegal drug.)

2. "It's your decision." Two decades of societal permissiveness toward drug use are reflected in the conclusion that you must decide for yourself whether or not to use drugs. In what other area do we tell kids that it's *their* decision whether or not to break the law?

3. "Do drugs." Some books and other materials used in schools contain virtual commercials for illegal drugs. For example, the three books on drug abuse most commonly found in school libraries today are *Chocolate to Morphine* and *The Natural Mind,* both by Andrew Weil, and *Licit & Illicit Drugs* by Edward M. Brecher and the editors of Consumer Reports, published by Little, Brown in 1972.

What adventurous youngster would *not* want to try mescaline or LSD, for example, after reading in *Licit & Illicit Drugs* (page 337) that mescaline users have found its "most spectacular phase comprises the kaleidoscopic play of visual hallucinations in indescribably rich colors . . . the 'seeing' of music in colors or the 'hearing' of a painting in music." Page 364 describes a 1960s study finding LSD valuable as "a therapeutic tool, a road to love and better relationships . . . a door to religious experience . . . a release from anxiety or troubles."

"Little Change." Otto Moulton is considered by most leaders of the national parent movement for drug-free youth to be the nation's foremost expert on information generated by the drug culture. He has visited hundreds of schools in over 40 states. In each town or city, he checks school and public libraries, as well as bookstores. "In 1979," he says, "the drug information was almost invariably incorrect, outdated and/or actually promoting drug use. Today little has changed. Some of the bad material has been updated. But most schools are not about to throw out materials they have already paid for, especially when they don't know where reliable material can be found, or, in many cases, *even what it is.*"

In 1987 Beverly Kinard, founder and president of HOPE (Helping Other People Educate), surveyed 100 chain bookstores in cities and towns from San Francisco to Boston. She found only one store with one book containing up-to-date information on drugs. She found *Chocolate to Morphine* in all the bookstores. Several teachers told her that they used the "suggestions" at the end of the marijuana section for class instruction. These include: "Define what benefits you want from pot" and "set limits on usage."

Why Wait? In America today the "Just Say No" message is being heard loud and clear from the White House on down. Even rock groups, those former promoters of the do-drug message, are beginning to clean up their act, as are movies, television and radio.

In October 1986 the President signed into law the Omnibus Anti-Drug Abuse Act, which among other things provided $200 million for fiscal 1987 and $250 million each for fiscal 1988 and '89—all so the Department of Education could help the states rid their schools of drugs. Most of the fiscal year '87 money has been distributed, and much of it is already available at the school-district level.

But what is actually being done? Says William Lennox, director of the Department of Education's Drug Abuse Policy Oversight Staff: "In November 1987 we will set up a committee to make on-site visits to schools in order to develop criteria for

Some Recommended Anti-Drug Materials

- A booklet listing drug prevention resources is available from Committees of Correspondence, Dept. RD, 57 Conant St., Danvers, Mass. 01923. (617) 774-2641. Cost, including postage and handling, is $5.
- Boy Scouts of America offers a four-color, 24-by-36-inch body chart showing how illegal drugs affect body organs. Drug Abuse Task Force, S200, Dept. RD, 1325 Walnut Hill Lane, Irving, Texas 75038-3096. Cost: $5.
- *What Works: Schools Without Drugs* is a 77-page booklet produced by the Department of Education and available free from Schools Without Drugs, Dept. RD, Pueblo, Colo. 81009.
- Just Say No Foundation provides free information on setting up a program in your area: Just Say No Foundation, Dept. RD, 1777 N. California Blvd., Walnut Creek, Calif. 94596. 1-800-258-2766; in Calif., 415-939-6666.
- Medical Education Research Foundation publishes *Marijuana: The Myth of Harmlessness Goes Up in Smoke,* an 8½-by-11-inch illustrated booklet plus teacher's guide. Address: 1100 Waterway Blvd., Dept. RD, Indianapolis, Ind. 46202. Cost: $2.50.
- PRIDE (Parents' Resource Institute on Drug Education) offers an anonymous student survey (already taken by over 850,000 students) on drug-use prevalence. PRIDE's computer compiles the data for school administrators. An excellent tool to galvanize schools and communities. Cost: 56¢ per student. Write for free information: PRIDE, 100 Edgewood Ave., Suite 1002, Dept. RD, Atlanta, Ga. 30303. 1-800-241-7946.

good curricula. We expect to have this guide ready by September 1988."

Why must we wait until September 1988 for new guidelines, which may or may not then be acted upon? Especially since, while we wait, an already appalling situation is growing worse. With millions of dollars available to schools through Department of Education grants, "curricula" entrepreneurs have been flooding the marketplace with bad advice. Notes Carla Lowe, co-founder of Californians For Drug-Free Youth, and a consultant on drug abuse to the State Department: "Many school districts are buying new materials without knowing whether they're good or bad. Accurate information about the harm drugs do is the best weapon we have. But we're shooting ourselves in the foot."

What to Do? Along with the $200 million allocated this year to the Department of Education, the 1986 Omnibus Anti-Drug Abuse Act established the Office of Substance Abuse Prevention (OSAP), with a $41.5-million budget. Part of OSAP is the National Clearinghouse for Alcohol and Drug Information, with its own hefty budget and a mandate to disseminate to schools information on drug-abuse education provided by the Department of Education. Says Section 4144 of the act: "Any materials produced or distributed with funds made available under this subtitle shall reflect the message that illicit drug use is wrong and harmful."

Over a year has passed since the law was enacted. Yet, as Congressman Rangel points out, "the act has received no priority. A list of recommended resources could be compiled in a few weeks by the National Clearinghouse and distributed free of charge to all schools, school departments and boards of education. This would be the simplest, most useful and cost-effective step we could take at once to better the drastic situation of drug education in our schools."

Secretary of Education William J. Bennett has announced a public-service campaign to help "slam the door" on drug use in our schools. To learn more about the campaign, and to ask about the availability of effective anti-drug materials, call the Department of Education's toll-free number, 1-800-541-8787.

Meanwhile, it is urgent that the National Clearinghouse take immediate steps to distribute a comprehensive list of accurate, up-to-date books, films and other materials with a *no-use* message. Such resources exist, and many schools are eager to learn about them. A law mandating that the government disseminate information about these materials has been in place for over a year. Let's not waste any more time in getting this list to schools, teachers and educators all across the nation.

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PSYCHIATRIC ANNALS

The Clinical Syndrome of Marijuana Dependence

By [illegible]

There is little question that the need for clinical treatment of marijuana dependence will escalate. Many persons who have used marijuana for several years are now beginning to realize that they are dependent and will not be able to cease use without medical intervention.

Dependence upon cannabis sativa was initially described in the United States about 40 years ago.[1] In 1944, 35 "confirmed marijuana addicts" were admitted to a military hospital and developed withdrawal symptoms. In the same decade, Fraser in India reported on soldiers who had been ganja smokers for some years and, after joining the army, exhibited severe withdrawal symptoms due to difficulty in obtaining cannabis products.[2] Since these initial reports, a number of studies clearly document that tolerance, dependence, and withdrawal symptoms may occur after chronic administration of cannabis.[1-7] Supporting data comes from clinical observations, animal studies, and a carefully controlled trial where humans were given known quantities of tetrahydrocannabinol (THC) and then observed for tolerance and withdrawal symptoms.[3-7]

Until very recently, cannabis dependence had not been a significant clinical concern in the United States. This is accounted for by two factors. First of all, the form of cannabis usually consumed in America is marijuana, and its THC content throughout the 1970s generally ranged from about 1% to 3%. This contrasts with other countries where the more potent forms of cannabis, including hashish, ganja, and dagga have been traditionally used, and where observation on cannabis withdrawal symptoms have frequently been made.[1] In the decade of the 1980s, however, potent forms of marijuana with a THC content of 5% to 15%, as well as hashish, have emerged as the usual forms for self-administration. This high THC content makes it relatively easy to consume over 180 mg per day, whic. was the daily dose given to human volunteers for 11 to 21 days by Jones and co-workers, and which showed an opioid-like withdrawal syndrome when it was abruptly discontinued under controlled conditions.[7] A second factor that has helped make cannabis dependence an increasingly common clinical entity in the United States is the recent development of low-cost, urine screening technology that can detect marijuana metabolites.[8] Wide-spread urine screening in the workplace, criminal justice system, and clinical settings are now identifying persons dependent upon marijuana. This practice has resulted in routine referrals for treatment in my ambulatory clinics located in West Covina, California (East Los Angeles County). This article reviews pertinent literature and summarizes some of my clinical experiences.

EVIDENCE OF DEPENDENCE

In 1971, Deneau and Kaymakcalan succeeded in producing self-administration of THC in monkeys.[5] When THC was abruptly discontinued,

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TABLE 1
Commonly Observed Cannabis Withdrawal Symptoms*

Insomnia	Anorexia
Nausea	Photophobia
Myalgia	Cannabis craving
Anxiety	Depression
Restlessness	Mental confusion
Irritability	Yawning
Chills	Anergy

* These symptoms have been observed in animal and human studies

the monkeys exhibited a withdrawal syndrome that was not dissimilar to the opioid abstinence syndrome. Other investigators were able to repeat these experiments and make similar observations.[1] Self-administration has also been induced in rats following a forced injection period.[1] In early studies, rats given THC chronically also appeared to develop an opioid-type withdrawal syndrome when THC was abruptly discontinued.[1] These observations were confirmed when, in 1974, Hirschhorn and Roseerans gave naloxone to rats treated with THC for five weeks and precipitated an opioid-like withdrawal syndrome.[3] Kaymakcalan duplicated this study and also found that naloxone produced withdrawal symptoms in THC-treated rats.[4] The most common withdrawal signs observed in both studies were diarrhea, teeth chattering, wet-dog shakes, salivation, ptosis, piloerection, yawning, and increased activity.[1]

After the human observations of withdrawal in the 1940s, there were no reports of cannabis dependence and withdrawal symptoms in humans until the 1970s.[1] In a research project sponsored by the World Health Organization (WHO) in 1976, 50 long term cannabis users in India were compared with 25 non-user controls.[1] It was found that the majority of users (98%) felt uncomfortable if they were unable to obtain their daily supply or dose of cannabis, and in addition to a strong craving for the drugs (86%), the majority also showed mental irritability and feelings of anxiety (74%) as well as profound lethargy and physical weakness (60%). About 70% of the users reported some kind of physical discomfort in the absence of the drug. There are reports from other countries, including Greece and Egypt, where there is a relatively high hashish consumption. Tennant and Grossbeck observed dependence in American soldiers in West Germany who were able to obtain large amounts of hashish.[9] Bensusan described five young South Africans who had marijuana withdrawal symptoms for one to three days and who were able to relieve them by re-administering marijuana.[10] Teitel reported three cases of manic-depressive illness that followed withdrawal after prolonged use.[11] Other clinicians have reported that heavy marijuana users may develop tolerance rapidly, become dependent, and experience flu-like withdrawal symptoms following cessation of use.[1]

To substantiate whether withdrawal symptoms exist with chronic marijuana use in humans, controlled human studies have been done. Volunteers have been given bedtime dosages of THC and monitored in sleep laboratories. When THC is administered nightly for only four to 15 nights and then abruptly discontinued, there is insomnia and increase in REM sleep and eye movements that last for up to 12 days.[12] In addition to controlled sleep studies, Jones and co-workers gave oral THC to volunteers for 11 to 21 days and then substituted placebo. They observed a variety of withdrawal symptoms similar to those described in clinical reports and animal studies.[7]

Based on numerous reports and studies, it is clear that there is a cannabis withdrawal syndrome. I have frequently observed marijuana-dependent patients in withdrawal, and my observations support previous reports. In particular, my patients have reported insomnia, nausea, myalgia, restlessness, and irritability. Table 1 summarizes the common withdrawal symptoms that have been reported in human and animal studies. A major question is whether this syndrome is identical to the opioid withdrawal syndrome. To date there are no reports of naloxone challenges in cannabis-dependent humans. A recent animal study, however, shows that THC will deplete endogenous opioid peptides, so marijuana dependence and withdrawal may be at least partially mediated through the endogenous opioid system.[13] THC administration also has effects on the catecholamine system.[14] Another study suggests that marijuana withdrawal may be mediated through the serotonergic system.[15] Rats made dependent on THC were given chlorimipramine, which is a potent inhibitor of serotonin re-uptake. Following this challenge, they developed a clear and quantifiable withdrawal syndrome similar to that observed when naloxone was given.[3,6]

CLINICAL TYPES OF DEPENDENCE

Two types of marijuana dependence will con-

TABLE 2
Two Clinical Forms of Marijuana Dependence

	Frequency of Self-Administration	Likely Dependence Metabolite(s)	Usual Referral Route	Patient's Perceived Dependence	Usual Severity of Withdrawal Symptoms	Relapse Rate
Type One	Multiple times each day	THC 11-OH-THC	Voluntary self-referred	Significant	Moderate	High
Type Two	Every 24 to 48 hours	THC-C	Involuntary. Detected by mandatory screening	Minor to moderate	Mild	High

front today's clinician (Table 2). Type One is an individual who will self-administer marijuana several times per day, usually at an interval of about two to four hours unless asleep. This individual may voluntarily present to the clinician with the complaint that their daily dosage has escalated and that they are unable to cease use without medical assistance. The patient may or may not relate mental impairment primarily related to memory, motivation, time-keeping, abnormal thoughts, and work or school performance. In addition, they may relate a number of withdrawal symptoms that occur when they attempt abrupt cessation. The variety of symptoms generally resemble those described in the controlled animal and human studies (Table 1), although they may report others. The precise relapse rate following withdrawal is unknown, but it occurs.

CASE REPORTS

Case 1: Marijuana Dependence: Voluntary Admission to Treatment

MV was a 25-year-old male who presented with the complaint that he could not "stop marijuana by myself." He was a 12-year user having begun marijuana smoking at 13 years of age. He had used marijuana daily for about five years and was using two to three joints per day at the time of admission to outpatient treatment. The patient was married and held a regular job as a warehouse superintendent. He claimed he was having considerable conflicts with his wife and employer. In addition, he had noticed in the two months just prior to admission that he occasionally heard voices that were not real, did not always have total "control over his mind," and had some thoughts of suicide. He denied use of any other drug or excessive alcohol intake. His treatment admission breath alcohol was negative, and his urine contained marijuana metabolite, but no other abusable drug. The patient was administered desipramine, 25 mg, three times per day and was given weekly psychotherapy for approximately six months. During the first ten days of treatment, he reported insomnia, abdominal cramps, diaphoresis, tachycardia, and anxiety. These symptoms subsided, and he submitted a urine void of marijuana approximately 30 days after admission. Most of the thought disturbances noted above disappeared after about two to six weeks of treatment. He denied any marijuana use during the six months after entering treatment, and he submitted monthly urine tests that showed no marijuana.

Case 2: Volunteer with Unsuccessful Treatment

JS was an 18-year-old male who voluntarily presented because he "wanted to stop." Consumption of drugs consisted of about 3.5 grams of marijuana and hashish per day for one year prior to seeking treatment. He self-administered every one to four hours while awake and complained of chronic cough, anorexia, depression, and weight loss. When he had tried abruptly to cease marijuana by himself, he had hallucinations, depression, and anergy. Urinalysis testing revealed the presence of marijuana, but no other drugs. The patient entered a counseling program, but received no medications. Only one return appointment was kept, and he was lost to followup.

Type Two form of marijuana dependence is primarily being identified as a result of mandatory urine screening and treatment referral in the workplace. Seldom does a Type Two voluntarily present for treatment, although it may occur. In this form, the patient is usually self-administering marijuana every 24 to 36 hours and may give a history of carrying on this habit for several years. As in Type One, reported impairment relative to memory, motivation, time-keeping, and job performance is

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variable. In contrast to Type One, however, the patient may report few if any symptoms of withdrawal upon abrupt cessation. Relapse, however, is common.

Case 3: Mandatory Work-Site Detection and Referral

HS was a 37-year-old male salesperson. He was reported to the management of his company to be a marijuana user who also sold it to other employees while on company premises. A mandatory urine test revealed the presence of marijuana metabolite, and in order to retain employment he was required to undergo withdrawal and enter a periodic urine-testing program. Upon interview, he stated that he had used marijuana every evening for approximately 22 years. He believed this habit had not been injurious to himself until approximately three months prior to treatment when he began to notice some defects in his short term memory. Physical examination was normal. Plasma analysis showed there to be 148 ng/ml of 11-OH THC and 80 ng/ml of THC-C. He was administered desipramine, 25 mg. three times per day and tyrosine. During the first three weeks following cessation of marijuana, he reported mild insomnia, depression, anergy, and craving. Urine analysis showed no marijuana metabolite after about 30 days. After six weeks of abstinence, he reported improvement of short term memory and improved job performance.

METABOLIC BASIS FOR TWO FORMS OF DEPENDENCE

New data on the metabolism and pharmacokinetics of marijuana provide a sound rationale as to why two basic clinical forms of dependence appear to exist. When a marijuana cigarette is smoked, THC is converted to two major metabolites, 11-Hydroxy-THC (11-OH-THC) and 11-Nor-THC-9-Carboxylic Acid (THC-C). THC and 11-OH-THC both have psychoactive effects, and they remain in the plasma at concentrations above about 5 ng/ml to 10 ng/ml for only about two to six hours.[16-18] During this period they appear to produce a short-term characteristic "high" or euphoria. This time period correlates well with the self-administration frequency of Type One marijuana dependence. The THC-C metabolite remains in plasma at concentrations above 5 ng/ml to 10 ng/ml for at least 48 to 72 hours. Although this metabolite may produce little or no euphoria, it is likely the compound that sustains Type Two dependence. A similar phenomenon also exists with some benzodiazepines, such as diazepam, and with the opioid methadone. For example, methadone will provide analgesia and euphoria for about four to six hours, but it and its metabolites will remain in plasma for 24 hours and sustain dependence. A similar time course may be observed with

A number of studies clearly document that tolerance, dependence, and withdrawal symptoms may occur after chronic administration of cannabis.

diazepam, which also has long-lasting metabolites. For example, some withdrawal symptoms and even seizures may not appear for several days following cessation of diazepam dependence.[19] I have recently observed that withdrawal symptoms following abrupt cessation of marijuana dependence may not appear for several days.

The following is an illustrative case in which plasma concentration of THC-C was assessed at three intervals during the first week following abrupt cessation of Type Two marijuana dependence. Withdrawal symptoms did not occur until the eighth post-drug day at which time plasma concentration of THC-C was undetectable. The delay in withdrawal symptoms is undoubtedly related to slow clearance of plasma and tissues of marijuana metabolites, particularly THC-C.

Case 4: Delayed Withdrawal Symptoms

A 27-year old male was admitted to a day-treatment program for marijuana dependence. He had been identified at work for being "under the influence" on more than one occasion and was, therefore, referred for treatment. Drug consumption consisted of intermittent cocaine use and daily use of about one marijuana joint. He perceived that he had been "addicted" to marijuana for about 15 years, and that he had skipped marijuana use on very few days during this time. A physical examination was normal except for mild nasal-septum inflammation and a swollen uvula. Urine analysis showed the presence of marijuana metabolite and marijuana plasma analysis by high performance liquid chromatography (HPLC) showed no 11-OH-THC and THC-C to be 8 ng/ml. A 24-hour urine specimen showed secretion of 2-methoxy-4-hydroxy-phenyglycol (MHPG) to be 143.0 MCG/24 hours (normal is 1164 to 2216). Since his continued employment was dependent upon attending the day-care program until his urine was void of all drugs, compliance with treatment and testing procedures was good. Withdrawal medication consisted of desipramine, 25 mg, administered three times per day, and the amino acid, tyrosine. On the third treatment day, his urine still contained metabolite, and his plasma contained 3 ng/ml of THC-C. On the eighth day of attendance, he complained of a flu-like illness consisting of nausea, vomiting, diaphoresis, chills, myalgia,

TABLE 3
Clinical Patients to Screen for Covert Marijuana Dependence

Psychiatric patients under age 35
Adolescents and young adults with recurrent respiratory ailments
Adolescents and young adults with recurrent accidents and unexplained somatic complaints
Patients under age 35 who abuse alcohol, cocaine, phencyclidine, hallucinogens, and amphetamines

anorexia, and insomnia. The patient did not relate these symptoms temporally to his marijuana use, since he had ceased use eight days previous. Plasma analysis showed no detectable presence of 11-OH-THC or THC-C, but marijuana metabolite was still present in urine at this time. The apparent withdrawal symptoms resolved within 48 hours. Marijuana metabolite remained in his urine until the 34th day of treatment.

SCREENING

There are some clear clinical indications to screen for marijuana dependence. Proper screening requires urine testing, physical examination, and history-taking relative to frequency of use (Table 3). Once detected, a treatment program can be developed. Patients who should particularly be screened by urine test are those who are under age 35 and who exhibit psychiatric symptoms, deviant behaviors, use cocaine, phencyclidine, or amphetamines, abuse alcohol, or have recurrent respiratory ailments. The association of various psychiatric symptoms and chronic cannabis use has often been described.[9] Although it is difficult, if not impossible, to always determine whether psychiatric symptoms pre-date or post-date the cannabis dependence, the association is so high that it is prudent to screen for it. In particular, chronic cannabis use has been associated with chronic thought disorders that are characterized by delusions, hallucinations, depersonalization, poor ability to perform at work or school, and inappropriate interpersonal relationships. Physical examination can often give clues to marijuana dependence. In particular, chronic marijuana smoking produces a swollen uvula and signs of chronic bronchitis. A generally unappreciated clinical candidate to screen for marijuana dependence is the adolescent or young adult who presents with apparent abuse of another drug or alcohol. For example, the underlying marijuana dependence may pharmacologically potentiate another drug, but remain unrecognized if a urine screen is not done.

Case 5: Marijuana Dependence Underlying Alcohol Abuse

A 17-year-old girl was arrested for being "drunk in public" on more than one occasion, and was referred for treatment. As part of a routine urine drug screen done for all persons under age 35 with substance abuse or psychiatric problems, she was found to have marijuana metabolite in her urine. Upon questioning, she stated that she drank alcohol only once or twice per week, but smoked marijuana daily. In addition, she questioned whether she could cease all marijuana use. Physical examination on admission to treatment revealed strabismus on the right and non-reactive pupils. She was administered desipramine, 25 mg, three times per day and tyrosine. She participated in outpatient counseling weekly. After approximately one week, the strabismus disappeared and pupils began to react. Marijuana metabolite could not be detected in urine after approximately two weeks of treatment. After three months of treatment, no known episodes of drunkenness occurred.

TREATMENT

At present there is no recognized medical withdrawal regimen for marijuana dependence. Outside of this review, the author cannot identify any reported use of a medical regimen for this purpose. Additionally, the use of the tricyclic antidepressant, desipramine, and tyrosine, a precursor of norepinephrine, as reported here, is not necessarily the optimal treatment. Recent studies of cannabis administration given to animals and humans indicate that it reduces noradrenergic activity and endogenous opioids.[13,14] For this reason desipramine, which is a potent blocker of the reuptake of norepinephrine, may be an effective withdrawal agent. For example, a case described here showed extremely low urinary excretion of MHPG, which is a metabolite of norepinephrine. Although this regimen appeared clinically effective in the cases reported here, plus others treated by me, only a double-blind, placebo-controlled study can prove true effectiveness. Regardless of pharmacologic effectiveness, I have observed that patients who present for treatment and who do not receive withdrawal medication for at least a few days tend to drop out of treatment just as did one of the illustrative cases described above. This appears to apply to both Type One and Type Two dependency.

Although there has been a scarcity of attempts at medical withdrawal, there are recent reports of hospitalization and withdrawal attempts.[20,21] Swatek found that many patients would drop out or fail to reduce marijuana use enough to ever clear

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their urine of marijuana metabolite.[20] This study points out the necessity to regularly monitor urine for marijuana metabolite as an indicator of successful treatment. I have found that assessment of the plasma concentration of 11-OH-THC and THC-C to be useful in determining whether the patient is ceasing self-administration of marijuana.

Regular psychotherapy to accompany urine monitoring and possible medication appears essential in most cases. Patients dependent upon marijuana tend to have a plethora of psychiatric symptoms and considerable problems with interpersonal relationships, motivation, and reality functioning.[9,11]

TRENDS AND RESEARCH NEEDS

There is little question that the need for clinical treatment of marijuana dependence will escalate. Many persons who have used marijuana for several years are now beginning to realize that they are dependent and will not be able to cease use without medical intervention. This realization is enhanced by the availability of more potent forms of cannabis that were not available just a few years ago. Some persons are probably becoming dependent as a result of these potent forms, where they might not have done so if their only consumption was the low potency forms that were formerly available. Perhaps the biggest impetus for dependency treatment will be the identification of dependent persons in mandatory urine screening programs operated by industry.

Research is needed to develop a medical withdrawal treatment for marijuana dependence. From a prevention perspective, we need information as to how frequently and for what length marijuana must be used to develop dependence. For example, I have clinically observed that withdrawal symptoms will occur in persons who use marijuana on a daily basis, but I am not clear as to whether they will occur in persons who use marijuana every second or third day. Since THC has long-acting metabolites whose pharmacologic activity is uncertain, our concepts of dependence must be refined. Lastly, there is almost no available data on relapse rates with marijuana dependence.

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Anchorage Chamber of Commerce

Crime Commission

November 15, 1985

Dear Reader:

The material contained herein was compiled from various sources by the Anchorage Chamber of Commerce Crime Commission in support of our recommendation to recriminalize marijuana in the state of Alaska.

Because of a State Supreme Court Decision on this subject, it will be necessary for the Legislature to hold extensive hearings to determine if, in fact, marijuana is harmful to one's health.

It is the Crime Commission's contention that since the decriminalization of small amounts of marijuana in Alaska approximately ten years ago, much new information has been developed concerning this issue.

We feel that this scientific evidence substantitates the Commission's position that marijuana is a harmful substance. We further believe that if the Legislature were to hold the same type of hearings that were held ten years ago, the preponderance of evidence would result in outlawing the possession of marijuana for health reasons, an act which should then stand up to any further Supreme Court reviews.

We ask the reader to review the material carefully and draw his own conclusions as the Crime Commission has.

Sincerely yours,

Pat Wellington
Vice Chairman

nm

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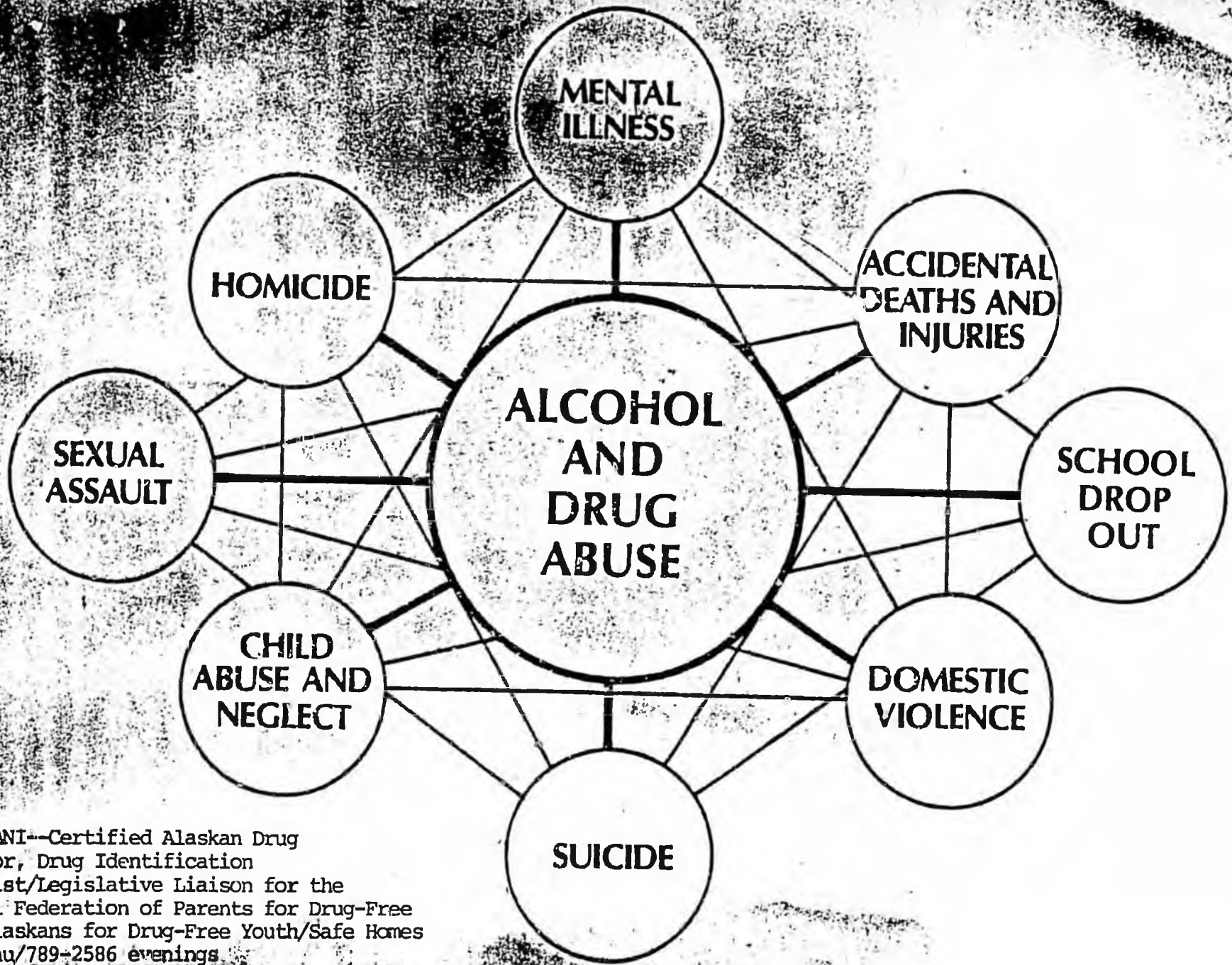

BOBI TRANI--Certified Alaskan Drug Counselor, Drug Identification Specialist/Legislative Liaison for the National Federation of Parents for Drug-Free Youth/Alaskans for Drug-Free Youth/Safe Homes of Juneau/789-2586 evenings

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PANDAA

PARENTS' ASSOCIATION TO NEUTRALIZE DRUG & ALCOHOL ABUSE

ADOLESCENT CHEMICAL USE

This is a special edition of the PANDAA newsletter. It is a guide for parents and professionals to identify adolescent chemical abuse problems. It is for sale in bulk or on a single copy basis. To purchase, use the form on page 11. This guide has been written by parents who have learned about the subject through experience, extensive research, and from their own recovering children and their friends.

WHY DO KIDS DO DRUGS?

Parents must realize that whatever type of home they have, the kids also live in another world - different than what our adolescent world was like. At present, the only way to keep your child from being exposed to the drug culture is to lock him up, without exposure to newspaper, TV, radio, movies, and magazines. Outside influences begin to affect our children at a very young age. TV and movies depict alcohol use as an ingredient for a good time. Drug usage is also portrayed as "cool" and expected behavior. Our kids' role models - TV, movie, and rock stars are open about their drug use, and receive no legal consequences. Rock music lyrics often promote alcohol and drug use. Many professional athletes have been suspended for drug use. The children see widespread alcohol and drug abuse at concerts, outdoor sports events, in school, and in shopping centers. Not only is it socially acceptable in these public places, but there seems to be no consequences from law enforcement personnel. By the time a child is 10 years old he is very saturated with "drink alcohol and do drugs" messages, and the philosophy, "If it feels good do it." It is very easy for a child to rationalize going against values that "old fashioned parents" may have taught.

Alcohol and drugs are easily available to our young people. Many homes have well stocked liquor supplies. Some young adults make extra money by stationing themselves at convenience stores to buy alcohol for underage kids. Some restaurants buy mailing lists of student groups, and mail notices of a special happy hour for students from a specific group or college campus. The breweries have sales representatives on college campuses. On at least the first few encounters, the marijuana is usually given to them free. Marijuana is easier for our kids to buy than it was for our generation to buy cigarettes. They can buy any drug they want at school, shopping centers, convenience store parking lots, etc.

When asked why they started doing alcohol and/or drugs the most frequent answer of the kids was peer pressure. They had ususally refused participation several times before they gave in to peer pressure. Curiosity, love of thrills and danger, desire for acceptance by a group, were other influencing factors. Experimentation continued because it was fun.

> "I started getting high off pot when I was 11, with my best friend. He was 2 years older and I really wanted to be like him. My friend's 16 year old brother did drugs and we would steal his drugs and get high. I did it at first to keep from being called "chicken" or being left out. For almost two years my parents were not fully aware I used drugs. I was sneaky and a good "con" which kept me from getting caught."

Alcohol and drugs were not used to alleviate parental conflicts, low self esteem, etc. until usage was well established. None of them intended to become dependent on alcohol or drugs. If they read literature on drugs they carefully chose reading that favored drug use, and when they observed their drug using friends and role models there were no apparent bad effects from the alcohol or drugs. Indeed, it seemed like these were the people who really knew how to live and had their act together! Some reported that drug education delayed their first encounters and they were very cautious in the beginning. As time went on the horror stories did not materialize or they did not recognize what was happening to themselves.

WHAT DOES "DO DRUGS" MEAN?

When we speak of kids "doing drugs" we are speaking mainly of alcohol and marijuana. As usage continues and tolerance is built up, alcohol and pot often become boring, and they may progress to using uppers, downers, and hallucinogens. Heroin is rarely part of the adolescent scene. Another frequently used term is "partying" or "to party", which means to drink and/or do drugs. For many kids their weekend social life is "partying". Keg parties are held at homes where the parents may or may not be present. Sometimes the parents buy the kegs, with the excuse that at least they aren't doing drugs, or at least they aren't out on the street. Drugs are usually available at these parties. Keg parties are often advertised at school with flyers - even, occasionally, at intermediate level schools.

As usage progresses kids will do drugs under almost any circumstances, and will try anything they can find. Girls have told of raiding medicine cabinets for any labeled or unlabeled pills while babysitting, and of getting the children they sit for high. Many kids admit to getting their pets high. Some tell of getting high with their teachers, school counselors, therapists, policemen, probation officers, at school and on their jobs. Kids will try anything to get a "high", from drinking vanilla or lemon extract to eating nutmeg.

A PERSONAL STORY

Professionally I am associate professor of Chinese at the George Washington University. I have three children. I would like to relate to you our family's experience with drug abuse.

While my son, age 15, and daughter, age 13, were doing drugs, I was unaware for a long time that this was their major problem, even though I myself had smoked quite a bit of marijuana about ten years ago in the early 70's. Indeed, that was part of the problem. I assumed "pot" to be a relatively safe drug, even though, if I could have looked honestly at my own life back then, I would have seen - as I now do - the extent to which my decreasing energy and motivation at the time could be laid at the doorstep of this drug. Luckily, I had weaned myself away from it, and, again, assumed a kid could do the same. I was wrong on this count as well. So even with my own experience, I failed to recognize for a long time what was happening.

What I did see was my son becoming increasingly hostile, volatile in his outbursts of anger - punching big holes right through the wall - and then darkly withdrawn into his cave-like room, which was designed as a shrine to heavy-metal rock groups and the death-like imagery they projected. He was also clearly in great pain and loneliness, although this was covered over for me by the outward behavior.

As for me, I was frightened both for him and of him; and beyond that, furious with him, practically hating him at times. And I was unbearably guilty; I was sure he was doing drugs because I was his adoptive father and he sensed that I rejected him. I was so confused

CONTINUED ON PAGE 11

to try to justify "responsible drug use." Proponents of responsible use contend that "careful use" in people who have no genetic predisposition toward addiction is relatively safe. The problem is that what may be careful use to one person is abuse to another. Alcohol may be a problem for some people; cocaine or marijuana for others. There is no effective way to predict who will become impaired or addicted. Drug use is like Russian roulette, and the earlier that an individual is exposed to mood altering chemicals, the greater risk of addiction. I have yet to meet an addict who intended to become addicted when he started using drugs or alcohol.

The disease of addiction is most effectively handled through a combined approach of prevention, intervention, and rehabilitation. This is the goal of the parents' movement. We must give our children a set of values and good self esteem; we must teach chem how to "say no" and be certain that they do.

We must try to make waters safe by enhancing prevention efforts, decreasing the supply of drugs, and working to rehabilitate individuals so as to not lose them to this disease.

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St. Francis Hospital
Topeka Kansas
Member Board of Directors
National Federation of Parents
for Drug Free Youth

RECOMMENDED READINGS

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SIGNS AND SYMPTOMS OF CHEMICAL USE

WARNING SIGNS

When children begin to use alcohol and other drugs few signs are initially noted by parents since many changes are expected during adolescence. Parents rarely find their child intoxicated, "high", or otherwise impaired. Likewise, hard evidence of usage such as finding the actual drugs or alcohol is often a matter of occasional accidental discovery. Parents must rely most often on the subtle signs and symptoms and the inference of drug use which can be drawn from various signs.

Parents may have cause for concern if their child has rebellious attitudes towards parents and other authority figures, changes friends, is very eager for acceptance by friends, uses bad language, is irresponsible toward work and school, strives to develop a "cool" image, or frequents rock concerts. Some changes may start before alcohol or drug use begins as the child becomes attracted to the drug culture.

THE DUAL LIFE

The alcohol or drug-involved child is apt to lead a dual life in the early stages of usage. A clean image is maintained in front of parents, teachers, and straight friends and a totally different image is projected among drug-using friends. Although their drug use may be well hidden, they put an emotional distance between themselves and their parents and other adults. Many are able to maintain a good appearance, good grades, athletic, and other extra-curricular activities for a surprisingly long period of time (years). The ability to lead a dual life also deceives the user into believing he has control of usage.

BEHAVIORAL SIGNS

As he is drawn more to the drug culture attitudes change, and what was once unacceptable (gross, crude, or illegal) behavior is now "cool" and acceptable. Sports, extracurricular activities, and hobbies, may be discarded. Carelessness, laziness, depression, cheating, stealing, lying, conning, vandalism, bad language, rapid emotional ups and downs, poor concentration and memory, falling grades, curfew violations, school and work absences, disrespect for authority, paranoia, interest in witchcraft, and sexual promiscuity point to possible drug use.

The family relationship deteriorates, family activities are shunned, meals are eaten quickly with the child retiring to his room and listening to loud rock music for long periods of time. Eye contact with parents and other authority figures is avoided. Everyone is "on his case." All of his failures are blamed on others.

> "I began to worry about my 14 year old when he became hostile, not just toward me, but to his sister. She had, up to now, been his best friend. I was bewildered by his urge to hurt those who loved him most. This puzzled me and I felt alone and wounded. When he ridiculed his best friend and abused other "friends" verbally I worried even more. Then other strange behavior began. He became insanely jealous of his sister and anyone he thought might get a crumb more of any treat he felt he deserved. He blew up at a moment's notice if he was asked to help around the house. He rarely talked, but when he did he revealed an alarming absence of reality in his thinking, planning a future career as an artist with no thought of education or marketability of his work.
>
> At home he was either arguing, complaining or locked alone in a bedroom, bathroom or basement. His moods swung from apathy to hatred. Hardly ever was there any peaceful ground between."

For some, threats to run away become an effective method to get their way. Many do run away and stay at friends' homes or in the woods. Parents of his friends may be told by the runaway that his parents are abusing him.

The "druggie look" is expressed in a child's flat facial expression, ragged, worn clothes, "bop" walk (walk with a bounce), slouched stance and generally depressed appearance. Girls often use heavy makeup, wear long bangs over the eyes, sexy clothes and jewelry. Both girls and boys strive to appear older. Personality changes can evolve slowly, over the years or occur very rapidly in a matter of months.

PHYSICAL SIGNS

Most physical signs do not occur until alcohol and/or drug use are well under way. Marijuana irritates the whites of the eyes, and the use of Visine or similar products alleviates irritation and redness. A persistent cough is very common. Other suspicious conditions are a runny nose, nasal sores, a facial puffiness, dilated or constricted pupils, glassy eyes, a skin rash similar to measles, poor muscle coordination, and stains and burns on lips, inside the mouth, finger tips or fingernails. There may be a craving for sweets, excessive or depressed appetite, excessive thirst, bad breath, or a weight gain or loss. Frequent illnesses are common.

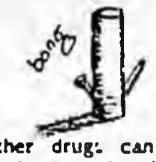
Children who "do drugs" are frequently tired because many of the drugs depress the central nervous system. Also, many teenagers are tired because a druggie lifestyle frequently involves sneaking out of the house at night (often through a window) in order to join friends, and returning in the morning before the family awakens. The child catches up or lost sleep in class or at home in the afternoon.

It is important to note that alcohol use alone can manifest many of the above behavioral and physical signs and should be considered just as serious as other drug use.

PARAPHERNALIA

Many drugs require paraphernalia to prepare them for consumption. Some drugs such as PCP and even the insecticide, RAID, are sprayed on substances such as dried parsley leaves and sold in tiny foil packets or baggies. Marijuana is stored and distributed in plastic bags, small jars, or film canisters. Marijuana seeds, about the size of large bird seed, may be found in baggies, pockets, or small containers. The handrolled marijuana joint requires rolling papers and quantities of matches to keep it lighted. The marijuana ash is smaller, more fragile and whiter than tobacco ash.

Marijuana joints (reefers) and other types of drug-treated cigarettes which are smoked down to the butt (roach) are often held by roach clips to avoid burning fingers. These clips resemble the alligator clips found in hardware stores. Fancier ones such as feathered and highly decorated clips can be purchased in many stores and gas stations.



Marijuana, hashish, and other drugs can be smoked in various types of pipes ranging from ordinary tobacco pipes to elaborate smaller ones that can easily fit into a pocket. Small probing tools are used to clean the sticky brown tar residue left from the smoking process. Some drugs can be smoked without pipes by burning them like incense in a partially covered container and inhaling the smoke.

Bongs are especially favored for marijuana smoking and are often shared by a group. A bong is an apparatus that cools, filters, and concentrates the smoke giving the user a better high. It consists of a cylinder 6 to 12 inches high which holds water. A tube leading into the side holds the "bowl" in which the drug is burned. By sucking air at the top of the cylinder, smoke is drawn from the bowl through the water and inhaled. It can also be used to smoke hashish, PCP, quaaludes, and other drugs. Bongs come in many styles and materials, and are often homemade.

Many kids will grow marijuana plants from the seeds they clean from their marijuana.

> "My daughter convinced me that the potted plants growing on her window sill were a school project. Feeling very proud of her new interest in science I helped her keep them watered. Much later I found out I was watering marijuana plants."

"Snorting" is another method of drug use popular among cocaine users. Any powdered or pulverized drug can be snorted. The drug is usually deposited on a mirror and aligned with a razor blade. The "line" is sniffed through a short straw, rolled dollar bill, or tiny spoon.

Items which may indicate intravenous drug use are syringes, eye droppers, spoons for heating and dissolving powders, and cords or belts used for tourniquets. Balloons or paper bags are used for inhalants.

OTHER SIGNS

Much of the alcohol used at first comes from parents' homes. Water is often added to liquor bottles to fool parents. It is well to do a taste test when checking supplies. Soft drink glasses and cans easily disguise alcohol. Girls often hide small bottles of alcohol in their purses.

Medications purchased by the child as innocuous as cough syrup or any over the counter drugs may indicate problems other than coughs or sore throats. These preparations may be used to alter moods when consumed in sufficient quantities. Often they contain alcohol.

Breath sprays mask alcohol use and smoking. Incense, candles, or room deodorizors remove smoking odors from a room.

Popular hiding places for drugs are stereo speakers, trophies, lamp bases, books, albums, stuffed animals, air conditioner vents, parents' and child's out of season clothing, parents' rooms, car trunks, attics, garages, tool sheds and bushes.

Faked or forged ID cards are easily obtained and used to buy alcohol. Bikes, clothes, stereos, etc. may appear or disappear if they are being used for trade in drugs. School yearbook inscriptions often reflect changed values, as do posters, drug culture clothing, jewlery, record albums, and magazines.

Frequent short telephone calls, hanging up when parents answer, prank and late calls are cause for suspicion.

Favorite hang outs include shopping centers, especially stairways, hallways and game rooms; convenience stores and pizza parlors; school smoking lounges; parks and secluded sites.

PUTTING THE CLUES TOGETHER

It is very helpful to write down all the behaviors, events, and physical evidence which have caused concern with either parent. Recall dates as well as you can and continue to keep the list. Such record keeping reduces exaggeration and minimizing, and helps both parents see their child's behavior more realistically. Bad attitudes, disrespect for authority, and a decline in the family relationship are some of the most tell-tale indicators of substance abuse, and warrant room checks, monitoring of phone calls, spot checks of school attendance, and relating concerns and observations to the parents of the child's friends. Impromptu urine testing for marijuana is of limited value since many factors affect the results of the test. The kids know tricks to bring about negative tests. Determination of which drugs the child is using is unnecessary. The fact that any drug use is causing problems in his life indicates that help is needed. A parent's best guide is probably his or her own "gut feeling" about the child. That "gut feeling" can be confirmed by an evaluation at a drug rehabilitation facility.

REFERENCES: See page 11, Nos. 1-6.

CHEMICAL DEPENDENCY IS A DISEASE

The disease of chemical dependency is established when the user needs mood altering chemicals on a periodic or continuous basis to feel good. The user is unable to control or stop usage, and a psychological and/or physical dependence is developed. Tolerance to the drug also develops, which means that larger doses are needed to produce the original results.

Physical dependency is present when the drug becomes a part of the person's normal body chemistry and unpleasant physical symptoms, such as vomiting, tremors, sweating, muscle cramps, or even convulsions occur when the chemical is abruptly withdrawn. Physical withdrawal symptoms last for 3 to 10 days depending on the drug. Drugs that cause a physical dependence include nicotine, alcohol, narcotics, hypnotic sedatives, and some tranquilizers.

Psychological dependency on any mood altering chemical is much more difficult to overcome than the physical dependence because it lasts for the rest of the user's life. In other words, he is never cured, but is always in either a recovering or active state of the disease. To stay well he can never again use any mood altering chemical.

The cause of this disease is unknown. It is a primary, progressive, and chronic disease which becomes a family disease as it progresses. It progresses faster in women and adolescents. If allowed to progress it can result in death. It is not a symptom of a disease, it is the disease. The undesirable behaviors associated with chemical use are caused by the chemical use rather than the chemical use being caused by other underlying factors such as inadequate parenting, learning disabilities, low self-esteem, etc. No one intends to become chemically dependent when they begin using alcohol or drugs. Most studies show there is no preaddictive or prealcoholic personality. But, once the disease has begun, behavior patterns become very similar in all abusers. Fortunately, these personality changes are reversible if treatment intervenes to arrest progression of this illness. Vernon Johnson, founder of the Johnson Institute, believes all abusers are guilt-ridden people having a very high set of values and morals which appear to be nonexistent because of their destructive and anti-social behavior resulting from their chemical abuse.

The illness is often divided into four stages. The stages are very similar for adults and adolescents but the following description will focus on the adolescent disease in today's drug culture. Chemical dependency can develop in six months in some adolescents, while it usually takes many years for an adult. Adolescents do not often become physically addicted to alcohol but they become psychologically dependent on it. If drugs are involved the progression of the disease tends to be more rapid than when only alcohol is used. Many adolescents begin tobacco use before or along with alcohol and/or marijuana use.

STAGE ONE

The first stage may be referred to as "learning the mood swing." The user learns that the chemical makes him feel good. If only alcohol is involved, this is still classified as social drinking. If other drugs are involved it could be classified as "experimentation". Few unpleasant effects occur. The chemicals involved are probably tobacco, beer, wine, pot, and/or inhalants. They are probably given to and not bought by the user. The child usually refused participation several times, and often did not get intoxicated on the first alcohol encounter or high the first several times he tried pot, because he had not learned how to inhale it. For peer acceptance, he may have faked being high. When he did learn how to use it effectively, very small amounts got him high because no tolerance had been built up. In stage one he drinks and does drugs only when it's convenient and available, mainly on weekend social events. For most there are no observable behavior changes yet, although some kids begin to adopt "druggie" attitudes and behaviors before usage begins. The parents are unaware of any usage unless they accidentally discover evidence or occasionally recognize the child is high or intoxicated. Ususally such a discovery is considered a "normal phase" by the parent.

STAGE TWO

As he enters stage two, he begins to "seek the mood swing." He plans his use of chemicals, buys them, and may use them alone. He begins to feel unpleasant symptoms as his high ends and tolerance increases. New chemicals may be introduced such as hashish, hash oil, "uppers" and "downers". Usage increaes from weekends ("weekend warrior"), to week nights, to week days. The child begins the dual life, gradually progressing to a more obvious druggie dress and life style. Druggie friends are often met away from home.

Unexplainable mood changes begin, including withdrawal, anger, and aggression. Verbal abuse towards parents, profanity, and rebellious attitudes become a constant friction point between parent and child. The child prefers to isolate himself from his family, and spends many hours in his room often with loud musical accompaniment. As drug use and tolerance increase, stealing from parents and siblings begins to pay for drugs. The first signs of the amotivational syndrome appear. That is, there is loss of motivation and drive. Everything is a "hassle." Hobbies and extracurricular activities may be dropped. All of the child's problems are blamed on other people.

As school grades drop, parents may react with strong disciplinary action. The child will bring up his grades, often by cheating or changing grades on his report card. The improvement "cons" the parents into believing the problem is improved or solved.

The child begins to violate his normal moral values. Vandalism, theft, shoplifting, lying, and/or sexual promiscuity is common. As he experiences shame and guilt for these acts, he gets high or is able to wipe out their memory by "blackouts" or selective amnesia.

Drug use increasingly becomes a necessity to feel good rather than a choice. The youngster can no longer control his drug use. Unfortunately, to most parents, school personnel, and counselors the problems are still not distinguishable from normal adolescent growth problems. Chances are slim that the parents can handle the problem alone. The child is already in need of outside help, but it is unlikely that he will receive the right kind of help.

STAGE THREE

The third stage is the dependency stage. Now his life centers on getting high. He may advance to hallucinogins, cocaine, or opium smoking. He is high most of the time. Tolerance increases and attempts to reduce dosage or stop usage fail. Solitary use is frequent. Suicidal thoughts occur. Overdoses and flashbacks begin to occur. Behavior continues to deteriorate, police incidents occur, jobs are lost, and the child may drop out of school. Chronic cough begins. He feels distress when not high. Rationalization of chemical use becomes an art and guilt feelings run high. He cannot see what is happening to himself.

Family life deteriorates. There may be skipping school, sneaking out of bedroom windows during the night, and running away. The child is guilt ridden and self esteem is very low. He thinks he is "different" from his druggie friends. Drugs are no longer fun. It appears to him everyone else is having fun. He becomes careless and maybe obvious with his use and paraphernalia (may be a plea for the help he is unable to ask for). Parents often believe the child is only using drugs occasionally. The family uses rationalizations to deny the problems.

STAGE FOUR

In stage four, chemicals must be used to feel normal. Use is no longer fun. It is compulsive, uncontrollable, and is regular throughout the day. He may be shooting up. Drugs must be used just to function. Physical health deteriorates. Delusions and paranoia can be severe. Euphoria is rarely even experienced from the drugs. Suicidal thoughts are frequent. Overdose, blackouts, and amnesia occur. He is usually well known by the police. The user is often referred to as a burnout or a zombie. If intervention does not occur, death will result from suicide, overdose, an accident, physical illness, or other untoward behavior.

REFERENCES: See page 11, Nos. 1-6

THE FAMILY

As the alcohol or drug using person's behavior deteriorates, each family member experiences anger, shame, guilt, fear, hurt, and loneliness. To relieve the pain of these feelings and to make attempts to cure the abuser, various defensive behaviors develop. These responses may begin before anyone in the family is aware that the problem is actually one of chemical abuse. In the case of the adolescent, usually the parents take on the role of the primary enabler. There are many forms of enabling. The enabler may protect the user by rationalizing his behavior; bailing him out of trouble at school, the job, the law, or even trouble with the other parent; making special allowances that would never be given to the other children; or keeping the problem secret. One enabling parent may become a controller by taking on responsibilities that actually belong to the user such as getting him up on time, taking him to school, blaming others for his problems, or by striking up bargains with the user. The other parent often enables by withdrawing from unpleasant situations, working late at the office, getting deeply involved in community affairs, being a peacemaker between the child and other parent, or blaming the spouse. As each parent takes on different forms of enabling, frequent conflicts arise and often they begin to believe that their declining marriage relationship is the cause of their problems. The user can become very skillful in exploiting this situation to his advantage. The enabling behaviors become just as compulsive as the user's chemical use. The enabler can become just as disturbed as the user.

As one parent comes out of denial and recognizes that the problems are caused by alcohol and/or drugs the other parent may still be in denial. The parent who comes out of denial first is usually the one who spends the most time with the child and handles most of the crises. The second parent may come partially out of denial, but still deny the seriousness of the abuse. Nothing constructive can happen until the second parent comes completely out of denial and the parents are united in their approach. Sometimes denial is broken when that parent is left alone to experience the embarrassment, hurt, or anxiety of each crisis his child creates with the school principal, the police, or in the emergency room. Much help can be gained in this area by attending self help support group meetings such as Al-Anon, Families Anonymous, or Tough Love.

As the conflict between the abuser and his parents continues, the other children in the family adopt various survival behaviors. Some become too good to be true, or "heroes." They overachieve, are very responsible, give the family a good name, but can be bossy, obnoxious, and achieve for attention rather than for healthy motives. Later in life these children are often "workaholics" and enablers to their spouses and their own children.

Another child may become a "scapegoat" and be rebellious, irresponsible, act out, and disrupt class. The reward is negative attention, which takes the spotlight off the user. This child could easily be mistaken for an abuser, and often abuse is in his future.

The apathetic child is often referred to as the "lost child." This child withdraws, shows little emotion, avoids conflict, and develops few social skills. He is sometimes overweight. On the surface the child appears calm and serene, when in reality there is pain, confusion, and denial of the family's problem.

The family clown gets attention by being funny and distracting. (He is often the youngest in the family.) The child is unable to express feelings and despite the humorous behavior there is much pain.

Each family member's defensive behavior becomes compulsive and habitual. As the lifestyle becomes too painful to bear, the person looks for a way out. Hopefully, this will be through a self-help group such as Al-Anon or Ala-Teen or by the family becoming involved in a rehabilitation program. Other forms of escape the person may use are leaving the family or, worst of all, by suicide.

If appropriate help is not enlisted the siblings in the chemically dependent family are more likely to become chemically dependent themselves. They have chemicals available to them, they have not developed good coping mechanisms, and the whole family is involved in unhealthy compulsive behavior patterns. With the proper help the chemically dependent family can become a nurturing family again, but without help, the family situation can only deteriorate.

REFERENCE: See page 11, Nos. 1 - 6.

FREE DIRECTORIES REHAB PROGRAMS

Directory of Community Substance Abuse Programs in Virginia: Secretary for Community Substance Abuse Services, Div. Of Substance Abuse, Dept. of Mental Health and Retardation, PO Box 1797, Richmond, VA. 22214; Call 804-786-1524.

National Directory of Drug Abuse and Alcoholism Treatment Programs. #(ADM) 83-321. NCDAI, PO Box 1908, Rockville, MD. 20850.

DOES MY CHILD NEED HELP?

By the time both parents recognize that the problems they have been experiencing are caused by chemical use rather than by other factors, the child has usually been abusing for at least one to three years, and is already chemically dependent, even though his use may be restricted only to alcohol and marijuana. If the parent finds that strict rule enforcement, close surveillance, spending more time with the child, professional counseling, etc. do not solve the problem, it gradually becomes obvious that the parents cannot "fix" their child alone. Outside help is needed from those experienced in the field of chemical dependency.

A child's drug use is not the parents' fault. The main cause is peer pressure. The child made his choice to do drugs. That choice progressed into the disease of chemical dependency. He needs treatment just as a diabetic child needs treatment. Few parents of diabetic children would withhold treatment because their child did not want injections. Untreated diabetes and untreated chemical dependency are fatal. A characteristic of chemically dependent persons is denial of their disease, and so they rarely seek help. In the case of an adolescent, it is the family's responsibility to intervene so recovery can be initiated.

Recovery from chemical dependency is very difficult, taking a long time, just like breaking a nicotine habit. Group therapy seems to be more effective than individual counseling. A good first step for parents is attendance at one of the free self-help groups such as Al-Anon, Families Anonymous, or Tough Love. There the parents will learn how to recognize their own unhealthy reactions to their child's behavior, how to make the child responsible for his actions, and how to use crises created by the child constructively. Often when the child is no longer able to manipulate parents he becomes ready to accept treatment. A child who asks for help and is motivated may do very well by attending every night or enrolling in an outpatient program. These children's programs will be more successful if their parents attend their own self-help group meetings. The less motivated children will probably require very intensive, long term programs. There are many types of treatment programs. It is advisable to meet and talk with parents and kids who have been through the programs that are available.

CRITERIA TO LOOK FOR IN A PROGRAM

1. It treats drug and alcohol abuse as a disease rather than as a symptom of a disease. It believes the unacceptable behavior is caused by the chemical use rather than by an underlying cause. It makes the user responsible for his own actions.

2. It promotes an alcohol-and-drug-free life style with drug free counselors. Recreational alcohol or drug use is not allowed. Mood altering prescription drugs are not part of the therapy. Out-patient programs often use urine screening to monitor marijuana use, and Antabuse to monitor alcohol use. Antabuse is a medication that makes one very ill when alcohol is ingested. Parents have the right to know results of urine tests, and the side effects of Antabuse.

3. It uses the twelve steps of Alcoholics Anonymous or includes AA meetings as a part of its program. These tools for self-change have a long successful history.

4. It provides daily support in the form of group counseling and/or AA meetings for at least 6 months. Aftercare continues on a less frequent basis, often in the form of AA meetings or self-help meetings.

5. At least some of the counselors should be recovered abusers who can relate by personal experience and read through the "cons" of their clients.

6. It provides counseling and education for the total family including siblings. This may be in the form of Al-Anon and Ala-Teen meetings. The family learns to recognize and to change its undesirable behavior responses it has developed in response to the abuser's unacceptable behavior. It strives to re-establish good family relationships.

7. The client must learn to live free of alcohol and drugs in a drug oriented society. After adequate progress in a structured, controlled, drug free environment the client begins a gradual re-entry into society, learning to remain alcohol and drug free at home, school, job, and during leisure time. Therapy continues during re-entry.

REFERENCES: See page 11, Nos. 1-3.

MARIJUANA

Marijuana (Cannabis sativa) is a plant which contains over 420 chemicals. The effects of most are unknown. In 1964 its principal psychoactive component (intoxicating chemical), delta-9-tetrahydrocannabinol (THC), was identified. The THC content of marijuana has increased dramatically in recent years due to improved plant genetics and cultivation techniques. Seizures made by the U.S. government in 1965 averaged a THC content of 0.1-0.2%, by 1970 the average THC content climbed to 1.0%, and by 1983 the average THC content had climbed to 2-5%. The most potent strain, sinsemilla, averages a THC content of 11-14%, and is grown illegally extensively throughout the U.S. The potency of marijuana has increased from 50 to 100 times since 1960.

Two marijuana derivatives are also widely used. Hashish or "hash" is the pure resin extracted from the flowering top of the marijuana plant dried and compressed into brown or black cakes or balls. The THC content averages 10-20%. Hash oil is a concentrated viscous liquid that varies in color from clear to black. Its average THC content is 30-40%. Pure THC is never sold on the street because it is very unstable and too costly to manufacture. What is sold as THC is actually PCP or some other drug.

Some slang terms for marijuana are grass, Mary Jane, pot, sens, reefer, weed, hemp, and roach. Marijuana looks like dried parsley mixed with stems and seeds. It is usually bought in small plastic baggies, called nickle or dime bags. One ounce of marijuana will make about 40 joints (cigarettes). A joint sells for about a dollar. Joints are hand rolled, smaller than tobacco cigarettes, and twisted on the ends. The end of a joint, a roach, is often held with a "roach clip" and smoked. Marijuana is also smoked in pipes and bongs (described under paraphernalia). Thai sticks are marijuana buds bound onto short sections of bamboo. Hashish is smoked in pipes or bongs. Hash oil is dropped on a cigarette or joint, or smoked in a special opium pipe. Dried marijuana can be eaten but is only one third as potent.

THC is fat soluble and is stored in the fatty tissues of the brain, reproductive organs, liver, kidney, and lungs. "It takes 30 days to eliminate a single dose of THC. ."[14] In comparison, alcohol is water soluble and excreted from the body in six hours. "Carefully conducted studies with known doses of marijuana or THC leave little question that tolerance develops with prolonged use."[15] Marijuana is psychologically addictive. There is evidence that it is also physically addictive, although there are no major physical withdrawal symptoms because of its slow metabolism and excretion.

IMMEDIATE EFFECTS

A single marijuana cigarette induces a "high" within minutes which lasts from 2 to 5 hours and usually does not result in a hangover. It gives an increased sense of well-being, and a dreamy, carefree state of relaxation. The user may experience sensations of floating and a more vivid sense of touch, sight, smell, taste, and sound. There is often a craving for sweets and dryness in the mouth and throat. The eyes may be irritated and red, and have a glassy look. The state of intoxication may not be noticeable to an observer, even an experienced drug user. Marijuana suppresses the nausea resulting from a large alcohol intake so that users are able to consume large (even fatal) quantities of alcohol.

EFFECTS ON DRIVING SKILLS

In a study done in 1974 by Dr. Harry Klonoff, 38 drivers covered a 16 mile route from a university campus to the traffic-heavy downtown area, and back again. They were rated by the system used to examine drivers for licensing. Final figures for the road test showed that those on the low dose (one joint with 1.2% THC) had a 42% decline in driving skills, while the high-dosage drivers (two joints with 1.2% THC) had a 63% decline. Unusual driving behavior included missing traffic lights or stop signs, poor handling of the vehicle in traffic, and unawareness of pedestrians and stationary vehicles. A 1972 study of driving behavior in a safety-controlled area showed a "marked" decline in driving abilities was still present 5 to 6 hours after smoking, a "definite" effect 8 to 10 hours after smoking, and a lingering effect as long as 24 hours later.

EFFECTS ON THE LUNGS

Marijuana burns at a higher temperature, and its smoke is inhaled deeper and held in the lungs longer than tobacco. Marijuana has 50% more cancer causing materials than tobacco. Benzopyrene, a known cancer causing agent, is 70% more abundant in marijuana smoke than in tobacco smoke. Smoking less than one marijuana joint a day decreases vital lung capacity as much as smoking 16 tobacco cigarettes a day. Marijuana has an irritant effect on the airways, resulting in inflammation and airflow obstruction of the airways. Heavy pot smoking can cause sore throats, bronchitis, sinusitis, pharyngitis, emphysema and other respiratory difficulties in a year or less. Marijuana smoke weakens the defenses of the lung against infection and disease.

EFFECTS ON THE HEART

During the "high", which can last from 2-5 hours, the heart rate increases from the normal 70-80 beats per minute to as much as 130-150 beats per minute. The blood pressure also increases. As a result, the heart muscle requires more oxygen. The marijuana smoke increases the amount of carbon monoxide in the blood, thereby reducing the amount of oxygen delivered to the wanting heart muscle, and weakening its pumping action. Only 10 puffs of a joint reduces the amount of time one can exercise before chest pain occurs by 50%.

EFFECTS ON REPRODUCTIVE SYSTEM

Possible effects on the male include lowered sperm count, enlarged breasts, damaged sperm, and decreased testosterone (male hormone) levels. These effects seem to stop when usage is discontinued. The female may experience irregularities in the menstrual cycle, failure to ovulate, and lower female hormone levels. THC crosses the placental barrier and enters the fetal bloodstream. It also passes into breast milk.

EFFECTS ON THE BRAIN

In a study done on monkeys by Dr. Robert Heath of Tulane University, a heavy smoking group smoked 3 "monkey sized" joints with 2.5 to 3% THC per day, five days a week. A moderate smoking group, smoked one "monkey sized" joint twice a week. A light smoking group received one tenth the dose of the heavy smokers. A fourth group was given an equal dose of THC intravenously to control the variables of smoking effects. A control group was given inactive marijuana to smoke. The heavy, moderate, and intravenous groups showed lasting changes on their brain recordings after only 3 months of usage. The marijuana use was continued for an additional 3 months, and the abnormal changes persisted. The marijuana was discontinued for an 8 month period. Studies were then done on their brains with electron microscopy. The heavy, moderate, and intravenous groups had changes in brain function and in brain structure. Cellular changes were greatest in the areas which control emotion and memory. The findings correlate with the behavioral changes seen in marijuana users.

BEHAVIORAL EFFECTS

Two Philadelphia psychiatrists, Drs. Harold Kolansky and William T. Moore, conducted one of the earliest well-documented studies of the effects of cannabis on the psyche between 1965 and 1974. Only patients who displayed no psychological problems or predisposition to mental illness before marijuana usage began were used. The only drug used by patients was marijuana and/or hashish. They smoked two or more times weekly, usually two or more joints each time. Common symptoms displayed included mental confusion, inability to concentrate, diminished attention span, loss of memory, loss of motivation, lack of goals, and declining academic performance. Irritability and outbursts of aggression were common, especially if the patient was questioned about his personality change, new philosophy, drug use, or if his drug supply was threatened. Control of impulses and judgment was impaired. Most felt a growing sense of isolation from others, a desire to shun social activities, and deep-seated feelings of anxiety and depression. An altered sense of reality, and symptoms of paranoia were observed in many. All of these symptoms began with marijuana use and were reduced or disappeared within 3 to 24 months after marijuana use was stopped.

Dr. Jason Baron states, "Once marijuana no longer relieves the anxieties and conflicts, then a drug with stronger effects is often tried. Of the 6,000 patients treated by our program over the years, at least 90% started their drug usage with marijuana. Do not let marijuana smoking continue in your child, or he may become the first of many drugs he uses during life."[19]

REFERENCES: See page 11, Nos. 1 & 13-20.

MARIJUANA AND EFFECTS ON YOUNG ADULTS

by Harold Voth M.D.

In my experience there is only one certain way to be cured from marijuana smoking. The user must be totally isolated from the drug for a minimum of three months. Only after a period of sustained abstinence will the user become aware of the profound effects the drug has had on him and, at the same time, become free of its addictive effects.

The inability of the user to perceive himself or gain insight into what has happened to him over time is one of the truly pernicious and remarkable aspects of the effects of the drug. Talking rarely works; forthright decisive action by someone willing and able to take responsibility for the fate of the user is necessary. The chronic and heavy, and probably even moderate user, cannot take responsibility for himself.

CONTINUED ON PAGE 6

FROM PAGE 5 - DR. VOTH

How the person or persons exercise their responsibility to the user depends on the age of the user, his life circumstances, the severity of the retrogressive changes and deterioration of the user, and so on. I recommend sparing no effort whatsoever in achieving this objective. Searches are in order, use of police to back up parental authority if necessary, hiring a companion for the user, confinement to the home and hospitalization are all methods that I have recommended and have seen used.

Someone who cares must intervene, totally, consistently and with unrelenting perseverance. Efforts short of an all-out effort generally fail.

In summary, I believe chronic marijuana use affects judgment, motivation, perception, cognition, and will. In addition, the drug causes an overall deterioration of personality; it leads to an estrangement from the mainstream of life; it lowers performance in all areas; and it leads to a social phenomenon in which users bond together into both loose and tightly bound subsocial groups. The effects on the user's family life is frequently devastating.

In my opinion, the influx of marijuana into the United States constitutes a national crisis and should be combatted by the use of any and all methods until the flow of the substance has been completely stopped. It is remarkable that our federal government does not utilize our armed forces to supplement the coast guard and the county and state police to search out and destroy the ships and planes along with the cargo of drugs they carry...such an all-out effort seems entirely justified to me, in light of the incredible harm which is being done to millions of Americans...most of them our youth.

REFERENCE: See pg. 11, No. 7.

ALCOHOL

About 75% of Americans drink alcohol because they believe it helps them relax and is associated with social gatherings and "good times". While most new drinkers do not particularly enjoy the taste of beer, wine, and liquors, they persist until a taste for them is developed over time. Later many people begin to seek the relaxing effects of this drug to "forget" their troubles and to ease the stress of living.

IMMEDIATE EFFECTS

Alcohol is directly absorbed into the bloodstream from the stomach and small intestine, which if full, absorbs it more slowly than if empty. The blood carries alcohol to the brain, where it affects every level of the nervous system. Alcohol is a depressant, although as blood level rises or in small doses it causes a drinker to feel stimulated and confident. The rate of alcohol absorption is affected by a drinker's body weight (women, smaller, and younger people are affected faster than large men), presence of food in the stomach, and dilution of the drink. People who have just learned to use alcohol are more quickly and profoundly affected than "seasoned" drinkers, whose bodies have built up a tolerance to the drug. When the amount of alcohol in an individual's blood is somewhat high he tends to talk loudly and less distinctly, becomes socially uninhibited, or more courageous, and less attentive. An intoxicated person will have difficulty keeping his balance, will have a thwarted memory, and suffer from fluctuating moods. A very high blood alcohol level can cause muscle tremors, stupor, and eventual unconsciousness. A protective response by the body to an overdose of alcohol is vomiting. Death can occur from an alcohol overdose, particularly if tolerance is low, if other drugs or medications have been used, or if any other absorption factors mentioned above are present.

Contrary to popular belief, neither coffee, long walks, nor cold showers will speed the excretion of alcohol from the system. Only time will help a person become sober. Another myth is that beer and wine contain less alcohol than hard liquor. The alcohol content in a 12 oz. can of beer is the same as that of one 5 oz. glass of wine, or 1 1/2 oz. of 80 proof liquor (an average mixed drink).

INTERACTION WITH OTHER DRUGS

Of the 150 most frequently prescribed drugs, more than half contain at least one ingredient known to react adversely with alcohol. The interaction of other drugs with alcohol may be classified as antagonistic, additive, or supra-additive. The effectiveness of both drugs will be diminshed when the interaction is antagonistic. Alcohol inhibits the action of anti-convulsants and some anti-biotics. If the effect is additive, effects that are similar in the two drugs will be intensified. Antihistamines combined with alcohol will produce more sedation than if either drug were taken alone. Alcohol combined with marijuana results in poorer performance driving tests than when either substance is used alone. A supra-additive interaction produces effects more than double - in other words two plus two will not equal four but maybe five or even ten. A blood alcohol level as low as 0.10% combined with barbiturates has caused death. To prevent undesirable interactions, read labels and check with your doctor or pharmacist.

EFFECTS ON ADOLESCENTS

Since the average beginning age of alcohol use is 12.5 yrs. more research is needed on its effects on adolescents. Scientists think it is highly possible that alcohol can cause certain degenerative changes in the brain, especially in the pituitary gland, which governs growth, and the hypothalamus, which is closely associated with emotions and stress. The younger the age at which an individual starts to ingest alcohol, the greater the chances that he will develop into a chronic alcoholic. For the action of the alcohol is channeled directly toward the adolescent's imbalanced hypothalamus and autonomic nervous system, thereby obstructing his emotional maturation on both psychological and physiological levels. The regular or frequent ingestion of alcohol during adolescence may produce a permanent imbalance of the hypothalamus and a concomitant irreversible malfunctioning of the autonomic nervous system, thereby leading to the development of chronic alcoholism. In brief, the direct action of the alcohol on the hypothalamus produces chronic alcoholism."[11]

EFFECTS ON DRIVING

Alcohol is known to reduce a person's ability to judge distances, speed and angles, as well as one's ability to handle machinery. Because of its uninhibiting effects, alcohol causes a tendency in drivers to take risks and feel overconfident in spite of adverse conditions. It also causes impaired reflexes, forgetfulness and sleepiness. Over 60 deaths every day in this country are due to drunk driving.

CHRONIC EFFECTS ON BODY ORGANS

Continued use of alcohol damages and eventually destroys brain cells, since its action is six times as great on nerve cells as on other cells in the body. From 50% to 70% of alcoholics entering treatment have some central nervous system impairment. Long term alcoholics may develop the Wernicke-Korsakoff syndrome, (the alcohol amnesia syndrome).

Alcohol is directly toxic to the liver and can cause fatty liver, hepatitis and cirrhosis (degeneration). Alcoholism can be associated with pancreatitis, stomach ulcers, and cancers of the mouth, throat, larynx, stomach, intestines, liver, and pancreas. Many authorities feel alcohol abuse is the most common cause of vitamin and mineral deficiencies in adult Americans.

Alcohol has a toxic effect on the heart muscle, causing heart palpatations and difficult breathing. It can lead to heart failure. High blood pressure is common among alcoholics.

Many hormonal imbalances are also caused by alcohol, especially in the reproductive system. It is closely associated with male impotence, infertility, and menstrual disturbances in women. It causes increased insulin secretion, causing diabetic-like symptoms in some people.

In pregnant women, even small amounts of alcohol can pass through the placenta and affect the fetus. Fetal Alcohol Syndrome identifies a characteristic combination of birth defects in infants born to alcoholic mothers. It is the third leading cause of mental retardation in newborns. Alcohol passes into breast milk to the nursing infant.

PHYSICAL DEPENDENCE AND WITHDRAWAL

Physical dependence can develop after 3 to 5 years of very heavy drinking, but more often it requires 10 to 20 years of heavy drinking. Early stages of the withdrawal syndrome may be characterized by nausea, vomiting, irritability, tremors, sweating, and insomnia 6 to 8 hours after heavy drinking has stopped. A more advanced syndrome, delirium tremens (DTs), can include increased blood pressure, heart rate, and temperature; visual, auditory, and tactile hallucinations; severe confusion; heavy tremors; and possible convulsions 2 to 4 days after abrupt withdrawal. Even with proper medical care DTs can be fatal.

CROSS TOLERANCE

A by-product of increased tolerance in heavy drinkers is a cross-tolerance for certain drugs. It occurs only when the person is sober. He may either be less sensitive or more sensitive to the other drug. Alcoholics require higher doses of ether to be anesthetized. Barbiturates or sedatives will have less effect, consequently the sober heavy drinker may take larger doses. Other drugs may require lower doses for the desired effect. Some chemicals may also be more toxic for the alcoholic. Carbon tetrachloride will damage the liver of an alcoholic more than that of a non-alcoholic.

REFERENCES: See page 11, Nos. 1 & 8 - 12.

STIMULANTS

Chemical agents which stimulate the central nervous system are called stimulants. Two of the most prevalent legal stimulants are nicotine, found in tobacco, and caffeine found in coffee, tea, chocolate, and some bottled beverages such as Coca-Cola and Pepsi-Cola. These stimulants relieve fatigue and increase alertness. More potent stimulants which have a high potential for dependency and tolerance are under regulatory control of the Controlled Substance Act. They include cocaine and the amphetamines.

The effects of amphetamines and cocaine are very similar, although the amphetamines are slower and longer acting. Possible effects of stimulants are increased alertness, euphoria, increased energy, a feeling of being powerful and able to master any task, followed by irritability, anxiety, and apprehension. Physical effects include dilated pupils, increased pulse rate, elevated blood pressure, insomnia, loss of appetite, dry mouth, and bad breath. Very high doses can produce tremors of the hands, arms, and legs, hallucinations, paranoia, disorientation, and seizures. If taken by intravenous injection, a sudden "flash" or "rush" usually occurs, followed by a very depressing "crash," which the abuser often counteracts with another dose.

Chronic stimulant users are usually polydrug users. They rely on alcohol and/or other depressant drugs to relieve their tenseness, depression, and insomnia caused by their stimulant use. Chronic users can develop a measles-like rash, weight loss, and probably because of poor nutrition, have trouble with their teeth, gums, nails, and hair. They may begin grinding their teeth, have muscle twitches, exhibit memory loss and paranoia with hallucinations, and have decreased sex drive. Brain damage can occur. When used intravenously over a period of time the user is subject to the complications of unsterile and adulterated injections such as blood infections, AIDS, hepatitis, lung abscesses and endocarditis.

Overdoses may be indicated by dizziness, tremors, an agitated state, headache, flushed skin, chest pains, sweating, vomiting and cramps, high fever, and possible convulsions. Fatalities have been reported among athletes who have been under extreme exertion after using moderate doses of stimulants.

Immediate withdrawal symptoms may last for several days with profound depression, apathy, fatigue, and disturbed sleep for up to 20 hours a day. Anxiety, tenseness, impaired perception and thought processes, and suicidal tendencies may persist for weeks or months.

COCAINE

"An incredible 22 million Americans - one out of every 10 - report that they have used cocaine at least once. And every day, some 5,000 teenagers and adults try it for the first time".[22] It is the fastest growing drug of abuse. In a recent study, the average daily cocaine user spent a weekly average of $637 for cocaine, with a range of $100 to $3,200.[22] It is often called the "Great Addictor".

Cocaine is distributed as a white crystalline powder. In professional medicine it is used as a local anesthetic. Illegally it is used for its euphoric effects. It is usually sniffed or "snorted" through a straw, rolled up dollar bill, or tiny "coke spoon". Because it constricts the blood vessels in the nose, it often results in a stuffy, running nose and nasal irritation, relieved by nasal decongestant sprays. Chronic snorting can lead to erosion and even perforation of the nasal septum. For immediate, more intense, but shorter results it can be injected intravenously or smoked in a free-base form. Using special kits available in paraphernalia stores, the user removes the hydrochloride salt and inert adulterants from the cocaine converting it to free-base, which is suitable for smoking. The conversion process is very dangerous because it uses ether, a highly flammable and explosive substance, which is usually evaporated over a flame. "Freebasing" and IV injection also entail the risk of respiratory failure and death. Depending on the avenue of administration, effects can last several hours but the euphoric high lasts only 15 to 40 minutes followed by a let-down and desire for more of the drug. Chronic cocaine users are sometimes afflicted with tactile hallucinations such as imaginary insects crawling under their skin, often referred to as "coke bugs."

Some slang terms for cocaine are big C, coke, nose candy, snow, white, and snowbirds. Synthetic cocaine composed of a "caine" drug such as lidocaine and glucose is being sold legally as an incense in head shops and through the mail under such names as Toot, Florida Snow, Supercaine, Ultracaine, Base-O-Caine, and Superior Caine. Deaths have been reported from these preparations which are not controlled by the Drug Enforcement Administration.

AMPHETAMINES

Amphetamines are used medically for narcolepsy (uncontrollable desire for sleep), hyperactive behavior in children, and for weight reduction. Vast quantities are produced illegally for the illicit market, especially methamphetamine ("crystal methedrine"), the most potent amphetamine. They are ususally taken orally but can be injected intravenously. Some brand names are Benzedrine, Biphetamine, Desoxyn, and Dexedrine. Look-a-like pills are often sold as amphetamines. Slang terms include speed, uppers, ups, beans, bennies, black beauties, bumblebees, hearts, pep pills, co-pilots, and footballs.

Other stimulants which may be abused are Ritalin and Cylert used medically for hyperactive children, and the appetite suppressants such as Preludin, Didrex, Pre-State, Voranil, Tenuate, Tepanil, Pondimin, Sanorex, Plegine, and Ionamin.

REFERENCES: Page 11, Nos. 1, 21, 22,& 29.

DEPRESSANTS

Substances classified as depressants under the Controlled Substance Act have a high potential for physical and psychological dependency with tolerance developing rapidly. In street language they are "downers" or "downs." Sedatives or sleeping pills and tranquilizers make up this classification. Most of these drugs are taken orally. Therapeutic low doses produce mild sedation and relief of anxiety, irritability, and tension. Higher doses, used by abusers, may relieve anxiety, produce temporary euphoria or the other extreme of mood depression and apathy. They are often used to sooth "jangled nerves" brought on by stimulants, to soften "flashbacks", or to ease a withdrawal from heroin. Intoxicating doses can result in impaired judgement, slurred speech, distorted vision, and often unrealized loss of motor control, making driving dangerous. The user may be quarrelsome and appear intoxicated with no odor of alcohol. Large doses could also induce sleep, stupor, respiratory depression, coma and even death. When mixed with alcohol or other drugs the effects can be very dangerous, sometimes causing death. A moderate overdose resembles alcohol intoxication. A severe overdose causes dilated pupils, cold clammy skin, weak and rapid pulse, either slow or rapid breathing and possible coma. Withdrawal symptoms of depressant addiction are more severe and dangerous than of heroin addiction. Withdrawal should only be attempted in a controlled hospital environment.

SEDATIVES

The following include the more common street drug depressants. Among the barbiturates are Nembutal, Seconal, Amytal, and Tuinal. Some slang terms, often indicating the color of the pills, are barbs, bluebirds, blue devils, red birds, red devils, yellow jackets, and yellows.

Commonly abused non-barbiturate sedatives are Placidyl, Chloral Hydrate, Doriden, Noludar, and Methaqualone (Quaalude). In 1980 Quaaludes followed marijuana as the drug of choice of teenagers. In 1984 this drug was virtually eliminated from the streets when the only legal manufacturer of Quaaludes in the U.S. discontinued their production, and the DEA declared war on illegal importation of the drug.

TRANQUILIZERS

Tranquilizers are the least toxic of the depressants but are highly addictive. Because they are fat soluble, they are eliminated from the body slowly, and withdrawal symptoms do not occur until 7 - 10 days after the drug is discontinued. They are used therapeutically to relieve muscle spasms and anxiety. Since both alcohol and tranquilizers are found in many homes, they are easily abused together by young people. The most common tranquilizers are Valium, Librium, Equanil, Miltown, Serax, Tranxene, and the more potent ones, Thorazine, Mellaril and Halcion. Valium is the most frequently prescribed drug and the most frequently abused drug in drug related emergency room admittances in this country.

REFERENCE: See page 11, No. 29.

LISTEN TO WGTS 91.9 FM

STRAIGHT TALK

RADIO SHOW

TUESDAY EVENINGS - 6:30 TO 7:30

Bill Burns interviews a guest who is experienced in a specific aspect of substance abuse. Call in with your questions about symptoms of drug and alcohol use, rehabilitation programs, parent awareness groups, etc. The program is produced by the Panel on Drug Awareness (PDA), a non-profit media production company.

HALLUCINOGINS

Hallucinogens, often called psychedelics, affect perception, sensation, thinking, and emotions. The user may have difficulty distinguishing between fact and fantasy and may refer to seeing sounds or hearing colors. Other possible effects may include dilated pupils, incoherent speech, lack of coordination, cold, sweaty hands and feet, vomiting, laughing, crying, shivering, goose pimples, irregular breathing, a strong body odor, and suicidal or homocidal tendencies. Chronic use can cause brain damage. The effects may be different in each person with each administration. Persons in hallucinogenic states should be upset as little as possible to keep them from harming themselves or others.

PCP

Phencyclidine or PCP is the most commonly used hallucinogen. Many authorities consider it to be the most dangerous of all drugs including heroin. Because it is so easily and inexpensively produced in bootleg laboratories, it is often sold as another drug, especially LSD. It is sold as a liquid, a white powder (angel dust), crystals, or in pills called "hogs" or PeaCe Pills. PCP can be taken orally or injected but smoking it after being sprayed on cigarettes, parsley or marijuana is the preferred route. The liquid is sometimes dropped in the eye for faster absorption. This can damage the eye. PCP has the odor of ether. One ounce of PCP yields 30-40 dime ($10) bags or foil packets. When sprayed on marijuana it costs about $15 for one fourth of a teaspoon. Some slang terms for PCP include KW, killer weed, green, tac, DOA (dead on arrival) rocket fuel, supergrass, and elephant tranquilizer. PCP sprayed on marijuana is called lovely or loveboat.

Diagnosis of PCP use is frequently missed because the user often looks normal, yet PCP can cause very violent and bizzare behavior, injuring the user or those around him. There are several reasons for this. Physical strength can be greatly increased under the influence of PCP. Police report incidences of users breaking handcuffs and becoming very violent. The drug is an anesthetic and numbs the user so he does not feel physical harm he may do to himself. The drug is also an amnesic so the user may not remember what he did under the influence of the drug. More deaths are caused by the resultant behavior than from the physical effects of the drug. Psychotic behavior may last for as long as 2 weeks after a single dose. Some adolescents are smoking PCP on a daily basis. When combined with marijuana on a daily basis the user can barely function.

LSD

Lysergic acid or LSD is once again a poplular street drug. It is a difficult and dangerous drug to manufacture. For this reason PCP is often sold as LSD. It is odorless, colorless, and tasteless. Doses of LSD are miniscule - an aspirin sized tablet makes 2 million hits and is worth $600,000. LSD requires very careful handling since it is absorbed through the skin when touched. It is sold in the form of tablets, thin squares of gelatin ("window panes"), and impregnated paper ("blotter acid"). The window panes can be put in the eye under the eyelid for quick absorption or for quick removal of evidence of possession. The blotter acid often looks like stamps which have pictures or Disney type characters (especially attractive to children) on them. It is put on the tongue or licked. Drops of LSD can be frozen in ice cubes or dropped into someone's drunk unknown to the recipient. Some slang terms for LSD are acid, green or red dragon, paper acid, white lightening, blue heaven, purple haze, sugar cubes, and blotter acid.

LSD is stored in the fatty tissue of the brain and slowly released back into the bloodstream. This can cause the user to experience "flashbacks", which are the recall of unpleasant effects of the drug weeks or months after the last dose.

MESCALINE

Mescaline is the active ingredient of the peyote cactus and is used as part of the religious rites of some American Indian tribes. It is sold as Peyote buttons which are sliced off the plant and dried to form a hard brown disc. The buttons are chewed and swallowed and have a very foul taste. It is very irritating to the eyes requiring the protection of sunglasses for a week after usage. Synthetic mescaline is rarely found on the streets because of its very high cost. A drug sold as mescaline is usually PCP.

MUSHROOMS

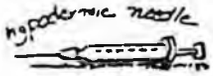
Psilocybin and Psilocyn are derived from certain mushrooms which are brewed in a tea. The taste is very unpleasant. They are chemically related to LSD. Kits are available for growing them through drug culture magazines. Substances sold as mushrooms usually are PCP.

REFERENCES: See page 11, Nos. 1 & 29.

CALL THE ABC

Suspected violations of alcohol control laws may be reported to the Virginia Department of Alcohol Beverage Control (ABC) by calling a toll-free number in service 24 hours a day, 7 days a week. The Department urges citizens to call. Know the name, address, and town where the violation occured.

CALL 1-800-522-3200



NARCOTICS

The term narcotics refers to opium, its derivatives, and synthetic substitutes. Narcotics are physically and psychologically addictive drugs. In professional medicine, they are the most effective pain relievers known. Drug abusers use them for their euphoric effects. Other effects may include drowsiness, stupor, poor coordination, confusion, watery eyes, pinpoint pupils, loss of appetite, slowed breathing and pluse rate, nausea, constipation, and excessive itching. Indications of overdose are deep sleep, stupor, slow shallow breathing, cold clammy skin, limp body, and a relaxed jaw. Coma and/or convulsions can occur. Death may result from respiratory depression. Chronic addiction can lead to malnutrition, neglect of general health, infections from contaminated syringes at sites of injections, blood infection, hepatitis, AIDS, or endocarditis. Physical withdrawal symptoms may include muscle cramps, chills and sweating, and nausea which may last 4 to 10 days after the drug is stopped.

The most commonly abused narcotics are the most addictive ones with tolerance developing rapidly. The intravenous route, "mainlining," is preferred by users. Heroin gives the most intense "high". It is a powder which may range in color from white to dark brown. It may also be snorted, smoked, or injected under the skin, "skin popping." Some slang terms for heroin are big H, boy, brown sugar, snow, stuff, junk, smack, scag, and horse.

Morphine, Demerol, Methadone, Dilaudid, and Percocan are other narcotics frequently abused. They may be taken orally but injection is preferred by abusers.

Opium may be smoked through a long stemmed pipe. It is also used in antidiarrheal preparations such as paregoric.

Codeine is less addictive and produces less euphoria than the above drugs. It is usually taken orally in preparations combined with Emperin Compound, Aspirin, or Tylenol. Codeine also acts as a cough suppressant and is found in some cough medicines such as Robitussin AC, Cheracol, and Elixir of Terpin Hydrate with Codeine. While Codeine is generally not preferred by narcotics addicts, it should be noted that it is a drug often present in many homes of adolescents who are experimenting with drugs. It should be kept in a locked container.

Darvon and Talwin are pain relievers, not classed as narcotics, but their misuse has caused them to be regulated by the Controlled Substance Act.

Fortunately, narcotics are not frequently abused by adolescents, but as young adults become bored with the other drugs they have been using and their tolerances build up they "graduate" to this classification.

REFERENCES: See page 11, No. 29.

* * * * * COMING IN APRIL * * * * *

PANDAA MOCKTAIL PARTY

DANCE TO THE STARLIGHT ORCHESTRA'S BIG BAND MUSIC OF THE PAST 40 YEARS

AN ALCOHOL FREE DANCE

PARENTS OF TEENS

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CARE

CALL 237-8121

Parents who have had a child recover from an alcohol and/or drug problem give their volunteer time to help you understand what is happening in your family. They will listen to you. They can relate their own personal experience to you. They understand the hurt, anger, fear, and disruption caused by drug and alcohol problems in the family. They will help and support you.

A parent is on call Monday thru Friday, from 9 a.m. to 5 p.m. to answer your questions, give you support, and mail information to you. Resource lists for those conducting drug awareness meetings are also available. The area code for callers outside the Washington DC area is 703.

DRUG INFORMATION SERVICE

A state-wide toll-free telephone information service provides telephone access to recorded information tapes, 2-3 minutes long, on drug and alcohol related topics. Trained operators are available to supplement the taped messages in the event of emergencies. It is a 24 hour service for push button phones, and a 9 a.m. to 3 p.m., Mon. thru Fri. service for rotary dial phones. Tapes and their No. Virginia code nos. include:

Marijuana
- 125 - a brief overview
- 121 - effects - females
- 126 - effects - males
- 120 - damage to lungs
- 127 - increased potency
- 119 - physical tolerance
- 128 - emotional impact
- 124 - body accumulation
- 117 - Amphetamines
- 129 - Tranquilizer
- 130 - Barbiturates
- 134 - Drug use by youth
- 135 - Alcohol
- 118 - Cocaine
- 133 - Codeine
- 132 - Heroin
- 131 - LSD
- 115 - Opium
- 114 - Morphine
- 113 - Methadone
- 116 - PCP
- 112 - Smoking

CALL 1-800-552-3784

DID YOU KNOW?

* Virginia law allows a judge to suspend the drivers license for up to one year of any underage person convicted of purchase or possession of alcoholic beverages. This is in addition to a fine for the offense. From Va. Code *4-62, & 4-112(c).

* You can be fined up to $500 and receive up to 6 mos. in jail for drinking or possession of any alcohol on school grounds during school hours or any school activity. From Va. Code *4-78.1.

* You can be fined up to $1,000. and/or be put in jail for up to 1 year if you purchase alcoholic beverages for anyone under 19 years of age. From Va. Code *4-112.1(a).

* If your minor child is abusing driving responsibilities, you can have his license suspended and ask that no duplicate be issued.

INHALANTS

It was once thought that "sniffing" was just a "passing thing" that kids "grow out of." Recent studies show that these youngsters often become our heaviest drug users. As nitrous oxide and butyl nitrite become more and more popular with college students, inhalant use is no longer just "kid stuff."

Inhalants are volatile substances inhaled intentionally for their intoxicating effects. Their effect is immediate because the substance passes directly into the blood stream. Effects usually last for a few minutes, but sometimes can last longer. Because the high is so short, users often inhale repeatedly during each sniffing episode. Inhalants can be classed into three main categories: 1. commercial solvents and aerosol sprays mostly used as cleaning or beauty agents, glues, or as fuels; 2. anesthetics; and 3. the volatile nitrites.

SOLVENTS AND AEROSOL SPRAYS

Some commonly abused items in this group are spray paints, hair sprays, vegetable oil sprays, cold weather car starters, air sanitizers, window cleaners, furniture polishes, insecticides, disinfectants, spray medications, deodorants, gasoline, transmission fluid, glues, paint thinners, nail polish and removers, magic markers, typing correction fluid, and shoe polish. Low doses may produce slight stimualtion, moderate doses cause one to become uninhibited, and high doses can cause loss of consciousness and sometimes death. Especially dangerous is inhaling from a bag. Other effects may be drowsiness, headaches, nausea, vision disturbances, watering of eyes, excess nasal secretions, coughing and salivation, chemical smell on the breath, sores on the nose and mouth, pallor, flushing, and poor muscular control. Long term use can cause damage to the central nervous system, liver, kidneys, blood, and bone marrow.

ANESTHETICS

Nitrous oxide (laughing gas) is used as a general anesthetic, especially in dental offices, and among other uses, as a propellant for whipped cream. For making whipped cream it is either in an aerolized spray can and considered a legitimate food additive, or in a small 8 gram metal cylinder used with a dispensing machine. These cylinders are called "Whippets" and are now sold in head shops and some record stores. Paraphernalia is sold to use with the cylinder, such as a balloon from which the gas is inhaled and a pipe ("Buzz Bomb") which combines with the cylinder. The production of Whippets has tripled in the last few years.

Adverse reactions can include shortness of breath, nausea, variations in heartbeat, and hearing loss. Long term use can cause nerve damage. Death can occur if the gas is inhaled without sufficient oxygen.

VOLATILE NITRITES

The most common nitrites in use are amyl nitrite and butyl nitrite. They are used as a euphoriant and as a sexual stimulant. The high produced lasts only a few seconds to a minute. Consequently users tend to inhale repeatedly during each sniffing episode. The nitrites temporarily dilate the blood vessels, causing the heart to beat harder and faster and fill the blood vessels with blood. Other effects include rapid pulse, headaches, dizziness, flushed face, lowered blood pressure, nausea and vomiting, fainting, and involuntary passing of urine and feces. Increased intraocular pressure with headaches can be a symptom of nitrite use rather than glaucoma. Long term use can cause an impetigo-like rash around the nose and mouth. It is felt that prolonged use may be linked to hepatitis and brain hemorrhage.

Amyl nitrite is a clear yellowish liquid with an ethereal, fruity odor. It was formerly used for treatment of the heart disease, angina pectoris, but has been replaced by other drugs. It is supplied in 0.3 ml. glass containers, enclosed in a gauze jacket of woven absorbent covering which is easily broken and inhaled. The popping sound when broken gives it the street name, "poppers" or "snappers."

Butly nitrite is a liquid which smells like dirty socks or a locker room. A fragrance is added to it and it is legally sold as a "room odorizer" in adult book stores, head shops, and by street vendors. FDA has no control over it. From 4 to 10 million vials of it are sold each year, mainly to older teenagers and young adults. Trade names include Rush, Bolt, Locker Room, Bullet, Jac Aroma, Climax, Loc-A-Roma, Shotgun, Satan's Scent, and many others.

REFERENCES: See page 11, Nos. 22 - 27.

LOOK-ALIKES

A popular addition to the drug scene are the look-alike drugs. Originally they were manufactured to resemble, or look like, prescription stimulants and depressants, with numbers, letters, or markings similar to the drugs they were copying. Because of the passage of "look-alike" laws and certain judgements by the FDA, the manufacturers are also selling pills that no longer look like controlled substances. They are sold in bottles of 100 or 1,000 in stores and through flyers in the mail, often referred to as "legal stimulants", allowing a young seller a very high profit margin. When sold as uppers these pills usually contain caffeine alone or in combination with ephedrine. When sold as downers they usually contain antihistamines.

CAFFEINE: At normal doses, caffeine is a mild stimulant that reduces fatigue and suppresses appetite. In larger amounts, or when there is a sensitivity to caffeine, it may cause restlessness, anxiety and insomnia. The amount of caffeine in look-alikes varies anywhere from 37.1 mg. to 323.8 mg. An average cup of coffee contains 100 mg. of caffeine. Serious side effects have been reported from using more than 600 mg. of caffeine a day.

EPHEDRINE: Medically, ephedrine is often used as a broncho dilator in asthmatic preparations and as a decongestant in prescription and over-the-counter preparations. It is similar to adrenalin. The effects of ephedrine are stimulation of the central nervous system, constriction of the arterioles which causes shrinkage of the mucous membranes and relief of nasal congestion, increased blood pressure and heart rate, dilation of the pupils, dilation of the bronchials, nausea, headache and anxiety.

ANTIHISTAMINES: Antihistamines are used to relieve symptoms of colds and nasal allergies, and to relieve itching caused by allergic reactions. Side effects include drowsiness, dizziness, dryness of the mouth and throat, and disturbed coordination. However insomnia, nervousness, and even convulsions can occur.

Each of the ingredients in look-alikes is dangerous when taken in sufficient quantities. To get a high, kids quickly learn they must ingest several of these pills, or even a handful. By October of 1981, 12 deaths had been associated with these drugs due to caffeine intoxication. There is also a danger that a child accustomed to the weak "copy-cat" drug will unknowingly buy the authentic drug, take several pills, and overdose.

REFERENCE: See page 11, No. 30.

* * * * * * * HOTLINES * * * * * * *

PANDAA Parents of Teens (Wash DC Area)
703-237-8121, Mon. - Fri., 9 am to 5 pm
National Federation of Parents
local, 649-7100, or 800-554-KIDS
Pride Drug Information - 1-800-241-9746
National Institute on Drug Abuse
local-443-6500, or 800-638-2045
National Cocaine Hotline - 1-800-COCAINE
Fairfax-Woodburn Center - 573-5679
Family & drug abuse emergencies
Families Anonymous-Richmond-804-771-9109

PANDAA

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Editor - Joyce Tobias

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PANDAA (Parents Association to Neutralize Drug and Alcohol Abuse, Inc.) was founded at Jefferson High School in Fairfax County, VA in April, 1980 by a group of parents concerned about teenage alcohol and drug abuse. The goals of the group are to combat substance abuse in the home, school, and community and to educate the public about all aspects of substance abuse. PANDAA is incorporated and has tax exempt status. There are no salaried personnel. All donations are tax deductible. Membership is open to any individual upon payment of $5.00 annual dues which includes a subscription to the newsletter. PANDAA is supported solely by dues and donations.

PANDAA publishes an educational 8 page newsletter 5 times a year. Its circulation is 5,000 copies. It is mailed to PANDAA members, federal, state, and local legislators, law enforcement personnel, civic leaders, civic clubs, youth leaders, churches, school counselors and principals, pediatricians, and treatment programs, and it is distributed at awareness meetings, workshops, and conferences.

PANDAA also publishes a 12 page GUIDE TO CHEMICAL USE for parents and professionals which includes why kids do drugs, signs of use, stages of use, effects on the family, treatment, and the drugs of abuse including alcohol. An order form for the GUIDE on page 7.

PANDAA works closely with the County School System strengthening school policies and educating school personnel.

The PARENTS OF TEENS program offers a confidential listening ear telephone service (237-8121) Mon. thru Fri. from 9-5 for parents in need of help and support in identifying an alcohol or drug problem. Materials on drug information, treatment programs, and resource lists for awareness programs may be received by calling this number.

The COURTWATCH committee observes drug cases weekly and is effecting changes in the judicial system. PANDAA also lobbies for legislation regarding substance abuse.

PANDAA does many speaking engagements and assists in the formation of new groups. It is a member of the National Federation of Parents and the Virginia Federation of Parents.

PANDAA BOARD OF DIRECTORS

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PANDAA PHILOSOPHIES

Our children have the right to grow up in a drug free environment. Parents have the responsibility to be informed about substance abuse, to communicate to their children a clear and firm "no use" position about alcohol and drug use, to set an example to their children, and to use consistent discipline combined with love and care. A parent's right takes precedence over a child's right to privacy whenever a situation is threatening to the child's health and safety.

PANDAA believes the use and abuse of both legal and illegal drugs has reached epidemic proportions. It has extended into every segment of our communities bringing with it corruption, violence, property loss, family disintegration and disregard for the law. It has become the number one health problem for the 15 to 24 yr. age group, the only age group with a rising death rate.

PANDAA opposes the use of illegal drugs or illegal use of mood altering prescription drugs. PANDAA considers any alcohol use under the legal drinking age abuse. We consider alcohol to be a DRUG which affects emotional and physical development in adolescents, and is capable of producing dangerous changes in behavior and well-being.

The initiation of adolescent alcohol and/or drug use is caused by pro-alcohol and drug media messages, drug using role models, peer pressure, curiosity, availability, acceptance by society, inadequate laws and enforcement of laws. Usage continues because it gives short term pleasure, it becomes a temporary problem solving tool, and society imposes few consequences for abuse. As usage continues it can develop into the disease of chemical dependency which affects the entire family and usually requires treatment. Adolescents can become chemically dependent in 6 months to 1 year while in the adult, dependency usually occurs after 5 to 20 years of usage.

The use of drugs is a clear choice and the user is responsible for any actions committed while under the influence of any drug. Juveniles and adults involved in alcohol and drug related crimes should be evaluated for chemical dependency and where appropriate treatment should be mandated, along with other appropriate consequences. We consider drug trafficking a violent crime which demands serious consequences.

The treatment of chemical dependency has a low success rate. Development of more successful treatment modes is needed. Treatment programs must be free of legal and illegal mood altering drugs including alcohol. They should be accessible, affordable, and acceptable to health insurance plans.

Schools have an obligation to the community and the families they serve to provide an alcohol and drug free learning environment for students. Schools should provide drug education, strictly enforced consequences for violations, substance abuse recognition training for school personnel, help families recognize chemical dependency, and require treatment for readmittance to school when chemical dependency has been diagnosed.

Elected and appointed officials have a responsibility to be informed, enforce the laws as written, and support improved and necessary new laws.

PANDAA GOALS

PANDAA's goal is to eliminate alcohol and drug abuse in our community by:

Offering support and educating families, professionals, and the community about the dangers and legal responsibilities of illegal drug and alcohol use, and prevention and intervention techniques.

Working with school officials, parents, and students for a drug free envitonment at school.

Working within the community to de-emphasize the "do drug" messages, opposing the aggressive commercial promotion of alcohol, and encouraging public and social support for those who choose not to use alcohol or drugs.

Supporting the efforts of law enforcement officials by courtwatching, lobbying, and other civic action activities.

Assisting in the formation and development of groups similar to PANDAA.

LEGISLATIVE GOALS

All persons convicted of a drug felony should have their bonds revoked when found guilty and experience incarceration until sentencing.

All juveniles and adults involved in an alcohol or drug related crime should be evaluated for chemical dependency and mandated to treatment when appropriate as a part of his sentence.

Any juvenile convicted of an alcohol or drug related crime should have his driver's license revoked until his 18th birthday.

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FROM PAGE 1 - A PARENT'S STORY

about my own feelings that I did not know at this point whether I did reject him or not. Psychiatrists, family therapists, and drug counselors reinforced my guilt by attributing his drug use to problems in my marriage, problems which were being exacerbated or actually caused by his drug use! This self-doubt, leading to self-hatred for being such a terrible father, was for me the worst aspect of the ordeal. Meanwhile, I was getting about three or more phone calls a week in my office from teachers, counselors, and the principle telling me he had come to school drunk, had been taking pills at school, was missing from class, etc. As I now know, he was in fact using his school as a place to obtain drugs and make contact with "druggie" friends.

Meanwhile, my daughter, in the sixth grade at the time, was following in his footsteps, getting more and more hostile, carving names of rock groups into her hand with razors, wearing tons of make-up, and basically spitting in the face of our family. My marriage was going down the drain along with my kids' lives. Everyone in the home was in tremendous pain. My third kid was withdrawing into himself, and also starting to experiment with drugs to gain the acceptance of his druggie siblings and friends.

Fortunately for us, we found a very rigorous drug rehabilitation program which worked for our family. Our kids have undergone what appears to be a transformation, but is really just the result of good, loving therapy leading to self-awareness. I personally feel better now than ever before in my life - happier with myself, more loving, and stronger than ever before. More has happened than just getting rid of drugs, much more. Each of us has grown with the support, love and help of this program, and I will be grateful from the depths of my heart to it forever.

COURTWATCH

What happens to drug dealers? Join the PANDAA COURTWATCH and find out. We attend trials and sentencings of drug related cases and compile our observations. With our data we are effecting changes in the judicial system and the laws. If you can help once a week or once a month call:

CALL 237-8121

VIRGINIA TEACHER IMMUNITY LAW

§8.01-47. Immunity of school personnel investigating or reporting alcohol or drug use: In addition to any other immunity he may have, any teacher, instructor, principal, school administrator, school coordinator, guidance counselor or any other professional or administrative staff member of any elementary or secondary school, or institution of higher learning who, in good faith with reasonable cause and without malice, acts to report, investigate or cause any investigation to be made into the activities of any student or students or any other person or persons as they relate to alcohol or drug use or abuse in or related to the school or institution or in connection with any school or institution activity, shall be immune from all civil liability that might otherwise be incurred or imposed as the result of the making of such a report, investigation or disclosure. Virginia Code 1950, §8:631.1; 1972, c.762; 1977, c.617; 1981.

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Position Statement on Psychoactive Substance Use and Dependence: Update on Marijuana and Cocaine

Am J Psychiatry 144:5, May 1987

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Position Statement on Psychoactive Substance Use and Dependence: Update on Marijuana and Cocaine

This statement is an adjunct to the position statement on substance abuse published in the June 1981 issue of the American Journal of Psychiatry, *which emphasizes diagnosis and treatment. It replaces the position statement on marijuana laws published in the May 1979 issue of the* American Journal of Psychiatry. *The statement was prepared by the Committee on Drug Abuse[a] of the Council on Psychiatric Services and was approved by the Assembly in November 1986 and by the Board of Trustees in December 1986.*

The misuse of psychoactive substances is the nation's foremost public health challenge. The use and abuse of alcohol, cigarettes, illicit drugs (heroin, cocaine, marijuana, etc.), and licit drugs (sedatives and tranquilizers) are by far the largest cause of preventable and premature illness, disability, and death in our society. The annual economic cost of alcohol and drug abuse has been estimated to be $136 billion, over four times that of cancer and nearly a third greater than that of cardiovascular disease (1). Illicit drug use has increased so rapidly over the past 25 years that it may be difficult for someone over age 50 to comprehend the extent to which drugs have permeated our society. Experience with illicit psychoactive drugs was restricted to 2% or less of the population in most areas of the country in the early 1960s (2). In contrast, the 1982 household survey (3) found that almost a third of the household population in the United States age 12 and older had had some experience with illicit drugs. Almost 60 million household residents had tried marijuana, and an estimated 20 million were current users. In 1982, it was estimated (4) that over 20 million had tried cocaine and over 4 million were current users. The prevalence of cocaine use and abuse has increased dramatically in the ensuing 4 years (4).

Illicit drug use is most prevalent in young adults. Typically, children begin experimenting with drugs of abuse by trying alcohol and cigarettes in early adolescence. By the time they complete secondary school, they have established attitudes toward drugs and patterns of use that will carry them through much of their lives. Most adults addicted to nicotine through smoking cigarettes established regular smoking in their teens. Adult users of cocaine and opiates generally began drug use in adolescence and may have been heavy marijuana users (5). In addition to exposing themselves to the risks of drug use (automobile accidents, overdose, or impaired physical, emotional, and psychological development), adolescents are establishing attitudes toward and actual patterns of use that have profound long-term consequences on health. By the time they graduate, more than half (54%) of high school seniors have tried marijuana and a fourth (26%) are current users. Cocaine use tends to begin a few years later than marijuana use, and heavy marijuana use is an important risk factor for cocaine use. Nevertheless, cocaine use now is increasing among our high school population. In the 1985 national survey of high school seniors (6), it was found that 17% had tried cocaine and almost 7% were current users.

In addition to statistics on the prevalence of use, there are now data from National Institute of Mental Health (NIMH) catchment area studies (7) on the lifetime prevalence of substance abuse disorders, which was found to vary from 15.0% to 18.1% among the three sites reported. These rates were significantly higher than the lifetime prevalence of any other group of disorders (except for phobic disorders at one site).

SOCIAL CONSEQUENCES OF USE OF MARIJUANA AND OTHER DRUGS

Young people may use drugs in an attempt to alleviate problematic family relationships. Over the short term, drugs may allow the young person temporarily to ignore intrafamilial strife, including developmental adjustments between child and parents and among siblings. Regular or heavy drug use undermines the adolescent's ability to work through these problems with other family members, thereby exacerbating family problems over the long term. The heavy drug user may withdraw socially from other family members, refuse to consider their needs and concerns, and put his or her own needs above those of the family. Theft from other family members (to obtain drugs) and lying (to hide drug use) undermine the trust necessary for coexistence within the family. Angry outbursts, property destruction, and intrafamily violence can ensue. Alienation of the drug user from the family, once present, is difficult to repair (8). Adult substance abusers also exert powerful effects on their families. Families react variably but often go through stages of denial, overprotection, personal mental illness, and family disruption. The effects on children in such families have been so profound that a national movement, the Adult Children of Alcoholics, has recently emerged to provide support and understanding (9–11).

Heavy drug use can precipitate financial problems in two ways. First, drugs themselves cost money; drug expenses are proportional to the cost of the drug, frequency of use, and dose consumed. Such costs mount as tolerance develops, habitual use becomes established, and larger amounts of drug are consumed more often. A second source of financial problems is unemployment or job loss. Early drug use may seem to facilitate work by alleviating fatigue or boredom or helping the user tolerate work-related stresses. Eventually, continued drug use undermines the person's energy, ambition, concentration, problem-solving abilities, performance, productivity, and social skills in dealing with co-workers and supervisors. Drug-induced paranoia, if present, further exaggerates interpersonal dissensions. In addition to individual financial loss, theft and unpaid loans from other family members can cause financial difficulties for the entire family.

The heavy drug user may resort to criminality to financially support the drug habit. Theft and illicit drug selling are the most

[a]The Committee on Drug Abuse includes Edward Kaufman, M.D. (chairperson), Edward Khantzian, M.D., Joseph Westermeyer, M.D., Dorynne Czechowicz, M.D. (consultant), Steven Mirin, M.D. (consultant), and Roger Meyer, M.D. (former member).

common illegal activities, but prostitution, robbery, and drug smuggling also occur. Easy money from criminal behavior impedes later rehabilitation, since the youthful person has been learning criminality rather than a licit occupation during this critical development period. Learning a job skill or profession requires hard work, willingness to make a commitment and risk failure, and learning responsibility, tasks not easily accomplished. Frustration, anxiety, and fear result to a greater or lesser extent, feelings that marijuana, cocaine, and other drugs can alleviate temporarily. Continued drug use undermines the persistence and industriousness needed to succeed at this developmental task. Drug intoxication and, later, withdrawal, impair the ability to concentrate, synthesize, and organize material, learn new material, apply general principles to specific problems, exert judgment in complex tasks and situations, and make timely decisions (12).

In developing friendships and, later, intimacy with persons of the opposite sex, most youthful persons experience anxiety, embarrassment, and fear of rejection. They may believe that drugs can relieve these aversive feelings as well as alleviate premature ejaculation (in males) and vaginismus (in females). However, prolonged heavy use can reverse these temporary gains in sexual performance, leading to anhedoma, amenorrhea, impotence, and rejection by a sexual partner (13). The lack of judgment seen in young drug and alcohol users often results in teenage pregnancy.

Adolescence is the time to acquire hobbies, sports, and other avocations that may last decades, even a lifetime (14). By and large, drug use does not enhance these activities. Drug use may in fact lead to abandonment of these pursuits and may intensify social isolation. Instead, the drug user pursues activities that focus on the drug use experience and that tend to be banal and boring if done without drug use. Thus, without drugs, the chronic user may be bored and at a loss for stimulating and rewarding activities. Recreational pastimes usually require a period of learning and acquiring skills, another lengthy process that is abandoned with drug use. Drug use during activities involving rapid psychomotor coordination, speed, and judgment (e.g., driving a car or motor boat, water or snow skiing) places the intoxicated person at risk of harming self or others.

In the process of becoming an adult, an adolescent learns to accept responsibility and cope with adversity. Maturation demands a focus outside oneself, task orientation, and the ability to delay gratification for a time. This personality development is impaired by the use of drugs, which furthers an egocentric and present-oriented attitude. If regular drug use began early in adolescence and was continued over several years, the recovering abuser often has the personality characteristics and maturation level of a much younger person (15). It is important to note that alcohol and cigarettes are "gateways," predecessors of marijuana use, which is in turn a predecessor of other drug use and abuse (16).

CONSEQUENCES OF MARIJUANA USE

General Medical Consequences

Two distinguished independent scientific groups separately have reported on marijuana in the past few years. The Institute of Medicine, National Academy of Sciences, prepared a report on marijuana and health that was published in 1982 (17). The Addiction Research Center, World Health Organization, prepared a report on the Conference of Adverse Health and Behavioral Consequences of Cannabis, which was published in 1981 (18). Both reports concluded that cannabis has both known and suspected health hazards that should be of serious national concern.

The health consequences of chronic marijuana use depend to some extent on the frequency, duration, and intensity of use, the age at which use begins, and biopsychosocial characteristics of the user, which may contribute to risk in still unspecified ways. For example, not all individuals who smoke tobacco cigarettes will go on to develop carcinoma of the lung, but the risk of this disorder is much greater among smokers, and the relative risk increases with the intensity, frequency, and chronicity of use.

Since the two aforementioned studies were published, further evidence of the harmful effects of marijuana has been established. In particular, the clearest evidence for harmful changes in physical health involves the pulmonary system (19–22 and a December 1979 report of the AMA Council on Scientific Affairs). Bronchitis and related inflammatory changes have been shown repeatedly. More recently, it has been shown that marijuana smoking causes a significant reduction in the gas-diffusing capacity of the lung. Moreover, there is considerable evidence to suggest that long-term use, like tobacco smoking, may lead to pulmonary cancer. Indeed, marijuana has up to 50% more aryl hydrocarbons in its smoke than tobacco, and high levels of these are associated with susceptibility to bronchogenic carcinoma. Many marijuana smokers also smoke tobacco, and it is postulated that the combined effects of smoking both substances may substantially increase the risk of cancer. Most important are the profound acute and chronic psychosocial, cognitive, and behavioral effects associated with marijuana use by youth. Acute toxicity is accompanied by negative effects on learning and memory, as well as psychomotor impairment. The typical effects of cannabis resemble a transient acute brain syndrome; they include deficits in attention span, concentration ability, short-term memory, information processing, and the performance of complex perceptual motor tasks. Thus, accidental injury to persons driving motor vehicles, piloting airplanes, or operating heavy machinery while intoxicated with marijuana is of special concern.

Even when marijuana use is discontinued, the memory loss continues for 3 to 6 months. This particularly affects adolescents who have been having difficulties in school. This consequent negative reinforcement leads them to return to marijuana use.

Specific Psychiatric Concerns

Psychiatrists have described three general complications associated with cannabis: acute adverse reactions, flashbacks, and prolonged reactions. Acute reactions are characterized by errors in judgment and confusion, which may be followed by an amnestic period. These are dose related and fall within the general category of deliria (23, 24). Anxiety may progress to acute panic reaction with overwhelming anxiety and a fear of losing control in response to drug-induced symptoms. Factors related to setting and or personality may lead to severe anxiety.

Flashbacks refer to brief, spontaneous recurrences of mental states experienced during marijuana intoxication that occur sometime after the last drug use. At this writing, the exact mechanism for flashbacks is uncertain.

Prolonged reactions secondary to marijuana use include psychotic and nonpsychotic reactions. Marijuana smoking may trigger a schizophrenic reaction in vulnerable individuals. Descriptions of long-lasting cannabis-induced psychoses appear mainly in medical journals in Asia and North Africa, where individuals may use cannabis at substantially higher doses than in the United States. Descriptions of cannabis psychoses vary by culture, and most reports suggest a persistent delirium, which includes bizarre behavior and the potential for violence and panic feelings in the absence of a "typical" schizophrenia-like psychotic state. There is fairly general agreement that persons suffering from marijuana psychosis do not develop psychotic thoughts or symptoms characteristic of schizophrenia. Most reports describe cannabis psychosis as lasting 1–6 weeks among very heavy users of high doses of cannabis. However, some reports describe longer-lasting marijuana psychoses in which the psychotic episodes do not clear in the usual time but persist in residual form. Repeated intoxications may result in recurrent psychotic episodes. There has been a problem in relating marijuana psychosis to the experience in Western countries because of differences in smoking patterns in the East and the West, the difficulty of translating the psychiatric symptom picture from one body of literature and culture into another, and the impossibility of generalizing from cases that come to psychiatric attention to the overall marijuana-using population.

Nonpsychotic prolonged adverse reactions have also been described. Chronic anxiety states, depressive symptoms, and changes in life style (including an "amotivational syndrome") have been linked to chronic marijuana use by a number of observers. The amotivational syndrome includes apathy, loss of effectiveness, and diminished capacity or willingness to carry out complex long-term

plans, endure frustration, concentrate for long periods, follow routines, or successfully master new materials. Verbal facility often is impaired both in speaking and in writing. Such individuals experience greater introversion, become totally involved with the present at the expense of future goals, and demonstrate a strong tendency toward regressive, childlike, magical thinking. It remains unclear whether those who are attracted to heavy marijuana use already were inclined toward an amotivational syndrome, of which the marijuana use was symptomatic, or whether the amotivational syndrome developed as a consequence of the chronic marijuana use. What is clear is that chronic marijuana smokers who develop amotivational patterns of behavior need to stop marijuana use if they are to be rehabilitated.

Finally, the question of marijuana's dependence-producing capability is raised frequently. Laboratory animals do not self-administer Δ^9-tetrahydrocannabinol as they do opioids, sedative hypnotic drugs, alcohol, and stimulants. Nevertheless, compulsive patterns of cannabis consumption do develop in human beings, and heavy use of marijuana in humans is associated with the development of a dependence syndrome. Moreover, heavy users of marijuana appear to be at substantially greater risk for other forms of drug abuse than persons who do not use marijuana. Finally, the long persistence of cannabinoids in the body after ingestion (up to 9 days after a single dose) raises the additional prospect of toxicity due to accumulation of the drug and its metabolites in the brain and other lipid-containing organs.

CONSEQUENCES OF COCAINE USE

The growing popularity of cocaine, as a drug of both use and abuse, is testimony of the willingness of human beings to consume psychoactive substances without regard to their effects on the brain or other body organs.

The adverse effects of cocaine on health may be divided into the general medical, specifically psychiatric, and social sequelae of acute and chronic use. The probability that adverse effects will occur is, in turn, related to factors such as dose, route of administration, and frequency and duration of use. Changing routes of cocaine administration (such as "free basing" or using "crack") increases the severity of health consequences. Frequent administration, even over short periods of time, leads to the accumulation of cocaine in plasma and presumably in brain tissue and increases the risk of adverse medical and psychiatric sequelae. Cocaine rapidly depletes endogenous neurotransmitters, leaving the user in a depressed state. Individual tolerance and vulnerability to the physical and psychological effects of the drug also play a role.

General Medical Consequences

Some sequalae of cocaine use stem from the drug's local anesthetic properties, its direct effects on small capillaries, and its ability to stimulate sympathetic nervous system activity. Other medical complications are the indirect result of the drug-using life style.

Until the upsurge of smoking crack cocaine, 80% of all cocaine use was by nasal inhalation (snorting). The direct effects of the drug on mucous membranes are responsible for a number of medical complications. These include rhinitis, erosion of the mucous membranes, and in severe cases, perforation of the nasal septum (25). Intravenous cocaine use, favored by some for the rapidity of onset and intensity of drug effects, is associated with all of the complications that one might expect with any type of unregulated intravenous drug use. These include skin abscess, thrombophlebitis, septicemia, hepatitis B, acquired immune deficiency syndrome (AIDS), and tetanus (26). Smoking the basified extract of cocaine (free basing or crack smoking) delivers the drug into the pulmonary capillary bed, where it is rapidly absorbed and results in a dramatically intense effect and a more rapid onset of addiction. Free basing and crack smoking have been associated with the development of chronic bronchitis and impairment in pulmonary diffusing capacity (27).

Cocaine's ability to stimulate the sympathetic nervous system may result in elevated heart rate and increased susceptibility to premature ventricular beats and, in some vulnerable individuals, ventricular fibrillation, respiratory arrest, and death (28). Acute elevations of blood pressure, with headache and the potential for cerebral hemorrhage, also have been described (29). Increased body temperature due to failure of the brain mechanisms controlling heat regulation, coupled with vasoconstriction and hyperactivity, has led to some deaths from hyperthermia (30).

Another untoward effect of cocaine is the development of status epilepticus. This may occur either as an acute response to high-dose use or as a result of a sensitivity to cocaine developed during chronic administration. The latter may be due to a so-called "kindling" phenomenon, in which brain neurons become increasingly sensitized to the effects of cocaine and fire in response to even relatively low doses of the drug (30).

All of the adverse medical complications of cocaine use are far more likely after acute administration of large doses. In many instances overdose is unintentional, since the user has little knowledge of the purity or even the amount of the drug consumed. Overdose deaths have occurred after the first use in apparently healthy individuals with no preexisting illness. In addition, repetitive use is associated with increasing sensitivity in some of the excitatory effects of cocaine. Finally, a small number of individuals suffer from a congenital lack of the enzyme pseudocholinesterase and thus are unable to metabolize the drug. In these individuals, even small doses can produce dramatic effects. The medical complications of cocaine use are more likely to occur in persons with preexisting heart or respiratory disease, hypertension, seizure disorders, or compromised immune function and in those who are taking other drugs whose effects are potentiated by cocaine.

Specific Psychiatric Complications

The acute subjective response to cocaine is characterized by euphoria, insomnia, increased energy, enhanced mental acuity and alertness, and an increase in sensory awareness. However, some individuals become hyperexcitable, while others, particularly those with underlying depressive disorders, experience dysphoria. Anxiety, concentration difficulties, decreased attention span, and memory problems also have been reported after use of cocaine. In individuals with underlying panic disorder, the drug can precipitate panic attacks. Some cocaine users may misperceive reality and/or experience auditory, visual, and tactile hallucinations. Flight of ideas, distractibility, pressured speech, restlessness, impulsivity, and poor judgment are common. Paranoia and delusions of persecution, coupled with profound irritability and grandiosity, may lead to assaultive and/or homicidal behavior by some cocaine abusers. These alterations in thinking, mood, and behavior may last a short time or, in certain vulnerable individuals, may persist long after the drug has been metabolized (31, 32).

Chronic cocaine use also is associated with untoward effects on psychological health. Several studies have demonstrated a direct relationship between cocaine dose, chronicity of use, and the development of cocaine-related psychopathology. Chronic cocaine users frequently complain of fatigue, headaches, impairment of recent memory, concentration difficulties, and sexual indifference. They also are more likely to develop a cocaine psychosis (described previously).

In some individuals the powerfully reinforcing effects of cocaine lead to increased frequency of use, escalation of dose, and the eventual development of psychological and physical dependence. The onset of dependence is particularly rapid with the use of crack. The primary reinforcing effects of the drug are probably mediated through the limbic system mechanisms responsible for the perception of pleasure—specifically, those neural circuits that use norepinephrine and dopamine as neurotransmitters. Other factors that contribute to the development of dependence include psychological variables, peer pressure, drug availability, and (perhaps) some sort of underlying biological vulnerability.

The tendency toward repetitive use is further enhanced by the occurrence of a cocaine withdrawal syndrome characterized by depression, lethargy, fatigue, feelings of guilt, anxiety, and feelings of helplessness, hopelessness, and worthlessness. In some individuals, particularly those with preexisting underlying depression, transient suicidal thoughts may emerge.

The cocaine withdrawal syndrome is particularly marked after chronic high-dose use. The signs and symptoms usually last 12–36 hours. In some individuals, however, the depression may last up to several weeks. To avoid withdrawal, some chronic users will self-administer the drug every 20–30 minutes. This pattern of use is more likely to be associated with the development of cocaine psychosis. The serious psychosocial consequences of cocaine use include loss of job and problems with one's family, friends, and finances.

In summary, both acute and chronic cocaine use are associated with adverse effects on health. In addition to medical and psychiatric sequelae, chronic cocaine use also is associated with the hazards of a drug-using life style. These include anorexia and associated weight loss, malnutrition and vitamin deficiencies, accidents, and a greater likelihood that one will be the perpetrator or victim of violence.

ROLE AND RESPONSIBILITY OF PSYCHIATRISTS

Psychiatrists should exercise a leadership role in drawing attention to the major public and mental health consequences of substance abuse in our society. Psychiatrists have a responsibility to educate the public about how ubiquitous drug abuse is and how it is both the cause and consequence of emotional problems. We must be aware that drug and alcohol abuse are often the primary problem among patients who present themselves to psychiatrists. Psychiatrists should take leadership responsibility in assuring that adequate training in substance abuse occurs at all levels of medical education and in influencing physician attitudes and behaviors as part of this training process. Psychiatrists also should interface with nonmedical care givers, such as educators, the clergy, counselors, and self-help groups, in imparting an understanding of the psychiatric implications of substance abuse. The psychiatrist's role in working with the family is essential.

Evidence has accumulated over the past decade that there is a significant association between psychopathology and substance abuse. In some instances, substance abuse has resulted from psychopathology and in other cases has been the cause of it. In either case, for most individuals regular reliance on drugs is incompatible with a life of meaningful relationships, productivity, and satisfaction. Substances of abuse are dangerous because they exert powerful deleterious effects on human emotions and behavior. Mind-altering drugs, including alcohol, create illusions that emotional distress can be avoided, that desired states or behaviors can be augmented, and that performance can be enhanced or improved. During adolescence, when particularly intense emotions, behaviors, and performance concerns loom large, this is a seductive and dangerous effect of drug use. However, these dangers also apply to other phases of life, when other developmental challenges are encountered and need to be mastered.

Psychiatrists should address the emotional and mental health needs of substance abusers. Psychiatrists should educate themselves and the public about how substance abuse affects the psychological and social functioning of individuals and their families and should take active roles in developing and establishing guidelines and protocols for the assessment and management of substance abuse problems. Psychiatrists should provide the public with information on the hazards of substance abuse through the media, public education campaigns, and contacts with other care providers and professional associations. Psychiatrists should take the initiative in developing guidelines and procedures for quality assurance and assessment of treatment outcome for substance abuse treatment programs. Finally, psychiatrists, through the American Psychiatric Association, should exercise an ongoing leadership role to assure nondiscriminatory reimbursement practices for substance abuse treatment services.

Each psychiatrist has a responsibility to understand and learn about substances of abuse; their psychoactive, toxic, and withdrawal effects; and how they interact with human emotions and behavior. Practicing psychiatrists must routinely obtain drug and alcohol histories, focusing not only on duration, amounts, and patterns of use but also on the effects that patients seek and obtain from the drugs they choose. Similarly, family histories of drug use and misuse patterns also should be obtained routinely. Psychiatrists should routinely consider whether their patients with psychiatric conditions suffer from concomitant substance abuse disorders and whether patients presenting with substance abuse disorders also might be suffering from coexistent treatable psychiatric problems. Psychiatrists should be cognizant of the life-threatening aspects of substance abuse as background for emphasizing the importance and necessity of obtaining control and abstinence at the onset of treatment. Accordingly, psychiatrists must learn how to use appropriate hospital and other residential treatment, support groups (e.g., Alcoholics Anonymous and Narcotics Anonymous), pharmacological treatment, and psychotherapeutic modalities [33].

Psychiatrists involved in the treatment of children and youth presenting with behavioral and emotional problems should be alert to the possibility that drug use may be a contributing factor. Close cooperation between psychiatrists, primary care providers, parents, and educators is needed to overcome the serious problems of alcohol and other drug abuse among our youth.

Finally, psychiatric practitioners are well suited to work with primary care providers in assessing and managing substance abuse patients in both outpatient and inpatient settings. They also are able to work with and interface with nonmedical caregivers, especially in consulting with self-help programs and drug counselors and helping them appreciate the mental health needs and psychiatric disabilities of their clients. The psychiatrist has a substantial contribution to offer in the management of the substance abuser. The psychiatrist can provide a dynamic understanding of the patient and can plan individualized multidisciplinary treatment and its implementation. It is the responsibility of the psychiatrist to emphasize the danger of drug use. To adopt a more neutral stance toward drug use by youth and refrain from warning of the dangers to mental health is to fail to fulfill an important public health responsibility of our profession.

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Facts About:

SUBSTANCE ABUSE

- Alcohol and drug abuse afflicts 25.5 million Americans. When its effect on the abusers' families and people close to those injured or killed by intoxicated drivers are included, such abuse affects an additional 40 million people.

- Alcoholism costs a total of $89.5 billion for treatment and indirect losses such as reduced worker productivity, early death, and property damage resulting from alcohol-related accidents and crime each year. Drug abuse drains a total of $46.9 billion in direct and indirect costs to business and the economy.

- Substance abuse victims can't control their use of alcohol or other drugs. They become intoxicated on a regular basis (daily, every weekend or in binges) and often need the drug for normal daily functioning. They repeatedly try to stop using the drug but fail, even when they know the drug causes or worsens a physical ailment. Use of the drug interferes with their family life, social relationships and work performance.

  Substance dependence victims suffer all the symptoms of abuse plus a tolerance for the drug so that increased amounts of it are necessary for the desired effects. Opioids, alcohol, and amphetamines also lead to physical dependence in which the person develops withdrawal symptoms when he stops using the drug.

- Ten million adults and 3 million children are alcoholics. These people will die 10 years earlier than nonalcoholics.

- Alcoholic drivers kill 28,000 people in traffic accidents each year.

- Alcoholism is a progressive disease that generally first appears between the ages of 20 and 40, though children can become alcoholic.
  - It takes five to 15 years of heavy drinking for an adult to become alcoholic; it takes six to 18 months of heavy drinking for an adolescent to become alcoholic.
  - Generally, abuse occurs in one of three patterns: regular, daily intoxication; drinking large amounts of alcohol at specific times, such as every weekend; and long periods of sobriety interspersed with binges of heavy daily drinking that lasts for weeks or months.
  - As drinking continues, dependence develops and sobriety brings serious withdrawal symptoms such as delirium tremens (DTs) that include physical trembling, delusions, hallucinations, sweating and high blood pressure.
  - Long-term, heavy drinking can cause dementia, in which the individual loses his memory, the ability to think abstractly, to recall names of common objects, to use correct words to describe recognized objects or to follow simple instructions.

- Drug abuse afflicts more than 12.5 million Americans. Of that, 7 million use addictive prescription drugs without physician supervision, 5 million abuse cocaine, and a half million are addicted to heroin.

- The five major classes of drugs are sedative-hypnotics, opiates, hallucinogens, marijuana, and psychostimulants. Not all are physically addictive, but all can lead to psychological addiction, in which the user needs the drug in order to function.
  - Abuse of sedative-hypnotics or barbiturates most often begins either as a prescription for insomnia among middle-class women between 30 and 60 or as a recreational experiment among men in their teens or early 20s. Often, abusers regularly take heavy daily doses and develop an addiction.
  - Abuse of opioids such as heroin or morphine generally follows abuse of other drugs such as alcohol, marijuana, sedatives, hallucinogens or amphetamines. About half of those who abuse the drugs develop a dependence or addiction.

- Successful treatment of drug and alcohol abuse includes a variety of therapies geared toward abstinence.
  - Psychotherapy helps the patients understand their behavior and motivations, develop higher self-esteem and cope with stress. Self-help groups such as Alcoholics Anonymous also are effective.
  - The only medication for alcoholism requires daily use of disulfiram (Antabuse) which induces violent physical reactions to alcohol.
  - Opiate addicts have been treated with methadone, a long-acting medication that maintains tolerance to opiates but substantially reduces the positive effects of herion. Another treatment relies on opiate antagonists, which block the effect of the abused drug.

~~WOMEN & CHILDREN'S [illegible] ASSOCIATES~~

CAROLYN BROWN, M.D.
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TEL:(907) 745-4711 DEA. No. _____

For Mary Kentteba Age _____

Address _____

℞ Date 4-16-96

This bill is nuts!
Please do what you can
to deal with it in an
objective way.

Dr. you are right
but renew the meds to
House Counsel.

REFILL 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ NR ☐
LABEL ~~☐~~ PRN ☐

☐ ~~SUBSTITUTION ALLOWED~~ ☐ ~~DISPENSE~~ AS WRITTEN

Carolyn
(Signature)

al-ic The major Substance Abuse Problem. 0351115628

For your information

K

April 16, 1988

I find CS for Senate Bill 32 an amazing document.

While the legislature is dealing with this serious problem, I wonder why the same attention is not given to the use of alcohol?

If one reads through CS for SB 32 and thinks alcohol in the same place of marijuana, it becomes apparent to the most casual thinking person that the use and abuse of alcohol in this state so far surpasses the use and abuse problems related to marijuana that to carry on with ciminalizing marijuana without giving the same attention to alcohol would make CS for SB 32 absolutely ludricous and absurd.

There is much to be said for giving serious attention and concern to marijuana. There is an even more critical mandate to give that same serious attention and concern to alcohol use in this state.

Why separate the two? I am aware of the alcohol lobby. I understand the economic impact of alcohol sales. I also see the victimization of innocent children, of women and men, of gainful employment, of domestic violence, and of meaningful productivity related to alcohol use in this state.

If one makes any attempt to be objective (not political, not economically astute, not consumed with one's own addiction), one cannot but deal with alcohol and marijuana in the same vein - however it is attacked and dealt with.

And where does that leave judgment about CS for SB 32? It appears to be a witch hunt for a junior witch when there are astronomical and agonizing costs accruing to the other witch. How can intelligent people deal with only one of these "societal" problems without giving some attention to the other.

Come, let us be reasonable. What is good for the goose is good for the gander.

Carolyn Brown

carolyn V. Brown, M.D.

Offered: 3/31/87 5-0131B
Referred: Judiciary & Finance

Original sponsors: Fischer and Faiks

IN THE SENATE BY THE HEALTH, EDUCATION AND SOCIAL SERVICES COMMITTEE

CS FOR SENATE BILL NO. 32 (HESS)

IN THE LEGISLATURE OF THE STATE OF ALASKA

FIFTEENTH LEGISLATURE - FIRST SESSION

A BILL

For an Act entitled: "An Act relating to marijuana; and providing for an effective date."

BE IT ENACTED BY THE LEGISLATURE OF THE STATE OF ALASKA:

* Section 1. FINDINGS. (a) The legislature finds that marijuana use is a serious health problem for the following reasons, each of which constitutes a legitimate and compelling state interest:

(1) marijuana and other cannabis preparations may contain over 420 different compounds;

(2) tetrahydrocannabinol (THC), one of the pharmacologically active compounds in marijuana, is not soluble in water, but goes into the fatty tissues of the brain, testicles, ovaries, and other internal organs, and takes as long as 30 days to be eliminated from the body;

(3) the buildup of THC in the system means that repeated administration of even small doses may lead to an accumulation of the drug higher than levels reached at any time after a single dose;

(4) the buildup of THC in the body causes the user to smoke more marijuana to achieve the desired high and may result in loss of sleep, appetite, and initiative, as well as moodiness and depression;

(5) it is possible for a human being to overdose from the use of marijuana, especially if it is used in conjunction with alcohol, because it increases the effects of alcohol;

(6) the THC content of commonly obtainable marijuana has increased from less than one percent 10 years ago to as high as 10 percent today;

(7) marijuana with THC content higher than one percent is generally available in the state, through both importation and local cultivation;

(8) marijuana may cause schizophrenia, illusions, and hallucinations, including a dulling of the senses, creating the possibility that the user is unable to respond to body signals such as pain;

(9) although it may take a heavy cigarette smoker as long as 20 years to develop lung cancer, one marijuana cigarette a day may cause lung cancer in three years;

(10) THC affects eggs, sperm, sexual hormones, and the development of a fetus and marijuana use may result in deformed or undersized offspring;

(11) other physical reactions to marijuana include irreversible changes in the brain, sinusitis, pharyngitis, bronchitis, emphysema, increased heart rate, and decreased blood circulation;

(12) other psychological reactions to marijuana include loss of memory, anxiety, panic, paranoia, psychosis, psychological dependence, and impairment in thinking, reading comprehension, verbal and arithmetic problem solving, and perception of distance and time;

(13) the use of even small amounts of marijuana by adults in the home subjects children present to a substantial health hazard; and

(14) marijuana and tetrahydrocannabinols have been found by the United States Congress to possess a high potential for abuse.

(b) The legislature further finds that

(1) patterns of marijuana use in the state have changed over the past decade;

(2) the daily use of marijuana in the state has increased to as high as four percent among the general population and as high as six percent among secondary school students;

(3) marijuana use in the state within both the general population and among adolescents is significantly higher than in the nation as a whole;

(4) there is a direct relationship between the use of marijuana at home by adults and the percentage of secondary school students who experience disciplinary and academic problems in public schools; over the last three years in the Anchorage School District, of the 230 students who have been s spended from school for possession or use of marijuana, 29 percent have indicated that marijuana is used by adults in their living environment;.

(5) the changing patterns of marijuana use and the relationship between marijuana use by adults and adolescents have significantly compromised the state's legitimate efforts to prevent the spread of marijuana use to adolescents and protect the health of adolescents; and

(6) these efforts constitute a legitimate and compelling state interest.

(c) The legislature further finds there is a legitimate and compelling governmental interest, based on testimonial and scientific evidence, that the public health and welfare will suffer if personal use of marijuana even in small amounts is allowed.

* Sec. 2. AS 11.71.060(a) is amended to read:

(a) Except as authorized in AS 17.30, a person commits the crime of misconduct involving a controlled substance in the sixth degree if the person

(1) uses or displays any amount of a schedule VIA controlled substance or possesses one or more preparations, compounds, mixtures, or substances of an aggregate weight of less than one-half pound [ONE OUNCE OR MORE] containing a schedule VIA controlled substance [ON A PUBLIC STREET OR SIDEWALK OR ON THE PREMISES OF A PUBLIC

CARRIER OR BUSINESS ESTABLISHMENT OR IN ANY OTHER PUBLIC PLACE]; or

[(2) KNOWINGLY POSSESSES ANY AMOUNT OF A SCHEDULE VIA CONTROLLED SUBSTANCE WITHIN THE IMMEDIATE CONTROL OF THAT PERSON WHILE OPERATING A PROPELLED VEHICLE;

(3) BEING UNDER 19 YEARS OF AGE, POSSESSES ONE OR MORE PREPARATIONS, COMPOUNDS, MIXTURES, OR SUBSTANCES OF AN AGGREGATE WEIGHT OF LESS THAN FOUR OUNCES CONTAINING A SCHEDULE VIA CONTROLLED SUBSTANCE;

(4) POSSESSES ONE OR MORE PREPARATIONS, COMPOUNDS, MIXTURES, OR SUBSTANCES OF AN AGGREGATE WEIGHT OF FOUR OUNCES OR MORE CONTAINING A SCHEDULE VIA CONTROLLED SUBSTANCE; OR]

(2) [(5)] refuses entry into a premises for an inspection authorized under AS 17.30.

* Sec. 3. AS 11.71.070 is repealed.

* Sec. 4. This Act takes effect immediately under AS 01.10.070(c).

ANCHORAGE TIMES
APRIL 3, 1988

1 in 10

That's the ratio of problem drinkers in Anchorage. But resources exist to help them triumph over the bottle

STORIES BY

ANN CHANDONNET

Editor's note: In Anchorage the problem of alcoholism isn't hopeless. Programs exist to help even the most confirmed drinker rediscover a life not dominated by mood-altering chemicals such as alcohol. The intent of this week-long series of articles is to help demystify the treatment process, and make it more accessible to those who wish to regain control of their lives. The series will be continued this week in the Neighbors section.

It's three minutes to noon on Fourth Avenue, and pedestrians scurry to grab a quick bite of lunch or squeeze in one more errand.

Tony K., 42, very drunk and unkempt, wanders unsteadily through the crowd, asking passers-by for spare change. Most ignore the sidewalk pest.

One of those passing is Arthur W., 37. Nicely dressed, with a neat moustache, Arthur W. is just another face in the crowd — a successful contractor wearing designer jeans under his London Fog overcoat. Arthur W. hurries to lunch. He hasn't had a drink since breakfast. If he doesn't have one soon he feels sure he'll lose the battle to control the shakes.

Dodging into an upscale restaurant, he's greeted by name. A double martini appears in his hand without his asking. He downs it in a gulp, and another appears. There are 50 minutes of his lunch hour left.

Tony K. and Arthur W. are both alcoholics. Arthur is already losing contracts through inconsistent workmanship and unprofessional temper tantrums. His home is mortgaged to the hilt. His wife goes to Al-Anon. His children peer into rooms before they enter, to see if he's there. His downward slide has begun.

• • •

Alcohol in Anchorage is not exclusively a native problem — something "out in the bush" and far away. One out of 10 Alaskans has a drinking problem, and the majority of those problem drinkers are white residents of the Anchorage municipality. They may never miss work. They may never drink on the job. But they come home at 5 p.m. with two six packs of beer that are gone before 11. Or they go for weeks without a bender — then slug back the straight bourbon and become violent with a girlfriend. Later they don't remember.

The conclusion is inescapable that alcoholism touches all our lives. The cost to society in dollars and lost potential is staggering.

Figures from the state Office of Alcoholism and Drug Abuse paint a stark picture: The average alcoholic in Alaska is not a "street person." He or she is between the ages of 20 and 55, married, a parent, educated and employed.

A decade ago, there were 15 Alcoholics Anonymous groups in Anchorage. Now there are 100, points out alcoholism counselor Bobbie Parker of the Women's Resource Center. "You can go to AA meetings from 6:30 in the morning to midnight if you want to," Parker says.

Alcoholism is not a problem limited to the one tipping the bottle. "Alcoholism affects the entire family," Parker explains. "The children of the family, even if they don't drink, are carrying on those behavior patterns into the raising of *their* children. It goes on and on."

Despite this gloomy picture, Parker is optimistic. "I firmly believe that inside every alcoholic there is a beautiful person

trying to get out — no matter what sex, age or ethnic background he is. But there is a lot of denial (that the problem exists). And denial is what kills people."

Although personal substance abuse may be easy to scoff at, statistics are not. Here are some Alaska substance abuse facts. Except as noted, they were derived from the annual report to the legislature in 1986 by the Office of Alcoholism and Drug Abuse, Department of Health and Social Services; and from a November 1986 report by the Anchorage Municipal Health and Human Services Commission.

- Of Alaska's 95 suicides in 1985, 80 percent were alcohol-related.
- In 1985, the equivalent of 4.35 gallons of absolute alcohol was sold per person over 21 in Alaska. The U.S. average was 2.52 gallons.
- Fifty-eight traffic accidents with fatalities in 1985 resulted in 69 alcohol-related deaths. Each fatality is calculated to cost $306,000, or a total cost to Alaska of $21,114,000.
- In 1986 there were 1,706 liquor licenses issued in Alaska, or one for every 178 Alaskans 21 or over.
- Fifty-five percent of all crime in Alaska is estimated to be alcohol-related. (Individual local police officers suggest this figure might be closer to 70 percent.)
- There were more than 9,500 reports of child abuse in Alaska in fiscal year 1986. In up to 80 percent, alcohol is a significant factor.
- Of clients using the emergency services of the Association for Stranded Rural Alaskans in fiscal year 1987, 12 percent needed services for alcohol treatment, according to figures provided by Mary Wolcoff, executive director of ASRAA.
- In 1985, 1,782 local drivers were arrested for driving while intoxicated in Anchorage.
- In fiscal year 1985, 10.5 percent of admissions at Alaska Psychiatric Institute were alcohol-related.

• • •

In November, Otis R. Bowen, secretary of the U.S. Department of Health and Human Services, unveiled a national initiative of government and private sector efforts to address alcohol-related problems.

Outlining his plan at the National Conference on Alcohol Abuse and Alcoholism, Bowen stressed that "alcoholism is a disease and highly treatable."

As is evident in Anchorage, Bowen emphasizes that alcohol has "a ripple effect" on public health concerns and the economy. That is, no citizen is immune to its effects. Alcohol consumption is directly linked with traffic deaths, suicide, fires, infant mortality and morbidity, recreational accidents with snowmobiles and three-wheelers, and a variety of diseases such as cancer of the esophagus.

Medical research has shown that children born to alcoholics are at the highest risk of developing attention deficit disorders, stress-related medical problems, eating disorders and some birth defects. Business and industry are affected by what Bowen called "the staggering economic costs" of lost productivity due to alcohol abuse. And America's health care system is becoming increasingly burdened by having to provide care for people who engage in "risk-taking behavior."

The estimated cost of alcoholism to American society in 1980, including the cost of reduced productivity, was approximately $90 billion, according to a study cited in the Jan. 21 issue of the New England Journal of Medicine.

Bowen says, "Recent evidence even points to the role of alcohol in AIDS and other immune-disabling disorders. Alcohol alters the state of the immune system and increases the speed with which the HIV virus weakens its host environment."

Some of Bowen's recommendations include:

- Encouraging colleges and universities to restrict campus promotions for alcoholic beverages.
- Taking further action on alcohol labeling.
- Securing radio and television programming to promote nonuse of alcohol by youths and others at high risk.
- Producing public service announcements on public health problems and the negative aspects of drinking during potentially dangerous activities, such as sports.
- Notifying small businesses concerning the benefits of employee assistance programs to combat alcohol abuse.
- Expanding health plans to cover alcohol and other drug abuse treatment.
- Reviewing Medicare reimbursement for alcoholism treatment.
- Adopting the terminology "alcohol and other drug abuse" in publications and reports, since "substance abuse" is, says Bowen, "too broad and diminishes public attention to alcohol-related issues."

T O M M.

Early drinking set the pattern

Tom M., 34, started drinking at age 12.

"It's been a long battle," he says wearily. "My father was alcoholic, and even though I promised myself as a kid that I would never turn out to be like him, I experimented with it. I found out with the first drink that it did something for me that I enjoyed — it gave me courage."

Tom M. drank for eight years without seeing a glimmer of the truth about alcohol. "But about the age of 20 I got my first DWI and that's when I started to take a real look at the problem."

Born and raised in Alaska, Tom M. joined the Navy in 1977, and with that came his first bout with treatment. "That dried me out for a month. I wasn't ready to accept that I had a disease, and thought I could handle it and drink socially. But with my first drink, it started the ball rolling again."

Tom M. gave in to the bottle: "I decided to just keep drinking until I died. Then there were numerous trips out to detox and other treatment centers. It wasn't until I was ready to admit within myself that there was no way that I could handle any alcohol that I got serious about staying sober."

His last massive bender reformed Tom M. "I ended up in a motel room alone with five prescriptions and two bottles of vodka. The prescriptions were tranquilizers, medication for depression, sleeping pills and a mood elevator. I decided to commit suicide. I was about halfway through one bottle of vodka and took some of my drugs. The next thing I remember, I was at detox, not knowing how I got there.

"I was upset that I was still alive, but I decided God would not let me die. I didn't want to hurt any more, so I decided to go into long-term treatment."

Treatment at Clitheroe, an alcohol treatment center run by the Salvation Army, is "going real well. I've been here four months now. The honesty is what turned it around — when I got honest with myself, with my counselors and my peers. I see myself sober now one day at a time."

Next he goes to Clitheroe's halfway house for three months "to kind of get my feet back into the community. If I can make it, anybody can," he says.

Andrew Weil, M.D.
& Winifred Rosen

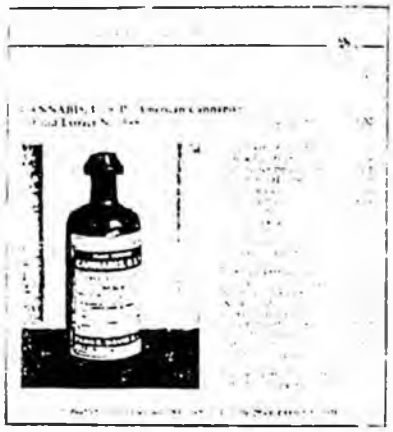
CHOCOLATE TO MORPHINE

UNDERSTANDING MIND-ACTIVE DRUGS

9

Marijuana

MARIJUANA is an ancient drug, used since prehistoric times in parts of the Old World. It is a product of the hemp plant, *Cannabis sativa*, a species that also provides a useful fiber, an edible seed, an oil, and a medicine. That is a lot for one plant to do, which explains why it has always been an important cultivated crop. Cannabis is probably native to central Asia. It tends to grow in waste places around camps and settlements and has been associated with human beings for so long that it is unknown in a truly wild state.



Tincture of marijuana (cannabis) was still listed in the Parke, Davis & Co. pharmaceutical catalog of 1929. (Courtesy of Tod H. Mikuriya, M.D.)

The intoxicating properties of hemp reside in an aromatic, sticky resin exuded by the flowering tops, especially the tops of female plants. The strength of a preparation of hemp depends on the resin content; some strains produce a great deal of resin, others little. If whole plants are chopped up, leaves, stalks, and all, the resin-rich tops will be diluted by much inert material. Carefully cultivated female tops, gathered before the seeds form, are sticky to the touch with resin, highly aromatic, and very potent. The resin itself can be collected and pressed into cakes or lumps; this is hashish. Also, the resin can be extracted with solvents and concentrated into a thick, oily liquid called hash oil. Any of these preparations can be either smoked or eaten.

Marijuana is unique among the psychoactive drugs, in a class by itself. The chemicals it contains resemble no other drug

molecules. Unlike most of the substances discussed in this book, they are insoluble in water but very soluble in oil. Therefore, they are absorbed unevenly when eaten, and they stay in the body for a long time because they accumulate in body fat. Marijuana is neither a stimulant nor a depressant, but has some features of both. Many people regard it as a mild psychedelic, but its effects are different from those of the true hallucinogens, and it is not necessarily mild. Moreover, the abuse potential of marijuana is considerably higher than that of psychedelics, because it can be used frequently or continually in combination with everyday activities.

As a psychoactive drug, cannabis has a much longer history in other parts of the world than it does in Western countries. Europeans and Americans grew the plant exclusively for its fiber for many years, and even when tincture of cannabis was widely used in Western medicine in the 1800s, few people took it to get high or reported that they felt high when they did take it. The knowledge of how to smoke hemp was probably brought to Brazil by black slaves who used the plant in Africa; the practice traveled north to Mexico and, finally, reached the United States.

Marijuana smoking began in the United States after World War I. Introduced by Mexican migrant workers, it caught on first among black people in southern cities. Many of its early users were musicians. Over the years, it spread to other subgroups, but was rarely associated with the white middle class

Marijuana growing on the United States government's experimental farm at the University of Mississippi. (Timothy Plowman)

until the 1960s, when it became a prominent symbol of the youth movement on college campuses. Since then, it has grown steadily more popular and today is the most widely used of all the illegal drugs.

From the very first, marijuana — which is known by many slang names, including pot, grass, and smoke — provoked a great deal of contention, mostly as a result of its associations. It was the drug of deviant subcultures and minority races even before it got mixed up with hippies and revolutionaries. Despite its growing acceptance today, the dominant culture still views it as a dangerous drug, worse than alcohol and tobacco, likely to lead to heroin.

In this highly charged atmosphere, arguments about marijuana tend to be more political than factual. And because pharmacologists and medical doctors are just as caught up in the politics of marijuana as other people, it's difficult to get neutral information about the drug. Much marijuana research sets out to prove preconceived ideas, and much of it is not worth reading.

Politics aside, the effects of marijuana are hard to describe, because they are so variable — more so than those of other drugs. Some of this variation has to do with set and setting, but some is inherent in the drug.

People who smoke marijuana for the first time often feel nothing at all, even if they take high doses of strong pot. As with other psychoactive substances, people have to learn to associate changes of consciousness with the physical effects of the drug. Compared to other drugs, however, the physical effects of marijuana are not spectacular. It makes the heart beat somewhat faster, causes the mouth and eyes to become dry, and reddens the whites of the eyes. Of these, the most noticeable change is the dryness of the mouth. Only people who wear contact lenses are likely to notice the dryness of the eyes. Increased heart rate is easily ignored, although it can become the basis of a panic reaction in anxious first-time users, who may interpret it to mean they are having heart attacks.

When people learn to get high on marijuana, their early experiences with it are often quite lively. Everything may strike them funny, and all sensory experiences become novel and interesting. Listening to music, eating, and making love can become more than usually absorbing. Time seems long and drawn out. People sometimes have strange illusions, such as seeing a room expand or feeling as though their legs have become enormously long.

Charles Baudelaire (1821–1867): a self-portrait by the French poet from 1844, drawn under the influence of hashish. (Fitz Hugh Ludlow Memorial Library)

(From *The Further Adventures of the Fabulous Furry Freak Brothers* by Gilbert Shelton. Copyright © 1979 Rip Off Press, Inc.)

With repeated use, these remarkable effects tend to fade away. Regular users may find that pot makes them relaxed or more sociable without greatly affecting their perceptions or moods. Very heavy users usually feel little from the drug, often smoking it simply out of habit.

Bad reactions to marijuana are more likely when high doses of strong material are taken in bad settings, especially by inexperienced users. Most are simple panic reactions, easily treated with reassurance that everything will be all right as soon as the drug wears off. The effects of smoking marijuana usually diminish after an hour and disappear after two or three hours. Some people, if they have smoked a lot of pot, feel tired or "fuzzy" the next morning.

Some users find that marijuana stimulates them and keeps them awake at night; others use it to help them fall asleep. It

... some people depressed and irritable, and others groggy ... several hours. Possibly, some kinds of pot are more sedative ... ners. In recent years, stronger and stronger marijuana ... become available. Some of the very potent sinsemilla ("without seed") from California is as potent as hashish and can ... disorienting to people who are not used to it.

Taken by mouth, rather than smoked, marijuana is a ... er drug, slower to come on, with longer-lasting effects. Because the resin is insoluble in water, marijuana tea is not very effective. But the crude drug can be added to food, and the active principles are easily extracted in alcohol or fat. Although some users like to eat cannabis, most prefer to smoke it because it's less trouble, and the effect comes on very fast. The main problem with oral use is the risk of overdosage. Since the stomach absorbs the drug unevenly, the right dosage is hard to estimate, and it's easy to take too much. Overdoses of cannabis are unpleasant, though not dangerous. They can make people extremely disoriented and delirious, as if suffering from a high fever, and are often followed by stupor and hangover. Perhaps because oral use requires more preparation and produces stronger effects, people who eat marijuana are less likely to become dependent on it than people who smoke it.

Whether they eat it or smoke it, users frequently combine marijuana with other drugs, such as alcohol, downers, stimulants, and even psychedelics. The effects of these combinations are not predictable, depending more on the individual than on the drugs. Because marijuana is not as powerful or as toxic as most of the other drugs, there is no special pharmacological danger in mixing it (as there is, say, in mixing alcohol with downers). Still, users should be aware that combinations they are not used to may disagree with them and may produce unexpectedly strong effects.

The medical safety of marijuana is great. It does not kill people in overdose or produce other symptoms of obvious toxicity. Used occasionally, it is no more of a health problem than the occasional use of coffee or tea, and certainly it is less toxic than alcohol and tobacco.

Long-term, regular marijuana smoking can, however, significantly irritate the respiratory tract, causing chronic, dry coughs that resemble the coughs of some cigarette smokers. Further, marijuana smoke may contain more tars than tobacco smoke, and can probably produce lung and bronchial disease in susceptible individuals. The risk depends on how much users smoke over how long a time.

Aside from respiratory irritation, heavy marijuana use does not seem to cause other medical problems. Of course, warnings of the medical dangers of cannabis have been well publicized, with reports of everything from brain damage to injury of the immune and reproductive systems, but these are based on poor research, often conducted by passionate foes of the drug. Studies of populations that have smoked cannabis for many years do not reveal obvious illnesses that can be linked to marijuana.

Much has been made of the fact that tetrahydrocannabinol, or THC, the most active chemical in cannabis resin, accumulates in body fat, staying around for weeks after the last dose of marijuana is smoked. Although this is true, and it is very different from the pattern of quick elimination of water-soluble drugs, it is not a problem in itself. If THC were a very toxic drug, its persistence in body fat would be cause for concern, but, THC and marijuana are less toxic than most of the drugs discussed in this book.*

I started dealing dope 'cause it was the only way I could afford to buy dope. Now I do it for the money.
— sixteen-year-old boy

Psychological problems related to regular use of marijuana are also subjects of controversy. Opponents of the drug charge that it interferes with memory and intellectual functioning and leads to an amotivational syndrome in which people lose their initiative and will to work. There is no question that young people who lack motivation often smoke a lot of pot and do very little else, but it is doubtful that marijuana made them that way. Heavy pot smoking is more likely to be a symptom of amotivation than a cause of it, and those same young people would probably be wasting their time in other ways or with other drugs if pot were not available.

*Marijuana may be quite toxic if it is contaminated with paraquat, a very poisonous chemical herbicide used to kill unwanted plants. In 1975 American drug enforcement authorities began encouraging officials in Mexico to spray this poison from helicopters on the illegal marijuana fields of that country. The growers soon learned that if they harvested their pot immediately after it was sprayed, it would still look healthy and could be sold to dealers as usual. In this way, paraquat-contaminated Mexican marijuana began to find its way to users in the United States.

The exact dangers of smoking paraquat are unclear, but it is certain that it cannot be good for you; the only question is how bad it is. Apparently it can cause serious lung damage over time and may affect other organs as well. There is no easy way to spot paraquat on a sample of pot, but some drug testing labs can analyze for it. Although public outcry put an end to American support for the Mexican program, the drug enforcement authorities are again pressing for use of paraquat on marijuana fields, both in other countries and in the major producing states, such as California and Florida. If they have their way, paraquat contamination will again be a risk to all users who do not grow their own pot or know who grew it. Some thoughtful legislators have urged that paraquat be mixed with some distinctive odor or color that would warn users of contaminated material, but so far that is just a suggestion.

As for its effects on memory and intellect, heavy users sometimes say that marijuana makes their minds fuzzy and can interfere with memory. These effects seem to disappear when people cut down on their use of the drug or stop using it altogether.

Although dependence on marijuana certainly occurs and has become more common as use of the drug has increased, it does not exactly resemble dependence on any other psychoactive drug. At its worst, marijuana dependence consists of chain smoking, from the moment of getting up in the morning to the time of falling asleep — a pattern similar to that of many cigarette smokers. But dramatic withdrawal syndromes don't occur when people suddenly stop using marijuana, and craving for the drug is not nearly as intense as for tobacco, alcohol, or narcotics.

Tolerance to marijuana also occurs. Even the strongest varieties seem to lose their power if people smoke them day in and day out. This leads heavy users to keep searching for more potent pot so they can feel stoned again. In fact, all they really need to do is cut back on their frequency of use; even a twenty-four-hour break from the routine of smoking all day long will allow a heavy user to become sensitive again to the psychoactive properties of marijuana.

Although dependence on marijuana has fewer physical components than dependence on more toxic drugs, it can still be very hard to break and very upsetting to people who find themselves caught up in it. Some heavy users are unable to stop smoking even though they no longer get useful effects from pot and, in fact, get effects they actively dislike, such as strong sedation and chronic coughs. Recently, self-help groups modeled on Alcoholics Anonymous have sprung up for people with unwanted marijuana habits.

Marijuana dependence can be sneaky in its development. It doesn't appear overnight like cigarette addiction, or in a matter of weeks like heroin addiction, but rather builds up over a long time. In most cases, people begin smoking pot only in special, usually social, situations. At first, because the drug causes such strong effects, they cannot imagine smoking it at other times. With increasing use, however, tolerance develops, and also people learn to adapt to being high. Soon they can perform normal activities while under the influence of marijuana. Users may then begin to smoke during the day, perhaps by themselves. With time, and unless precautions are taken, marijuana smoke can gradually pervade all their waking hours. At that point, the habit is not easy to break.

Eventually I became a daily pot smoker, sometimes starting in the morning. It was my main way of relating to other people. However, I started getting less and less effect from it that I liked. In fact, it began to make me groggy and sleepy most of the time and also gave me a cough. These unwelcome effects got worse and worse until I realized I would have to stop using pot. So I made a resolution to quit completely.

Well, it surprised me to find that wasn't so easy. It took me three years of trying before I really gave up smoking marijuana, even though I no longer got pleasant effects from it. I never realized how much of a habit I had and how hooked I was on it . . .

— forty-one-year-old man, lawyer

Even in heaviest usage marijuana does not lead to heroin or any other drug. Many junkies smoked marijuana before they tried opiates, but few marijuana users take narcotics. Many junkies also drank alcohol heavily before they discovered heroin, sometimes at very young ages, yet no one argues that alcohol leads to heroin. The reason, of course, is that alcohol enjoys general social approval, while marijuana is a "bad" drug and so invites false attributions of causality. Possibly, marijuana users are more likely than nonusers to try psychedelics and cocaine, because the distribution networks of these drugs overlap somewhat, but there is no quality of marijuana that induces its users to become consumers of other substances.

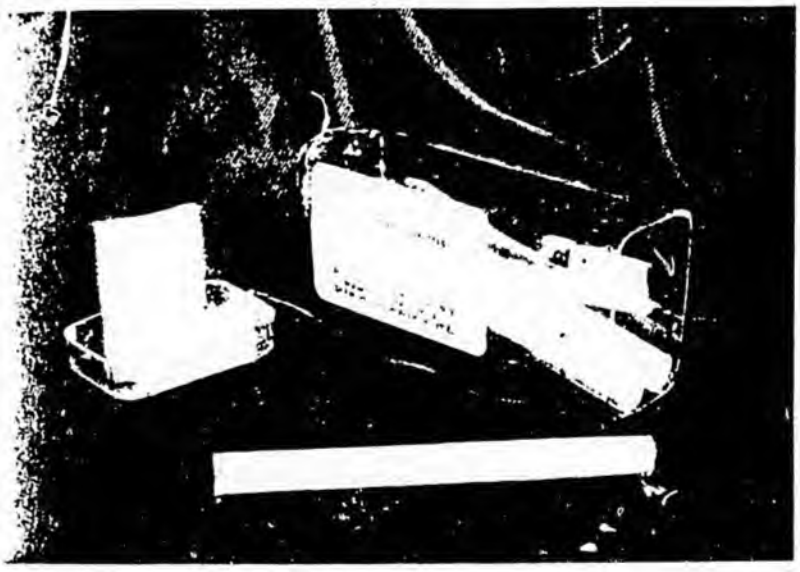
Adaptation to marijuana enables users to learn to perform well under its influence. Unlike alcohol, it does not invariably depress reflexes and reaction times. People who aren't used to its effects will not be able to drive cars well or do any number of other routine tasks well while stoned. Even experienced users need time to practice a given task under the influence of marijuana in order to bring performance up to normal. Some users feel that marijuana helps them concentrate and enables them to work better, but even they have to learn to adapt to its effects. Most scientific tests show that marijuana impairs performance of all sorts. It is easy to come up with such results if you give marijuana to people who are not used to it, give it in much higher doses than they are used to, or give them hard tasks to perform, especially tasks they have never done while stoned.

I have multiple sclerosis. About three years after it was diagnosed I discovered marijuana. A friend told me it was relaxing. My main problem then, aside from partial blindness, was tenseness and tremors in my muscles. Pot cured it, and I've smoked regularly ever since, about four to five times a week. If I go without it for a week, the muscle tremors come back . . . Most people with MS have repeated attacks and keep losing body function. I'm convinced that pot has kept me in remission all these years.
— forty-one-year-old man, part-time roofer

Many marijuana smokers drive cars, fly airplanes, ski, scuba dive, and engage in other hazardous activities after smoking. Many of them get away with it because they are experienced users with practice. This does not change the fact that marijuana can drastically interfere with performance in some circumstances. Pot and driving may not be as bad a combination for everyone as drinking and driving, but it is certainly not a good one. For teen-agers who drive recklessly to begin with, it can be especially dangerous.

Devotees of marijuana like to argue its merits, trying to persuade others that it is really a beneficial drug. In fact, cannabis was used in medicine in the past, and some doctors today feel that it is still a valuable remedy for some ailments. Current federal laws prohibit all uses of marijuana, but synthetic THC is available for research, and many states have now legalized marijuana for specific therapeutic uses.

Both THC and marijuana are good treatments for nausea and vomiting. Doctors have used them successfully with cancer



Government-manufactured marijuana cigarettes. A few patients with glaucoma have been able to obtain them legally for the treatment of that eye disease. (Jeremy Bigwood)

patients receiving chemotherapy, which involves very toxic drugs that often cause intense stomach upsets. This effect was first discovered by teen-agers with leukemia who happened to be pot heads. Cannabis may also help asthma patients breathe easier, but not in the form of joints because the smoke may make them cough. It also is a specific treatment for glaucoma, a serious eye disease in which fluid pressure builds up in the eyeball, causing losses of vision. Marijuana reduces this pressure. Finally, it relaxes stiff muscles in a condition called spastic paralysis that results from brain injuries and diseases such as multiple sclerosis.

Although many patients prefer the effect of marijuana to that of pure THC, federal agencies won't permit doctors to prescribe the natural plant. Yet THC is not the same as whole marijuana and may not be as safe. Recently, several pharmaceutical companies have come up with synthetic drugs related to THC and have tried to market them as antinausea remedies. In general, they are much more toxic than marijuana.

Aside from these specific uses, many people find that pot relieves the symptoms of various mild ailments, from headaches to menstrual cramps. Probably, they use the marijuana to get high and use the high as a way of taking their minds off discomfort. Sometimes taking your attention away from the symptoms of a n inor ailment will allow it to subside. The less frequently you smoke marijuana, the more likely it is to work for you as a medicine.

Of course, the same principle applies to getting high from pot. The less frequently you use it, the better and more intense will be your experiences with it. The main danger of smoking marijuana is simply that it will get away from you, becoming more and more of a repetitive habit and less and less of a useful way of changing consciousness. The ease of integrating marijuana smoking with all activities, from parties to sports to watching television, favors habitual use. Also, tolerance to the interesting effects of the drug often encourages users to smoke more of it, when in fact they should be cutting down to increase their sensitivity. The absence of dramatic negative effects, such as hangovers, further encourages overuse. Unless you set rules for when and where you will smoke, you are likely to find yourself using pot more than you should — to the point where all the interesting and useful effects of the drug disappear and you are left with a stubborn, unproductive habit.

(Michael R. Aldrich)

Some Suggestions for Using Marijuana Wisely

1. Define what benefits you want from pot. Do not use it just because other people do or because it is available. Be aware of the dangers associated with acquiring an illegal drug.*
2. If you get effects you like from marijuana, you will have to take precautions if you want to keep enjoying them.
3. Set limits on usage. For example, you may want to use pot only with certain friends, only on weekends, or only when you have no work to do. Such rules are necessary if you want to prevent your use from turning into a habit that gives you little satisfaction.
4. Remember that it can be dangerous to drive, operate machinery, or engage in hazardous activities under the influence of marijuana. The drug can cause illusions of time and space and always takes getting used to.
5. If you find the effects you like from marijuana becoming less intense or disappearing altogether, *stop using it.* You can resume after a break and get them back. The trick is to keep frequency of use below the level where you become insensitive to marijuana's interesting effects on consciousness. Odd as it may sound, less is more, and you can easily prove that to yourself.

*See pages 163-

9. If you find that the effects you like are disappearing, the worst things you can do are smoke more or look for stronger pot. Those actions will just increase the problem.
10. Consider using marijuana by eating it in some form rather than smoking it. It is more trouble to take by mouth and the effects are different, but the risk of dependence is less.
11. Be careful about combining marijuana with other psychoactive drugs.
12. Be careful about set and setting, especially if trying marijuana for the first time.
13. Do not use marijuana on the job or at school. Most people would not drink alcohol in those situations, and just because pot is less detectable is no reason to use it. The more situations in which you allow yourself to smoke, the more likely you are to become dependent.
14. If you develop a cough or wheeze, or become more susceptible to chest colds, marijuana may be doing harm to your respiratory tract. Stop using it, cut down on use, or switch to eating it.
15. If you find that you are using marijuana more than you want and are not getting useful effects from it, consider the possibility that it is controlling you more than you are controlling it. Try to do without it for a while. If you cannot, you may need outside help in breaking the habit.

Suggested Reading

Much has been published about marijuana in recent years, but few books worth reading exist.

The best general history of marijuana is *Marihuana: The First Twelve Thousand Years* by Ernest L. Abel (London: Plenum Press, 1980). *Marijuana Botany* by Robert Connell Clarke (Berkeley, California: And/Or Press, 1981) is about the plant itself. It is lavishly illustrated.

The Marijuana Papers, edited by David Solomon (New York: Bobbs-Merrill, 1966), is an anthology of historical, literary, sociological, and medical articles that is still valuable reading. *Marihuana Reconsidered* by Lester Grinspoon (Cambridge, Massachusetts: Harvard University Press, 1971) is a comprehensive overview of the drug by a psychiatrist. The origins and development of marijuana prohibition in America are discussed in Richard J. Bonnie and Charles H. Whitebread's *Marihuana Conviction: A History of Marihuana Prohibition in the United States* (Charlottesville, Virginia: University Press of Virginia, 1974).

One of the most readable and informative books on effects and uses of pot is *High Culture: Marijuana in the Lives of Americans* by William Novak (New York: Knopf, 1980). One example of a crusading antimarijuana book is *Keep Off the Grass* by Gabriel G. Nahas (New York: Pergamon Press, 1979). One example of a promarijuana book, written for users, is *A Child's Garden of Grass* by Jack S. Margolis and Richard Clorfene (New York: Ballantine, 1978).

Louisa May Alcott wrote a short story about hashish in 1865. Titled "Perilous Play," it is reprinted in *Plots and Counterplots: More Unknown Thrillers of Louisa May Alcott*, edited by Madeleine Stern (New York: William Morrow, 1976). A modern comic novel filled with references to marijuana is *The Fan Man* by William Kotzwinkle (New York: Avon Books, 1974). Its hero, a delightful character named Horse Badorties, is never without pot.

Although teen-agers make up the bulk of the movie-going public, few films have capitalized on the popularity of marijuana among young people. Three notable exceptions are *Up in Smoke* and *Nice Dreams* with Cheech and Chong, and Peter Fonda's classic from the 1960s, *Easy Rider*. An outrageous antimarijuana propaganda film from the 1930s, *Reefer Madness*, now plays on college campuses and in "art" movie houses, usually to the delight of mostly stoned audiences.

other points - effect on fetus — contact Div. Public Health - Testimony from NIH that 21.7% of low birth weight infants due to tobacco alone (nicotine is a vasoconstrictor which prevents blood from reaching placenta adequately)
- Fetal Alcohol Syndrome + Fetal Alcohol Effect (FSA + FAE) children often show incomplete development of brain, nervous system, lungs etc - extreme handicaps if they survive birth

A4 Anchorage Daily News Sunday, March 27, 1988

New evidence may burn cigarette makers

By JOHN KING
The Associated Press

BOSTON — Evidence presented in a New Jersey court that cigarette makers were aware up to 40 years ago that smoking might cause cancer and other ailments will lead to a flood of tobacco-liability cases, attorneys said Saturday.

The attorneys, including one involved in the New Jersey trial, said they expected the documents would lead to the first verdict against a tobacco company in a product-liability case. And now that the documents are a matter of public record, their availability will substantially reduce the cost of pretrial proceedings in other cases, the attorneys said.

"This is a product that is as dangerous as alcohol and as addictive as heroin," said Professor Richard Daynard of the Tobacco Products Liability Project at Northeastern University. "The evidence shows that."

The project, which assists attorneys involved in suits against tobacco companies, brought together lawyers involved in more than 100 tobacco liability cases nationwide as part of its fourth anniversary conference.

A lawyer for cigarette maker Philip Morris Cos., one of the defendants in the New Jersey case, said Daynard and other attorneys at the conference were taking the documents out of context. The attorney, Charles R. Wall, also criticized the group for discussing them while the New Jersey case was still under way.

"These issues will be decided in the courtroom where they should be decided," Wall said. "We disagree that there has been proof that cigarette smoking causes lung cancer."

Daynard and others at a Northeastern news conference said past cases blaming smoking for deaths have failed because of insufficient evidence that tobacco companies knew smoking was or possibly was a health hazard.

The documents gathered for the New Jersey trial include internal tobacco industry memos dating back to 1946 in which researchers for cigarette makers discuss growing evidence of a link between smoking and lung cancer and heart and respiratory problems.

They also include verification that cigarette makers developed less dangerous cigarettes, and memos in which the companies are advised that marketing those products would amount to an admission that other cigarettes were dangerous.

Rep. Nils Kippenan

Reagan Aide: Pot Can Make You Gay

Senior presidential aides looked on White House drug adviser Carlton E. Turner as a nattily dressed functionary with zero clout. He spent his time grinding out reports that nobody in the White House, save Nancy Reagan, cared much about. But suddenly that changed. Drug abuse became a hot issue, and Turner was in the spotlight. Now, Turner's views are making a few waves. He believes that pot smoking may lead to homosexuality; at the very least, he says, gays who use marijuana are risking damage to their immune system and vulnerability to AIDS.

Turner offers scant scientific backing for his claims. But he says that when he visits drug-treatment centers for patients under 18, he finds that roughly 40 percent of them have also engaged in homosexual activity. "It seems to be something that follows along from their marijuana use," says Turner, who is convinced that the drugs come first, the homosexuality second. "My concern is, how is the biological system affected by heavy marijuana use? The public needs to be thinking about how drugs alter people's lifestyles."

Turner also holds firmly to his belief that marijuana makes users more susceptible to AIDS, a disease that destroys the immune system. "No one is saying that marijuana will *cause* AIDS," he says, but he argues that marijuana suppresses the immune system and "if you're in a high-risk category, you certainly don't want to use something that will impair your immunological system." Turner, who holds a doctorate in organic chemistry from the University of Southern Mississippi, says that people who have contracted the AIDS virus certainly should not smoke pot, and he wants the Centers for Disease Control to investigate whether it is a cofactor in the progression of the disease.

Making waves: *Turner*
KEN HEINEN

Turner's assertions befuddle drug experts and gay-rights activists alike. Stephen Morin, a San Francisco psychologist whose patients include gay men, says there is no evidence that drugs play a role in the formation of sexual identity. Dr. Marvin Snyder of the National Institute on Drug Abuse says tests have shown that THC, the active ingredient in marijuana, does weaken the immune system in animals. But he says the immune system is fragile and many things, including some chemicals found in drinking water, can do the same thing. Meanwhile, Dr. Stanley Weiss of the National Cancer Institute says that a preliminary study found no causative link between pot and AIDS.

'Crazy ideas': One White House official said Reagan aides had been pleasantly surprised to find that Turner "wasn't a zealot who'd try to plant crazy ideas in Reagan's head." When asked about Turner's assertions concerning pot and homosexuality, however, one aide groaned and said the White House didn't want to get involved.

TERRY E. JOHNSON *with* MARGARET GARRARD WARNER *in Washington and* GEORGE RAINE *in San Francisco*

TO KNOW YOU–Dr Halfdan Mahler, Asst Director
[illegible] visits with children in northeast Thailand at the [illegible]
[illegible] during a recent 5-day field mission.

[illegible] participated in an evaluation of primary health care [illegible] undertaken by a joint WHO-Royal Thai Government team [illegible] Khon Kaen and Sisaket.

[illegible] is the first country to carry out such a programme [illegible] purpose to determine the effectiveness of [illegible] the village level. The second part of the exercise is [illegible] for 1985.

[illegible] according to officials is to ensure optimal support [illegible] member states. ■

[illegible] Nations, [illegible]g 40, Seeks [illegible]thing But [illegible]e Truth

[illegible] a truthful account of what the United Nations can and cannot do, of its successes and failures, of its means and limitations, of its dreams and realities.

[illegible] is calling for the world's [illegible] leaders [illegible] is most important [illegible] to undertake the assessment. "During my visits in many countries I am often struck by the low level of knowledge prevailing among the people about the United Nations, at the very time when a [illegible] address [illegible] May [illegible] 1985 will [illegible] the [illegible] peace,

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Drugs are big business

Any nation will drink more alcohol, smoke more cigarettes or abuse more opiates if the relevant drug is made more *available*. The key to reducing drug–and alcohol–related problems lies in controlling production, marketing, retailing and distribution

by Anthony W. Clare

Confronted by the deluge of statistics relating to the international epidemic of cigarette smoking, the inexorable rise in alcohol production and consumption, the proliferation of opiate dependence and the remorseless growth of the psychotropic drug market, it is hard to resist adopting one of two attitudes. The first, a resolutely pessimistic approach, is to conclude that societies in every quarter of the globe are hell-bent on drugging themselves into a terminal state of euphoria and malaise. The second, ruggedly optimistic, is to draw comfort from the fact that there has never been a society on this earth which has not experimented with, habitually relied upon and occasionally abused some mind-altering substance.

Which of these two positions the average individual adopts depends as much on his or her temperament as on the state of our contemporary and historical knowledge.

Professionals working in the health field–doctors, nurses, primary health care workers, lay healers–all occupy an uneasy position within the drugs debate. They feel, and indeed are, morally obliged to document and publicise the extent to which we all ingest, smoke, drink and inject nicotine, alcohol and drugs; yet in carrying out such a valuable task they find themselves slipping into or being pushed to adopt the role of moralisers, priests and social engineers. For while such drugs have profound biological consequences, the factors that primarily influence their use are psychological, social and cultural. Our understanding of a person's propensity to alter his or her mind with various chemical substances will not be advanced by way of a narrow medical perspective. The medical profession ought not to deduce that, because a certain drug behaviour in a certain individual can legitimately be construed as an illness, the general use of such a drug in some way reflects a pathological society.

Drugs destroy families

An English couple, both aged 37, have been jailed for ten and seven years respectively for the manslaughter of their 15-month-old daughter by giving her an overdose of a heroin substitute. Both had been medically prescribed the drug Methadone in an attempt to wean them off taking heroin. They told a London court that they gave the drug to the baby "to quieten her down."

The fact is that drugs–all kinds of drugs–constitute very big business throughout the world. In Zimbabwe, tobacco production is the nation's largest industry. In Malawi, 100,000 families rely on cash from tobacco, while in the Indian state of Andhra Pradesh, tobacco provides a living for 75,000 farmers and about two million other workers are engaged in curing, packing and processing. The soaring consumption of alcoholic drinks in Third World countries has just begun to worry health care workers at a time when it is taken by some economists as a sign of improving living standards and growing industrialisation. Spectacular growth rates in beer production have been achieved in countries as varied as Japan and Bulgaria, the Netherlands and Yugoslavia. In the past 20 years, Nigeria, Mexico and Brazil have become major beer producers by world standards and have joined such traditional producers as the Federal Republic of Germany and the United Kingdom at the top of the league.

The situation is little different when it comes to illicit drugs. Ever since a fully fledged opium market was opened up in South-East Asia in the nineteenth century by the United Kingdom and other European imperial powers, there has been a massive

Drugs are big business

Left:
Opium-smoking in South-East Asia. Commercial motives among the European imperial powers in the nineteenth century encouraged the opium trade.
Photo CIRIC ©

Right:
Why the insatiable need for drugs such as alcohol? Does it reflect the growing self-assertion of youth–since drug use and abuse is primarily an activity of the young?
Photo CIRIC © and WHO/P. Hendricks

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The situation is little different when it comes to illicit drugs. Ever since a fully fledged opium market was opened up in South-East Asia in the nineteenth century by the United Kingdom and other European imperial powers, there has been a massive international trade in the cultivation and distribution of opiates and related substances. Opium in the East, like rum and guns elsewhere, was offered by European traders in return for spices, silk and tea from China and the East. Now developed and developing countries alike are struggling to contain what has been termed "the global heroin economy," which includes street dealing in Manhattan, the problems of opium farmers in India, Pakistan, Sri Lanka and Thailand, and smuggling networks which criss-cross the world's airways and oceans. Heroin use is spreading in poppy-growing countries themselves.

While alcohol and nicotine tend to be regarded as licit drugs and the opiates in general are under elaborate international controls, other mind-altering substances, such as cannabis and industrially produced psychotropic drugs, occupy a sort of no-man's land. One popular Jamaican rhyme reverses the usual image of alcohol as the superior, status-related drug and ganja (marijuana) as the inferior, down-market product:

You drink white, rum you tumble down;
You smoke kali weed, you succeed.

The dramatic expansion of psychotropic drug prescribing in Scandinavia, the UK and North America in the 1960s and 1970s was largely sanctioned by the medical profession. Only recently has it begun to provoke alarm, and there is evidence that a similar epidemic of drug use is spreading to the Third World.

So why is there this seemingly insatiable need for drugs? Is it a reflection of the growing self-assertion of youth throughout the world, given that drug use and abuse, particularly of the illicit kind, is primarily an activity of the young? Does it reflect a world-wide loss of confidence, an international epidemic of anxiety and demoralisation that is being "treated" by a wholesale recourse to intoxication? Is it a quirk of statistics? After all, it is often pointed out that no reliable statistics have ever been kept of the amounts consumed in Africa, Asia and Latin America of traditional fruit- or cereal-based alcoholic drinks.

There is hardly an expert in this area who does not believe that many factors play their part in drug use. But most would agree that the strongest single cause of the high levels of consumption is the rate of production and the energy and enthusiasm with which the product is marketed. Any nation will drink more alcohol, smoke more cigarettes or abuse more opiates if the relevant drug is made more *available*.

Not surprisingly, doctors and nurses, primary health care workers and interested members of the public are beginning to realise that the key to reducing drug- and alcohol-related problems lies in controlling production, marketing, retailing and distribution. And this realisation, in turn, sets the stage for a difficult confrontation between those anxious to reduce the negative impact of drugs on society and those for whom the production and distribution of such drugs represents a livelihood.

To paraphrase Sir William Osler, the desire to take drugs is one feature which distinguishes man, the animal, from his fellow creatures. It is, as that wise Canadian physician observed, one of the most serious difficulties with which we have to contend. He foresaw in the success of the pharmacists in producing remarkable remedies the danger that we would become used to assuming that for every ill there is a pill. That danger, if international statistics do indeed mean what they appear to mean, is already upon us. A Pandora's box has been opened, and a host of evils have been poured on the world. But let us not forget that, in the ancient Greek legend of Pandora, it was said that hope alone remained at the bottom of her box as a comfort to mankind. ■

How one family is fighting the cigarette industry in a small Southern town

Taking on Big Tobacco in Dixie

Nathan Horton, right, died addicted to the weed. His widow Ella and stepson, Nathan, aim to send a message with their suit

■ Late last month, a gray tornado blew up out of the board-flat cotton country of the Mississippi Delta and spun into the rolling hills around the county seat of Lexington, missing the town by a whisker. In the local courthouse, a judge suspended proceedings for a few hours. And as the storm blew by, the defense in this evolving courtroom drama hoped only that it would dodge disaster as neatly as the citizenry of Lexington. After all, there was an awful lot at stake. Money, for one thing. And a winning streak unlike any other in the annals of big business.

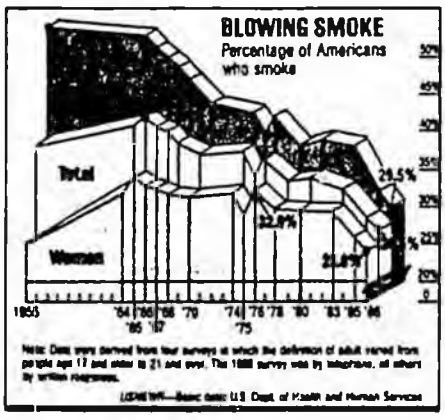
The *Nathan Henry Horton family v. the American Tobacco Company* is a case that is something of a humdinger. The facts are fairly straightforward, the implications anything but. The background: Nathan Horton, carpenter and ex-Navy seaman, smoked two packs of unfiltered Pall Malls a day. He did that for more than 35 years, right up until he died last year. He was 50. Horton's family—alleging that smoking causes cancer and that, in addition, the Pall Malls were contaminated with cancer-causing insecticides—has sued. They want $17 million. And according to some lawyers and tobacco-industry experts, they just might get it. A mistrial at week's end clouded the picture. But if the Hortons prevail when the case is retried, it'll reverse an extraordinary record for Big Tobacco, which has seen some 200 product-liability cases resolved in its favor over the years.

Peculiarities, plaintiffs' rights

For the $33.7 billion industry, it would be a particularly irksome development. Just last week, as the jury in the Horton case broke off deliberations, proceedings in another high-profile liability case against the tobacco industry were getting under way in New Jersey. And while the Horton case turns, in part, on a peculiarity of Mississippi law (jurors there may award a percentage of damages to a plaintiff even if they find a defendant only partially at fault), the determinative facts concern claims that, by the time warning labels were mandated on cigarette packages in 1966, many smokers were addicted and could not stop.

Win or lose, cases like the Horton family's spotlight increasing uneasiness about the industry. Since December, stock prices have dipped about 10 percent, on average, below the market—perhaps in anticipation of the coming lawsuits. And if the industry loses in Lexington, stock prices will drop further, though probably not to catastrophic levels because of the diversity of its holdings. American Brands, for instance, derives 50 percent of its profits from cigarette sales. But it also owns Masterlock, Jim Beam and Franklin Life Insurance. Franklin, by the way, offers discounts to nonsmokers.

The cumulative effect of the lawsuits is to fuel public debate over the dangers of smoking. There is also a more practical side, one that can only cause more uneasiness in the tobacco industry. With each new case, plaintiffs learn new legal stratagems while their lawyers uncover more and more about the tobacco industry through discovery proceedings. Richard Daynard, chairman of the 3-year-old Tobacco Products Liability Project at Northeastern University Law School, is encouraging plaintiffs' attorneys to share information as they explore new arguments. "I think there will be a large number of cases brought," says Daynard, "and many able and well-paid lawyers becoming involved."



And this, ultimately, is the significance of the trial in the little courthouse in Lexington. It is here, in this turn-of-the-century courtroom with the hard wooden seats, that the case of Nathan Horton may, better than any surgeon general's warning, finally give the lie to the tobacco industry's oft heard refrain that there is nothing to prove that cigarette smoking causes cancer. It's a message that seems to be getting through. While 350,000 smokers die in the U.S. of smoke-related illnesses each year, an additional 1.5 million stop puffing. At the same time, according to the Smoking Policy Institute, about 50 percent of U.S. businesses have instituted some sort of antismoking policy. And because of publicity surrounding cases like the Horton family's, those instances are increasing in number and severity. ■

by Sandra R. Gregg in Lexington

Lung study: 1 joint of pot as bad as 4-5 tobacco cigarettes

BOSTON (AP) — One marijuana cigarette is as bad for the body as four or five ordinary cigarettes, and regular pot users may face the same lung cancer risk as pack-a-day smokers, says the author of a new study.

"Our study deflates somewhat the myth that smoking just a little bit of marijuana can't be that bad for you compared with tobacco, since tobacco smokers generally smoke far more," said Dr. Donald P. Tashkin.

The reason is the way pot users smoke, tending to take deep puffs and hold them in.

The new study found that this style of smoking means one joint, or marijuana cigarette, deposits four times as much tar in the lungs as one tobacco cigarette. And it results in five times as much carbon monoxide in the bloodstream.

"The smokers of only a few joints of marijuana a day may have at least as great a risk of developing lung cancer, if not a greater risk, as the average tobacco smoker," said Tashkin, a researcher at the University of California at Los Angeles.

He estimates that three or four joints a day could pose about the same lung cancer risk as three-quarters of a pack or a full pack of cigarettes. There are 20 cigarettes to a pack.

Tashkin said his research suggests that pot smokers may also face an elevated risk of heart attacks.

His latest study was published in today's New England Journal of Medicine.

Experts have long suspected that marijuana smoke is harmful to the lungs, but there has been little hard evidence of this. Six years ago, a panel of the National Academy of Sciences concluded that pot smoking probably has similar effects as tobacco, and heavy prolonged use may lead to cancer.

Surgeon General C. Everett Koop has called marijuana "a major public health problem in the United States."

An estimated 25 percent of the population has tried marijuana, and millions are thought to use it regularly.

In earlier studies, Tashkin found that those who smoke three or four joints a day have as much bronchitis and damage to the major airways of the lungs as do pack-a-day cigerette smokers.

The researchers recruited 15 men who had smoked both marijuana and cigarettes for at least five years and looked for differences in how the men smoked them.

They found that the smokers inhaled three times more smoke from one joint than one cigarette. And a third more tar was retained from each puff of marijuana.

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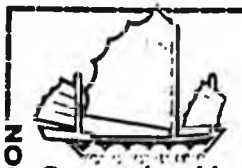

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Alcohol and the Family

The children of problem drinkers are coming to grips with their feelings of fear, guilt and rage

Believe it or not, there are still people who think that the worst thing about drinking is a hangover.

Oh, yeah, on New Year's Day I had a hangover that . . .

No. Forget hangovers.

Huh? So what should we talk about? Cirrhosis?

If you wish, but the liver, with its amazing powers of regeneration, usually lasts longer than the spouse, who tends to fall apart relatively early in the drinker's decline.

You're making it hard for a man to drink in peace.

Sorry, but even if spouses do not abuse alcohol, they can come to resemble drunks, since their anger and fear are enormous: way beyond what you'd find in a truly sober person.

I know, I know, it's terrible what goes on behind closed doors.

You make it sound like there are no witnesses. You're forgetting the children. They grow up watching one out-of-control person trying to control another, and they don't know what "normal" is.

I suppose it's hard for the kids, until they move out.

They may move out, but they never leave their parents behind.

Hmm. Listen, can we talk?

We already are. A lot of people already are.

We are, just now, learning more about heavy drinking, and, simultaneously, putting behind us the notion that what alcoholism amounts to is just odd intervals of strange, and sometimes comic, behavior: W. C. Fields, Dean Martin, Foster Brooks. Since 1935 the members of Alcoholics Anonymous have been telling us, with awesome simplicity, that drinking made their lives unmanageable; Al-Anon brought us the news that relatives and friends of drinkers can suffer in harmony; and then came Alateen and even Alatot, where one picture of a stick person holding a beer can is worth a thousand slurred words. The Children of Alcoholics (COAs)—loosely organized but rapidly growing throughout the United States—reaffirm all of the previous grass-roots movements and bring us new insight into alcoholism's effects on the more than 28 million Americans who have seen at least one parent in the throes of the affliction. The bad news from COAs: alcohol is even more insidious than previously thought. The good news: with the right kind of help, the terrible damage it does to nonalcohol-

Exercising old demons: *Gill treat undergoes g*

ics need not be permanent.

Imagine a child who lives in a chaotic house, rides around with a drunk driver and has no one to talk to about the terror. Don't think it doesn't happen: more than 10 million people in the United States are addicted to alcohol, and most of them have children. "I grew up in a little Vietnam," says one child of an alcoholic. "I didn't know why I was there; I didn't know who the enemy was." Decades after their parents die, children of alcoholics can find it difficult to have intimate relationships ("You learn to trust no one") or experience joy ("I hid in the closet"). They are haunted—sometimes despite worldwide acclaim, as in the case of artist Eric Fischl—by a sense of failure for not having saved Mommy or Daddy from drink. And they are prone to marry alcoholics or other severely troubled people because, for one reason, they're willing to accept unacceptable behavior. Many, indeed, have become addicted to domestic turmoil.

"Hurting so bad": Children of alcoholics are people who've been robbed of their childhood—"I've seen five-year-olds running entire families," says Janet Geringer Woititz, one of the movement's founding mothers. Nevertheless, the children of alcoholics often display a kind of childish loyalty even when such loyalty is clearly undeserved. They have a nagging feeling that they are different from other people, Woititz points out, and that may be because, as some recent scientific studies show, they are. Brain scans done by Dr. Henri Begleiter of the State University of New York College of Medicine in Brooklyn reveal that COAs often have deficiencies in the areas of the brain associated with emotion and memory. In this sense and in several other ways—their often obsessive personalities, their tendency to have a poor self-image—the children of alcoholics closely resemble alcoholics. In fact, one in four becomes an alcoholic, as compared with one in 10 out of the general population.

The anger of a COA cannot be seen by brain scans. But at a therapy session at Caron Family Services in Wernersville, Pa., Ken Gill, a 49-year-old IBM salesman, recently took a padded bat and walloped a couch cushion hard enough to wake up sleeping demons. "I came because I was hurting so bad and I didn't know why," he says. "A lot of things were going wrong. I

There's a Problem in the House

In "Adult Children of Alcoholics," Janet Geringer Woititz discusses 13 traits that most children from alcoholic households experience to some degree. These symptoms, she says, can pose lifelong problems.

Adult children of alcoholics . . .

- guess what normal behavior is.
- have difficulty following a project from beginning to end.
- lie when it would be just as easy to tell the truth.
- judge themselves without mercy.
- have difficulty having fun.
- take themselves very seriously.
- have difficulty with intimate relationships.
- overreact to changes over which they have no control.
- constantly seek approval and affirmation.
- feel that they are different from other people.
- are super-responsible or super-irresponsible.
- are extremely loyal, even in the face of evidence that the loyalty is undeserved.
- tend to lock themselves into a course of action without giving consideration to consequences.

was a workaholic, and I neglected my family." It took Gill only a few hours of exposure to the idea that he might be an "adult child," he says, to realize that his failings as a parent may be if not excused, then at least explained. Like a lot of kids who grew up in an alcoholic household, Gill, who is also a recovering alcoholic, never got what even rats and monkeys get: exposure, at an impressionable age, to the sight and sound of functioning parents. Suzanne Somers, the actress and singer, spent years working out her anger in the form of a just published book called "Keeping Secrets." "I decided that this disease took the first half of my life, and goddam it," she says, "it wasn't going to take the second half of it."

'Control freak': Not every COA has all of the 13 traits (chart, page 63) ascribed to them by Woititz in her landmark work, "Adult Children of Alcoholics" (*1983, Health Communications, Inc.*), and not all have been scarred (President Reagan, who has written of sometimes finding his father passed out drunk on the front porch, does not appear, from his famous management style, to suffer from any tendency to be a "control freak," a most common COA complaint). Some children of alcoholics are grossly overweight from compulsive eating while others are as dressed for success as, well, Somers. A few COAs are immobilized by depression. Another runs TV's "Old Time Gospel Hour." What these people *do* have in common is a basic agreement with George Vaillant, a Dartmouth Medical School professor who says that it is important to think of alcoholism not as an illness that affects bodily organs but as "an illness that affects families. Perhaps the worst single feature of alcoholism," Vaillant adds, "is that it causes people to be unreasonably angry at the people that they most love."

The movement is only about six years old, but expanding so rapidly that figures, could they be gathered for such a basically unstructured and anonymous group, would be outdated as soon as they appeared. We do know, though, that five years ago there were 21 people in an organization called the National Association for Children of Alcoholics; today there are more than 7,000. The 14 Al-Anon-affiliated children-of-alcoholics groups meeting in the early '80s have increased to 1,100. With only word-of-mouth advertising, Woititz's book has sold about a million copies; indeed, "Adult Children of Alcoholics" reached the number-three spot on The New York Times paperback best-seller list long before it was available in any bookstore—at a time, in other words, when getting a copy meant collaring a clerk to put in an order and *saying the title out loud*.

"We turned on the phones in 1982," says Migs Woodside, founder and president of the Children of Alcoholics Foundation in New York, "and the calls are still coming in 24 hours a day." The COAs Foundation sponsors a traveling art show that features the work of young and adult COAs; often, says Woodside, an attendee will stand mesmerized before a crude depiction of domestic violence or parental apathy ("Mom at noon," it says beneath the picture of someone huddling beneath the bedcovers)—and will then go directly to a pay phone to find help. "The newcomers all tend to say the same thing," says Woodside. "'Wait a minute—that's my story, that's *me*!'"

"It's private pain transformed into a public statement," says James Garbarino, president of the Erikson Institute for Advanced Study in Child Development, in Chicago, "a fascinating movement." But when you consider that denial is the primary symptom of alcoholism and that COAs tend by nature to take on more than their share of blame for whatever mess they happen to find themselves in, the rapid growth of the COAs movement seems just short of miraculous—something akin to a drunken stockbroker named Bill Wilson cofounding AA, now *the* model for a vast majority of self-help programs throughout the United States. After all, who would want to spill the family's darkest secret after years of telling teachers, employers and friends that everything was fine? ("A child of an alcoholic will always say 'Fine'," says Rokelle Lerner, a counselor who specializes in young COAs. "They get punished if they say otherwise.") Who would voluntarily identify themselves with a group whose female members, according to some reports, have an above-average number of gynecological problems, possibly due to stress—and whose men are prone to frequent surgery for problems, doctors say, that may be basically psychosomatic?

The answer is, only someone who had, in some sense, bottomed out, just the way a drinker does before he turns to AA.

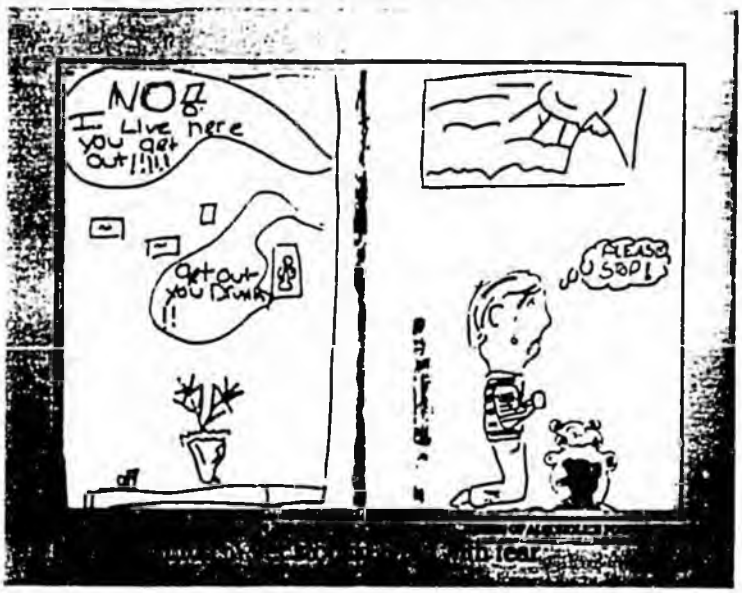
The concept of codependency is at the center of the COAs movement. Eleanor Williams, who works with COAs at the Charter Peachford Hospital in Atlanta, defines codependency as "unconscious addiction to another person's dysfunctional behavior." Woititz, in a recent Changes magazine interview, referred to it more simply as a tendency to "put other people's

Talking and playing their way to a healthy state of mind: *The*

needs before my own." A codependent family member may suspect that he has driven the alcoholic to drink (though that is impossible, according to virtually all experts in the field); he almost certainly thinks that he can cure or at least control the drinker's troublesome behavior. "I actually thought that I could make a difference by cooking my husband better meals and by taking the kids out for drives on weekends [so he could rest]," says Ella S., a Westchester, N.Y., woman. "For all I know, it's a deeply ingrained psychological, and possibly genetic, disease, and here I am going at it with a lamb chop."

Mental movies: Obsessed with her husband's increasingly self-destructive behavior, Ella's next step, in typical codependent fashion, was to hide Bob's six-packs, which made him, to put it mildly, angry. Soon they were fighting almost daily and Ella was running mental movies of their scenes from a marriage all night long. "I was wasting a lot of time and energy trying to change the past, while he kept getting worse," she says. "There was a kind of awkward violence between him and me all the time; our hearts weren't really in it, but it wasn't until he had an affair with an alcoholism counselor *that I got him to* that I left." If you're wondering about children, Ella has a seven-year-old daughter, Ann. Her omission is significant. If life were a horse race, then Ann has been, as they say on the past performance charts, "shuffled back" among the also-rans.

What COAs—all people affected by alcohol—need to learn is that the race is fixed: when there is no program of recovery—either through the support of a group or the self-imposed abstinence of an individual—the abused substance will always win, handily, no matter what the competition. The first step of AA begins, "We admitted we were powerless . . ." But what will become of Ann, who is codependent on *two* people? Perhaps, sensing that she is not exactly the center of attention, she will reach adulthood with a need for constant approval, a common COA symptom. Or maybe she will, even as a child, react to the chaos by trying to keep everything in her life under control, and thus give the impression that she is, despite everything, quite a trouper, a golden child.

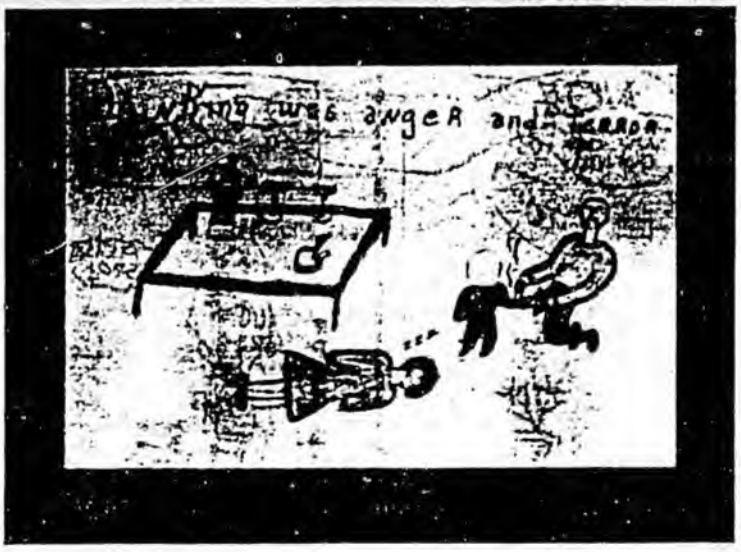


"[Some] don't fall apart until they're in their 20s or 30s," says Woititz, and in some cases, especially those marked by violence or incest and sexual abuse (three times more common in alcoholic households than in the general population), that's the wonder of it all. One eight-year-old patient at Woititz's Verona, N.J., counseling center woke up in the middle of the night to see her alcoholic mother shoot herself in the head. "The child called the 911 emergency number, got her mother to the hospital and basically saved her mother's life," says Woititz. "When I saw her she was having

f mind: *The board game Sobriety (left). Brooks with a father and son at her California counseling center*

TOM IVES

RICK RICKMAN



nightmares—that she wouldn't wake up and witness this suicide attempt. This is not a normal nightmare. The child had become mother to her own mother."

Each unhappy family, as Tolstoy said, is unhappy in its own way. Artist Eric Fischl, 39, in a short videotape he made for the COAs Foundation called "Trying to Find Normal," speaks of stepping over his passed-out mother, in their comfortable-looking (from the outside) Port Washington, N.Y., home and seeing her "lying in her own piss." His work, which has been the subject of a one-man show at the Whitney Museum in New York, is not autobiographical, he says, and yet "the tone [of it] has everything to do with my childhood." His painting "Time for Bed" (page 63) "relates to my memory of all hell breaking loose," he says. "I guess you could say the boy is me and his shame, embarrassment and sadness is mine as well. The little boy's Superman pajamas are on backwards, so it's like looking in a mirror. I painted the woman standing on a glass table with spiked heels on to give it a sense of fragility and danger. The man only has one arm because I wanted a sense of impotence."

Alcohol leaves every alcoholic and codependent who does not admit his powerlessness over the substance in a constant state of longing. Fischl didn't realize how sad he'd been until his mother died, in an alcohol-related car accident, in 1970. "The thing about having a sick parent is that you think it's your problem," he says. "You feel like a failure because you can't save her." Even when there is no incest, there is seduction. Fischl's mother kept "signaling," he says, "that if you could just come a little bit further with me in this, you can save me."

Some of the other things that alcohol ruins, before it gets to the liver: family meals ("Alcohol fills you up. My father was never interested in eating with us"); gloriously run-of-the-mill evenings around the hearth ("Alcohol makes you tired. My father was in bed most nights at 8"). When enough C_2H_5HO is added to a home, vases may start to fly across the room and crash

Heredity and Drinking: How Strong Is the Link?

Research on the genetics of alcoholism took a curious turn a few weeks ago when Lawrence Lumeng analyzed his DNA to demonstrate why he can't tolerate liquor. Lumeng, a biochemist at the Indiana University School of Medicine, is among the 30 to 45 percent of Asians whose response to spirited beverages is a reddened face, headaches or nausea. This "Oriental flush," past studies have shown, arises in those who have an inefficient version of a liver enzyme that is crucial to the body's breakdown of alcohol; this "lazy" enzyme allows the buildup of an alcohol product, acetaldehyde, which is sickening and leads many Asians to shun alcohol. Working with biochemist Ting-Kai Li, Lumeng says that he pinpointed the gene that instructs cells to make the odd enzyme. The experiment offers dramatic evidence that a bodily response to alcohol is genetically dictated—and is thus inherited as surely as eye color.

There is no evidence for the opposite proposition: that a specific gene makes a person *crave* alcohol. Considering the wide variety of reasons why people consume the stuff, it seems unlikely that a "drinking gene" exists. But researchers have firmly established that, compared with other children, an alcoholic's offspring are around four times more likely to develop the problem, even if they were raised by other, nonalcoholic parents. In families with a history of alcoholism, explains C. Robert Cloninger, a psychiatrist and geneticist at Washington University in St. Louis, "what is inherited is not the fact that you are destined to become an alcoholic but varying degrees of susceptibility" to the disorder. So real is the predisposition that many researchers advise adult children of alcoholics (COAs) to drink no alcohol whatsoever.

Even the brains of COAs show faint signs of unusual activity, according to controversial studies by psychiatrist Henri Begleiter of the State University of New York in Brooklyn. Begleiter has found that young boys who have never consumed alcohol produce the slightly distorted brain-wave patterns typical of their alcoholic fathers. Such signature brain waves, he says, may mark the son of an alcoholic as likely to develop a drinking problem and perhaps alert him to the risk. However, it

MARY ANN SARTER

Probing for genes: *Lumeng*

into walls. All kinds of paper—court-issued Orders of Protection, divorce decrees, bounced checks—come fluttering down. The lights go on and off. Does that mean Daddy's forgotten to pay the bill again, or that the second act is starting?

Every alcoholic household is, in fact, a pathetic little play in which each of the members takes on a role. This is not an idea that arrived with the COAs movement; a 17-page booklet called "Alcoholism: A Merry-Go-Round Named Denial" has been distributed free of charge by Al-Anon for almost 20 years. Written by the Rev. Joseph L. Kellerman, the former director of the Charlotte, N.C., Council on Alcoholism, "Merry-Go-Round" takes note of the uncanny consistency with which certain characters appear in alcoholic situations. These include the Enabler ("a 'helpful' Mr. Clean . . . [who] conditions [the drinker] to believe there will always be a protector who will come to his rescue"); the Victim ("the person who is responsible for getting the work done if the alcoholic is absent") and the Provoker (usually the spouse or parent of the alcoholic, this is "the key person . . . who is hurt and upset by repeated drinking episodes, but she holds the family together . . . In turn, she feeds back into the marriage her bitterness, resentment, fear and hurt . . . She controls, she tries to force the changes she wants; she sacrifices, adjusts, never gives up, never gives in, but never forgets").

Some of the earliest books in the COAs movement explored the drama metaphor more deeply and defined the roles that children play. Sharon Wegscheider-Cruse, in her 1981 book, "Another Chance" (*Science and Behavior Books, Inc. Palo Alto, Calif.*), wrote about the Family Hero, who is usually the firstborn. A high achiever in school, the Hero always does what's right, often discounting himself by putting others first. The Last Child, meanwhile, is withdrawn, a loner on his way to a joyless adulthood, and thus, in some ways, very different from the Scapegoat, who appears hostile and defiant but inside feels hurt and angry. (It is the Scapegoat, says Wegscheider-Cruse, who gets attention through "negative behavior" and is likely to be involved in alcohol or other drugs later.) Last and least—in his own mind—is the Mascot, fragile and immature yet charming: the family clown.

'Good-looking' kids: Virtually no one was publishing those kinds of thoughts when Claudia Black, a Laguna Beach, Calif., therapist, began searching for literature on the subject of the alcohol-affected family in the late '70s. "Half of my adult [alcoholic] patients had kids my age and older," she remembers, "but all I found was stuff on fetal alcohol syndrome and kids prone to juvenile delinquency." One thing that fascinated her about young COAs, she says, was that despite their developmental problems "they were all 'good-looking' kids"—presentable and responsible albeit

remains to be seen whether such brain scans are sufficiently reliable and informative to distinguish potential social drinkers from future alcoholics. The technique, comments psychologist Robert Pandina, scientific director of the Center of Alcohol Studies at Rutgers University, is "at this time not any more valuable" as a predictor of future drinking behavior "than collecting a good family history on an individual."

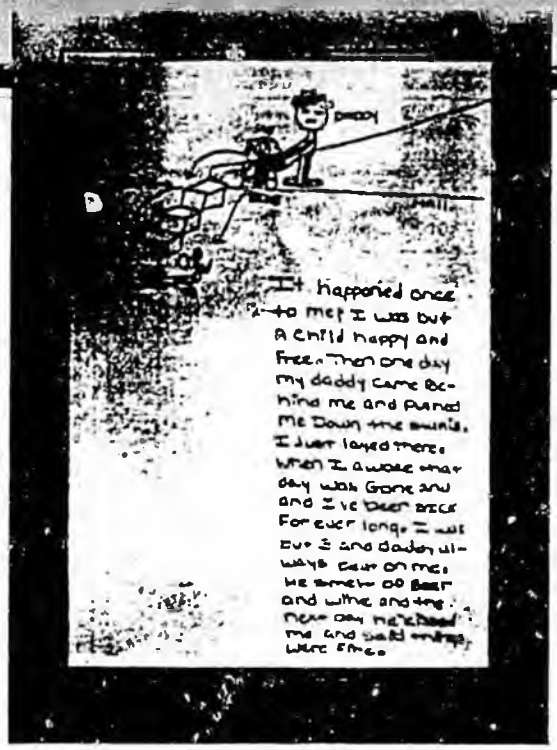
Other studies show that many COAs respond uniquely to booze. Marc Schuckit, a psychiatrist at the Veterans Administration Hospital in San Diego, has found that college-age sons of alcoholics often react less to a few drinks than other college men; in his studies, the drinkers' sons were generally not as euphoric or tipsy after three to five cocktails. Schuckit believes that this lower sensitivity makes it harder for the alcoholics' sons to know when to stop drinking, starting them down the road to alcohol problems. Preliminary experiments by Barbara Lex of McLean Hospital in Belmont, Mass., confirm that daughters of alcoholics respond similarly. Women from families with a history of alcohol abuse tend to keep their balance better on a wobbly platform after having a drink. Apparently women, too, can inherit traits that might predispose them to addiction, although there are far fewer females than male alcoholics.

Half a beer: The key unresolved issue, of course, is why some individuals from alcohol-scarred families succumb to alcoholism while others don't. Genes play some role in the development, most notably in abstinence. "People say that whether you drink or not has to do only with willpower," explains Indiana's Lumeng, "but the reason I can drink only half a beer is biological."

Yet heredity alone obviously isn't to blame for alcoholism's appalling toll. In fact, about 60 percent of the nation's alcohol abusers are from families with no history of the disorder. How much people drink is influenced by factors as prosaic as cost; partly to curb consumption, the National Council on Alcoholism is lobbying to raise federal excise taxes on beer and wine, which haven't changed since 1951. Social influences like cost and peer pressure "are just as important as genes," says Dartmouth psychiatrist George Vaillant. "All the genes do is make it easier for you to become an alcoholic." For now, the value of genetic studies is to warn COAs that they may well have a real handicap in the struggle against the family trouble.

TERENCE MONMANEY with KAREN SPRINGEN in New York and MARY HAGER in Washington

Tipsy? *Lab demonstration*



not terribly verbal. "They had friends but weren't honest with them. Everything was 'fine and dandy'."

The title of Black's important 1981 book, "It Will Never Happen to Me" *(M.A.C. Denver, Colo.)*, reflects the typical codependent's mix of denial and false bravado. In it, she makes the point that the children in an alcoholic household never have an environment that is consistent and structured, two of the things they need most—and she, too, talks of such stock juvenile "roles" as the Responsible One and the Adjuster. Her unique warning was that children who survive a parent's alcoholism by displaying unusual coping behavior often experience "emotional and psychological deficits" later on. They are also likely to become alcoholics, says Black, because "alcohol helps these persons become less rigid, loosen up and relax. When they drink, they aren't quite so serious." Though those things happen to almost everyone who imbibes, Black says that "for those who are stuck in unhealthy patterns, alcohol may be the *only* thing that can provide relief."

Well, she guessed wrong there: a movement, manifested by often joyous meetings, has come along in the interim. At hundreds of COAs gatherings around the country tonight, people will talk and listen to each other's stories, to cry, to laugh and generally, as Ken Gill says, "recharge their batteries." "This program kept me from being an alcoholic myself," said a woman named Heather at a gathering in an affluent section of San Francisco last week. "Because I was the oldest, everything was always my fault. It's like when you make your parents breakfast and you bring them one scrambled egg and one fried egg—in my house I always scrambled the wrong egg." Heads bobbed in agreement. Who else but COAs could identify with a story about what happens when kids cook for their own mother and father?

Discovering self-esteem: Talking and listening: this is the way we've learned to deal with problem drinking. And though it sounds wimpy, don't knock it; it's the surest way to alleviate not just the imbibing but the whole range of symptoms we call alcoholism. A woman named Nina stood up at a meeting in Boston last week, practically glossed over the fact that both her parents were alcoholics—and proceeded to speak about how well she was feeling and doing. COAs meetings and literature, she said, had allowed her to discover self-esteem. At another meeting, Carolyn told a story of complaining to her doctor about depression—and hearing the doctor shoot back a question about whether one of her parents was an alcoholic. "I was shocked," she said, and well she might be. Doctors, as a group, have yet to play a major role in helping mitigate the effects of alcohol, perhaps because the average medical-school student spends a grand total of between zero and 10 hours studying the affliction that kills 100,000 people annually.

An avalanche of information is coming, nevertheless, from another kind of M.D.—call them the Masters of Disaster, the people who've lived with alcoholism or worked with alcoholics so closely that they might as well be the victim. Robert Ackerman, a professor of sociology at Indiana University of Pennsylvania, has been studying the children of alcoholics for an exceedingly long time by the standards of the movement—since the early '70s. In his recent book "Let Go and Grow" *(Health Communications, Inc.)*, he reports on a survey he took to test the validity of Woititz's 13 generalizations about COAs, as well as seven more observations of his own. What he found was that "adult children of alcoholics identified about 20 percent more with these characteristics" than did the general population. Other professionals are reporting success with therapies involving hugging, acting out unresolved scenes from long ago and even playing one of several board games for children of alcoholics called Family Happenings and Sobriety. Cathleen Brooks, executive director of a program called Next Step in San Diego, reports that her clients often make life-changing strides after six to 18 months of primary treatment and make the decision never to drink or take drugs.

A founding mother of the movement: *Woititz*

The 7 million COAs who are under the age of 18 are harder to help, if only because their parents' denial tends to keep them out of treatment. For these children who never know what to expect when they come home from school each day, life, says Woititz, "is a state of constant anxiety." Some pediatricians think there is a link between such anxiety and childhood ulcers, chronic nausea, sleeping problems, eating disorders and dermatitis. Migs Woodside, from the COAs Foundation, says that the trained teacher can pick the child of an alcoholic out of a crowded classroom. "Sometimes you can tell by the way they are dressed or by the fact that they never have their lunch money," she says. "Sometimes you can tell by the way they suddenly pay attention when the teacher talks about drinking, and sometimes you can tell by their pictures."

Someday, 20 or 30 years from now, those children may feel a vague sense of failure or depression and be hard pressed to explain why. In the meantime, it's their Crayolas that are hard pressed. Beer cans—and not liquor or wine bottles—form a leitmotif in the work of young children of alcoholics. Occasionally, Woodside says, looking a little sad, the big stick figures can be seen tipping the cans into the mouths of the little stick figures.

CHARLES LEERHSEN with TESSA NAMUTH and bureau reports

MARIJUANA:

A SECOND LOOK AT HEALTH HAZARDS

Every Child Must Make a Decision about Marijuana.

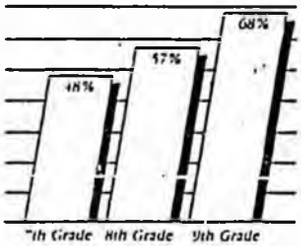
More than two and a half million adolescents smoke marijuana regularly. This includes one in twenty American high school seniors who smoke marijuana daily. Of greater concern is that one-third of high school seniors who smoke marijuana started in 9th grade or before. An increasing number first tried it in the 6th grade. These facts show that marijuana use is widespread among American youth and that the age at first use is declining. It is clear that every child will have to make a decision about marijuana. In order to help children make the smart decision, preventive measures must be taken early. This means teaching children the facts about marijuana and arming them with the skills to say "no" to pot.

Kids face a lot of peer pressure.

According to a 1985 survey by *Weekly Reader* magazine of over 100,000 students in grades 4 through 12, the main reason cited by students for smoking marijuana is to "fit in with other kids." In addition, this survey reported that more than one-quarter (28%) of 4th graders believe that kids their age feel "some" or "a lot" of pressure to use marijuana. These children face increasing peer pressure as they get older; see the bar graph above.

WHAT IS THE PROBLEM?

How much do kids push each other to smoke pot?



The Weekly Reader survey demonstrates increasing peer pressure among school children. A critical period, 7th–9th grades, is shown here.

Marijuana Isn't Kid Stuff.

Today's marijuana is often ten times stronger than the pot of the 1960's and 70's. Marijuana's potency is measured by the concentration of THC, the drug's principal intoxicating chemical. The average increase in THC from 0.5% to 4.5% makes today's marijuana more powerful and much more hazardous.

Kids are vulnerable. Smoking marijuana is especially dangerous during adolescence. Physical, psychological and sexual changes are rapid and complex. Any disruption of the normal processes due to marijuana smoking at this critical stage in development may have harmful and lasting effects. In particular, the THC in marijuana inhibits the hormone which sets adolescent development in motion.

What Makes Pot So Bad? Marijuana consists of the dried flowers, leaves and leaf stems of the plant *Cannabis sativa*. It is composed of over 400 substances which convert to over 2000 chemical compounds when marijuana is smoked or burned. The smoke contains a greater concentration of some of the cancer-causing substances (benzpyrene and benzanthracene) and lung irritants (acetone, acetaldehyde, and hydrocyanic acid) than those found in tobacco smoke. THC (delta-9-tetrahydrocannabinol) is the main psychoactive, or mind-altering, substance; it produces the marijuana "high." THC is fat-soluble and therefore is retained by the tissues of the lungs, liver, reproductive organs, and brain for up to one month after one marijuana cigarette has been smoked. Alcohol and nicotine, on the other hand, are water-soluble and leave the body in a few hours.

Marijuana Is a Gateway Drug.

The peer pressure that leads young people to try pot often leads them to try other, even more hazardous drugs. Half of daily marijuana smokers use amphetamines and one-third use cocaine.

The tobacco connection. An incredible *81%* of tobacco smokers have tried marijuana, compared with *17%* of non-smokers. Further, tobacco smokers are *14 times* more likely to use cocaine, amphetamines, and heroin.

A dangerous combination. The many users who smoke marijuana and tobacco subject themselves to a double hazard. The combined effects of these substances pose a far greater threat of lung disease.

Marijuana Causes Lung Disease.

There can be little doubt. Marijuana smoke has greater concentrations of the cancer-causing substances found in tobacco smoke. It has 12 times the "tar" and 10 to 20 times as much carbon monoxide. The lung's delicate tissues get greater exposure to these harmful chemicals because marijuana smokers inhale deeply and hold the smoke in their lungs to get the greatest "high". Smoking marijuana daily for 5 years or more produces the kinds of changes in lung tissue seen in people who have been smoking for 10 to 15 years. These changes are the same as those in people who develop chronic bronchitis, emphysema and lung cancer.

Reduced lung function. Marijuana irritates the lung's air passages making

Normal Lung Cells | *Cells Damaged by Marijuana*

AMERICAN LUNG ASSOCIATION
The Christmas Seal People

breathing more difficult. Further, it impairs the special lung cells that fight infection.

Because marijuana smoking is a recent phenomenon, the long-term effects of its use are not yet documented. It is likely, however, that as pot-smokers age, the continuous assault on the delicate tissue of the lungs will cause debilitating lung disease.

Pot Smoking Doesn't Just Hurt the Lungs.

Marijuana also interferes with normal functioning of the cardiovascular, nervous, and reproductive systems.

The heart and cardiovascular system. Marijuana can increase heart rate by as much as fifty percent, depending on the THC concentration of the particular marijuana cigarette. At the same time, oxygen supply to the heart is reduced, causing chest pain and other harmful consequences in people with underlying cardiovascular problems.

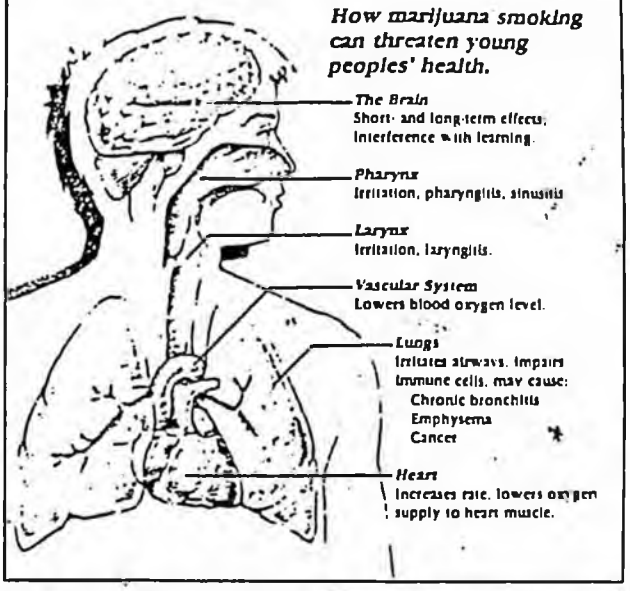
The brain and central nervous system. Marijuana use can result in both short-term and long-term effects on the brain. The short term effects include distortion of time and space perception and interference with thinking and learning. Some marijuana smokers experience "acute panic anxiety reactions" which include paranoia, abnormal fears, and extreme anxiety. Long-term regular users are often dependent on the drug and can experience "burn-out", a feeling of energy loss and apathy.

Sexual development and the reproductive system. In both males and females, marijuana causes impairment of normal sexual development. Marijuana smokers can develop tolerance to the drug but the sperm or eggs they carry inside can be adversely affected by marijuana's toxic chemicals.

Specifically, marijuana causes increased menstrual cycle abnormalities and interference with ovulation. When a pregnant woman smokes marijuana, the drug's chemicals enter her bloodstream, travel through the placenta, and enter the bloodstream of her fetus.

INSIDE STORY

How marijuana smoking can threaten young peoples' health.



In addition, marijuana increases the incidence of abnormal sperm cells (see photograph) and decreases sperm production, sperm motility and male hormone levels.

Healthy vs. Unhealthy Sperm

On the left is a healthy sperm, on the right the sperm of a chronic hashish smoker. Hashish is a stronger form of marijuana.

Other Consequences: Social and Psychological.

Children who smoke marijuana often exhibit a behavior pattern that includes: energy loss, diminished school performance, low motivation, absenteeism, difficult peer and parental relations and low self-esteem. Emotional and psychological development is interrupted when marijuana is used to avoid confronting normal adolescent "growing pains" and problems.

Parents Can Help.

Young children want the opinions and advice of their parents and other adults. They look to them for direction and guidance. Parents and teachers are vital role models during a child's social and psychological development.

Parents must be informed. It is important for parents to learn about the health hazards of marijuana so they can be confident that they are relaying relevant and up-to-date information to their children. As children get older and peer pressures mount throughout junior and senior high school, it becomes more difficult for parents to influence their children's behavior. Children accustomed to discussing the problems of drugs with their parents are more likely to continue this communication when they become teenagers. They will be better equipped to resist peer pressure and to say "no" to marijuana.

Driving High—A Deadly Road Hazard.

Marijuana impairs many driving skills including coordination, reaction time, and perception. Pot smoking can create the false impression that the user is driving capably, when in fact his or her critical driving abilities are badly impaired. Marijuana has been detected in the blood and urine of a disproportionately large number of highway accident victims. This finding indicates that a significant number of highway accidents and deaths are due to "drug driving".

Drugged, drunk and driving. Statistics show that teenagers frequently use marijuana and alcohol together. Since alcohol and marijuana affect the central nervous system in different ways, their combined use doubly impairs the user's ability to drive; and greatly increases the risk of tragedy on the highway.

AMERICAN LUNG ASSOCIATION

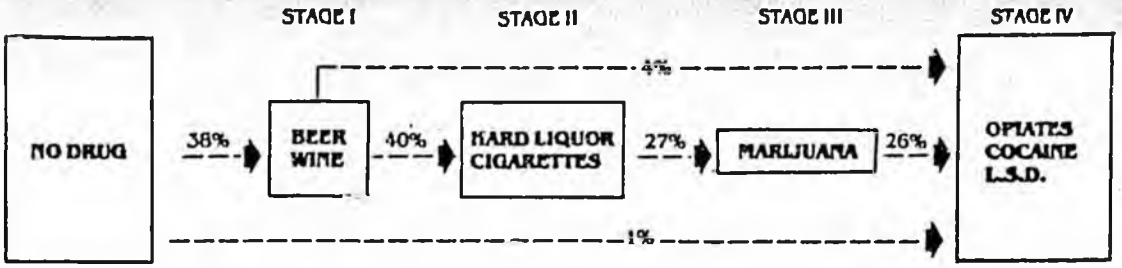
alcohol update
FACTS AND FIGURES FROM THE ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATIC

ALCOHOL AND DRUG ABUSE AMONG ADOLESCENTS

- Approximately 6.2 million young people age 12-17 have used marijuana at some time during their lives; 2.7 million have used marijuana in the last month; 4.8 million have used marijuana in the past year. (1)
- Nearly two-thirds (61%) of all American high school seniors use an illicit drug at least once before they finish high school; 40% have used drugs in addition to marijuana. (2)
- Cocaine has been tried by at least 17% of seniors in the Class of 1985--the highest rate observed so far in the National High School Senior Survey. (2)
- Approximately 80% of 1985 seniors acknowledged the harmful effects of using cocaine regularly (an increase of 10% since 1979); but only about 34% saw much risk in experimenting with it. (2)
- One out of every 20 high school seniors (4.9%) smokes marijuana on a daily basis. (2)
- Approximately 30% of high school seniors have smoked cigarettes during the last month, a substantial proportion of whom are daily smokers. (2)
- About one in 20 seniors (5.0%) drinks alcohol daily.
- Approximately 92% of all high school seniors have used alcohol; 66% used alcohol in the last month, and 86% used it in the past year. (2)
- Nearly half (45%) of boys and more than 1/4 (28%) of girls in the 1985 senior class report heavy party drinking (five or more drinks in a row) on at least one occasion in the two weeks prior to the 1985 survey. (2)
- Motor vehicle accidents involving alcohol are the leading cause of death for young Americans aged 15 to 19, accounting for 45% of fatalities in this age group. (3)
- Although 16-24 year-olds comprise only 20% of licensed drivers in the U.S. and account for less than 20% of total vehicle miles traveled, they are involved in 42% of all fatal alcohol-related crashes. Close to 8,000 people between 15 and 24 were killed in alcohol-related traffic accidents in 1984, and an additional 220,000 were injured. (4)

No. 1, April 1986

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • Public Health Service



STAGES OF DRUG USE

This diagram illustrates the successive stages in adolescent drug use observed in two follow-up surveys ("longitudinal") of 5,468 New York State High School students between fall 1971 and spring 1972, and 985 seniors 5 months after graduation. Students start using legal drugs, beer or wine, and go on to smoking cigarettes and drinking hard liquor. While 27% of students who smoke and drink progress to marijuana within a 5 to 6 month follow-up period, only 2% of those who did not drink or smoke previously, do so. **Marijuana is turn is a critical step on the way to other illicit drugs.** While 26% of marijuana users will experiment with L.S.D., amphetamines and opiates, only 1% of non-drug users and 4% of legal drug users do so. This sequence is found in each of the 4 years in high school and in the year after graduation (Kandel, D., Stages in Adolescent Involvement in Drug Use. Science, 190:912, 1975).

A 1980 study confirmed the statistical progression of marijuana to heroin and cocaine. "The linkage between marijuana use and later heroin or cocaine use is **10 times** greater than the evidence of linkage between cigarette smoking and lung cancer." (Clayton, R. and Voss, H. U.S. Jour. of Drug and Alcohol Dependence, Jan. 1982).

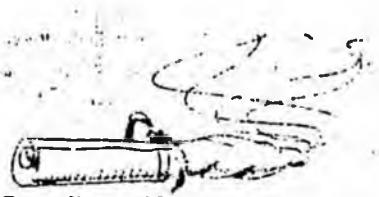
—Excerpted from "Keep off the Grass" Third Edition, Futura-McDonald, 1983

The Evidence Builds

School and Drugs Do Not Mix

Many times in this publication we have described the connection between drug use and school problems. A recent study in Clinical Pediatrics adds to the accumulating evidence that student drug use has a direct, negative effect on education.[1]

The sample for the study consisted of 35 adolescents in a drug treatment program who had smoked marijuana at least four days a week, every week, for at least four continuous months.



Regarding problems in school, the researchers found that:

- 31 percent reported having had serious academic problems—two or more D or F grades on their sixth grade report card—before marijuana use began.
- 60 percent reported at least three D or F grades per marking period after marijuana use became frequent.
- 51 percent said that they either skipped school or some classes every day.
- 71 percent had been suspended, 9 percent had been expelled, and 11 percent had dropped out of school.

The study also found relationships between the onset of heavy marijuana use and family problems, suicide attempts, and automobile accidents.

1. R.H. Schwartz, N.G. Hoffman, R. Jones. Behavioral, Psychosocial, and Academic Correlates of Marijuana Usage in Adolescence. May 1987: pp. 264-70.

Essay

Charles Krauthammer

The Ginsburg Test: Bad Logic

Did F.D.R. have a drink during Prohibition? (He did.) Douglas Ginsburg, nominated for the Supreme Court, did the '60s' equivalent, and within two days of the revelation was crushed in a political avalanche. Most Americans tell pollsters they don't think past marijuana use should be a disqualification for high office, but polls don't make politics. Not many Americans would disqualify a presidential candidate for a bit of plagiarism either. That didn't help Joe Biden. It remains to be seen how much damage the marijuana issue will do to presidential candidates like Albert Gore and Bruce Babbitt. But there is no doubt what would happen to the latest Supreme Court nominee if a joint or two turned up in his background. He'd be finished.

Polls or no polls, the fact is that marijuana use can jeopardize one's chance for high office. We are stuck with the Ginsburg test, so we might as well think it through.

▸ Is marijuana use wrong? Most of the penitents who have rushed to confess to smoking dope have agreed that it is. "It was a mistake," said Babbitt. "I wish I hadn't," said Gore. "I hope that the young people of this country, including my own daughters, will learn from my mistake," said Ginsburg, withdrawing. Conversely, Columnist Tom Wicker, in a biting critique of the phony moralism and "sudden piety" of Ginsburg's attackers, felt compelled to preface his remarks about marijuana smokers by assuring his readers that "I am not now and never have been one of them." An odd credential to flash. It undermines Wicker's premise that in the conduct of public affairs (which includes public debate) one's marijuana history is an irrelevancy.

In the '70s the hysterically antimarijuana film *Reefer Madness* was a camp classic to be mocked by stoned viewers at the midnight show in the local art house. The Zeitgeist of that generation is now wildly reversed. Public figures who used pot at that time express regret for the transgression. Political survival demands that they not offend the new cultural norm. Marijuana use now carries a moral taint.

▸ Why? In what way did Ginsburg or Gore or Claiborne Pell (a one-time, four-puff penitent) do wrong? The most obvious answer is that they willfully broke a law. True. But if what is at stake is respect for law, why the agitation about this particular law out of the thousands on the books, out of the dozens that every non-monastic citizen has broken at one time or another. If law is the issue, then the press ought to be asking public figures not "Have you ever smoked marijuana?" but "Have you ever broken the law, any law?" We could start with "Do you speed?" Or "Have you ever driven drunk?" Or "Did you ever read pornography before the relevant Supreme Court rulings that made it legal?" And, for the bolder reporter, "Have you ever engaged in any variety of carnality prohibited by state law at the time?" If lawbreaking is really the issue, then focusing on marijuana use seems to be a peculiarly narrow way to approach the question.

▸ And not just narrow, but unconvincing. What if it had turned out that Ginsburg smoked dope only on camping trips to Alaska, where marijuana possession for private use is, under state law, entirely legal? Would Ginsburg still be a candidate for the Supreme Court? Not a chance.

▸ Ginsburg's marijuana use was greeted with revulsion not because of its illegality, but because of its perceived intrinsic moral taint. Even without law, it is something that demands contrition. Why? Because, to summarize much that has been said on the subject, it is a decadent, nihilistic, frivolous giving over of one's consciousness and self-control to the pleasures of a waking stupor. Fine. But any moral reasoning that leads you to call immoral that kind of self-surrender must lead you to conclude the same about drinking, which can get you to a stretch of Lethe-land right next door to marijuana's.

This is not to imply, as pot propagandists do, that marijuana should be legalized. If you were inventing a new society, perhaps. You might prefer the intoxicant of choice to be marijuana, since alcohol can be more physically damaging and addicting. But such considerations are irrelevant to deciding what society ought to do about marijuana today. We are not inventing a new society. There is such a thing as history. We have millenniums of experience with alcohol. It is ineradicably part of our culture. The question today is not Will it be alcohol or marijuana? The only relevant question is Will it be alcohol and marijuana? Do we need to legitimize more intoxicants?

The answer is no. Which is why it makes sense for society to discourage marijuana use. Not because it is immoral—it is no more so than alcohol—but because it is destructive and society has the right to legislate self-protection.

▸ Marijuana is destructive in two ways. First, you can't learn on marijuana, and marijuana attracts the young. It kills their time, robs their attention and stunts their development. Use it often enough in your teen years, and you get to adulthood having lost crucial months, years, of emotional and intellectual growth. Second, marijuana is a gateway to harder drugs, the stuff like cocaine and heroin that can destroy people in very short order.

What, then, to do about the use of a substance that is not intrinsically immoral but that society wants to discourage because of its potential for harm? We have muddled through to a fairly good compromise: make the use illegal, but be extremely circumspect about enforcing the law. Illegality is important to prevent the predictably vast increase in use that would occur if you could get a pack of Acapulco Gold out of the machine that now gives you Kools. And non-prosecution is important because you don't persecute people for behavior that you find impossible to argue is morally wrong.

▸ Which makes the Ginsburg test so hard to justify. Did a few encounters with marijuana really make him morally unfit for the Supreme Court? Six out of ten Americans born in the '50s and '60s tried pot by age 25. A test that has the potential for disqualifying almost two-thirds of the population from high public service needs a compelling logic. The Ginsburg test doesn't have one. That won't save poor Ginsburg. But it might save a few others down the road. ■

TODAY'S DRUG SCENE

. . . . The Facts, The Choices . . . .

A HANDBOOK of DRUG FACTS and INFORMATION

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COMMITTEE FOR
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Marijuana potency increases

By MIKE ADAMS
The Baltimore Sun

Thousands of Americans are getting hooked on superpotent marijuana that is up to 40 times stronger than varieties of the plant that were available just a decade ago.

Some of the superpotent marijuana contains as much as 20 percent THC, a psychoactive compound that causes intoxication. Ten years ago, the THC content of marijuana generally ranged from one-half percent to about 5 percent. The new superpotent marijuana was developed by growers who have used the basics of genetic engineering to produce a more powerful plant.

Michael Leeds, an addictions specialist from Ukiah, Calif., said he has treated marijuana smokers who meet the criteria set for addiction. Leeds said he believes that the patients were addicted because they smoked marijuana compulsively, they couldn't stop using the drug and they continued to abuse marijuana in the "face of adverse consequences."

Leeds was one of several drug experts who spoke at the Maryland Drug Abuse Administration's conference on drug epidemics. About 100 people, many of whom are involved in the treatment of addicts, attended the session in Baltimore.

"Ten years ago, I would have had a lot of difficulty even talking about marijuana as an addictive drug," Leeds said. "Have you ever, and I'm sure you have, treated someone who's obsessed by pot? People who wouldn't go home if they didn't have marijuana or who wouldn't go in a party without pot or wouldn't travel, walk, talk or go to the show or go to school without marijuana.

"There are some adults and some children in our society who use marijuana compulsively," he continued. "In the 1970s we considered heavy users anyone who smoked pot more than once a week. In 1985, we call a heavy abuser anyone who smokes from three to five joints a day. Now that is a substantial change."

Leeds said very little is known about the health effects of prolonged use of the superpotent marijuana. Since the drug is relatively new, he said it will take about 20 years before its effects will show up.

Leeds said marijuana smoking is rampant among children and teenagers. He said continued use of the drug stunts the intellectual and emotional growth at a critical time during the users' development.

Leeds said many youths are using marijuana along with other drugs and alcohol. He said many of them do not understand the dangers inherent to this pattern of drug abuse.

"Getting high is relative to not being high," he said. "If you smoke pot daily, then you're high most of the time and that becomes a normal waking state for you. If you start using at 12 and smoke regularly until you're 16 then your friend says it's your birthday, let's party. What would you party on? Pot? Maybe, but pot is like air to some adolescents. It wouldn't be thrilling enough or breathtaking enough, so that opens the door to LSD, cocaine or opium."

Leeds said that the use of tobacco and alcohol are often the precursors to drug abuse.

"If children don't smoke any other thing, if they don't do any other smoking behaviors, then smoking that joint is an enormous risk," Leeds said. "On the other hand, if they have already experimented with tobacco products, and are smoking cigarettes, then the step to smoking a joint is a lot smaller. The same model holds true for the use of intoxicating beverages like alcohol."

Meanwhile, an underground chemist has produced a drug so powerful that an amount the weight of a postage stamp will keep 1,000 people high for a month. The drug is an analog of fentanyl, a legal drug that is used as a pain killer. Robert Roberton, the chief of California's division of drug programs, said the drug has killed more than 100 persons in that state. There are unconfirmed reports that the drug has turned up in Florida, New York and Detroit.

Another underground chemist turned out a bad batch of drugs that crippled people in California. The drug attacks the portion of the brain that controls motor skills, and its effects are irreversible. Its side effects are similar to Parkinson's disease.

"They were trying to make synthetic Demerol, but they heated the chemical too much and made MPTP instead," Roberton explained. "MPTP is a neu. otoxin. We estimate that 500 people got his bad batch and we're evaluating them now."

People who didn't say no

Hospital emergency rooms are the MASH units of the drug wars, places where rhetoric is irrelevant and "cool" turns deadly. In 1986, for the first time, the number of cocaine-related visits passed those from any other cause.

Drug-related emergency-room visits in 1986 and change since 1983—

	VISITS	CHANGE
Atlanta	2,045	Up 22%
Baltimore	2,703	Up 19%
Boston	2,757	Up 7%
Buffalo	1,442	Down 25%
Chicago	6,873	Up 40%
Cleveland	2,143	Down 8%
Dallas	3,037	Up 106%
Denver	3,164	Up 19%
Detroit	11,865	Up 21%
Indianapolis	1,114	Down 24%
Kansas City	1,940	Up 32%
Los Angeles	10,894	Down 5%
Miami	4,616	Down 1%
Minneapolis	2,373	Up 39%
New Orleans	2,552	Up 11%
New York	15,484	Down 31%
Norfolk	796	Up 20%
Oklahoma City	934	Up 23%
Philadelphia	7,178	Up 20%
Phoenix	3,305	Up 52%
St. Louis	2,276	Down 2%
San Antonio	1,821	Up 45%
San Diego	2,489	Up 20%
Seattle	2,621	Up 17%
Washington, D.C.	6,240	Up 65%

Note: Figures are for metropolitan areas

Emergency-room visits involving particular drugs in 1986 and change since 1983—

	VISITS	CHANGE
Cocaine	24,847	Up 245%
Alcohol with other drugs	21,801	Down 15%
Heroin or morphine	15,832	Up 23%
Tranquilizers	7,653	Down 30%
PCP, PCP combinations	6,421	Up 3%
Marijuana	6,046	Up 8%
Acetaminophen	5,591	Up 26%
Aspirin	5,589	Down 14%
Ibuprofen	2,491	Up 201%
Methadone	1,993	Down 8%
Over-the-counter sleep aids	1,850	Down 3%
Amphetamines	3,475	Down 8%
Codeine	1,038	Up 4%
LSD	1,002	Down 4%
Caffeine	459	Up 72%
Ampicillin	409	Down 15%
Hashish	256	Up 42%
Mescaline	199	Down 35%
Insulin	151	Down 64%
Mushrooms	114	Down 2%
Glues	107	Down 25%

Note: A sampling of 744 hospital emergency rooms reported in 1986 and 780 in 1983. Figures for individual drugs include those used in combination with other drugs. Visits due to alcohol alone are not available.

USN&WR—Basic data: National Institute on Drug Abuse

KAPPAN SPECIAL REPORT

Schoolchildren and Drugs:
The Fancy That Has Not Passed

BY RICHARD A. HAWLEY

I. BACKGROUND

COME NOW, haven't we schoolpeople heard *enough* about drugs? The question is more than fair. Stories about drugs in the print media — big busts, latest threats to health, controversial testing programs, involvement of celebrities — are so ubiquitous that each new one raises little more interest than the daily weather report. And most televiewers would agree that, if Geraldo Rivera made only one documentary on the subject, it would be one too many.

But while drug-related journalism may have lost the power to engage us, the issue of school-age children altering the course of development of their central nervous systems with toxic chemicals continues to command our immediate attention. However inured to it we have become, the "drug problem" has not gone away. In many regions and in whole school systems, student drug use is virulent. Nationwide it continues to be — and this is the technically correct word — epidemic.

According to the best and most far-reaching survey, Lloyd Johnston, Patrick O'Malley, and Jerald Bachman's *Drugs and the Nation's High School Students*, more than nine out of 10 members of the high school class of 1985 had used alcohol, more than half had tried marijuana (more than a quarter reported using it in the past month), one in six had used cocaine, and one in eight had used hal-

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Illustrations by Joe Lee

DUE TO A LACK OF PHOTOGRAPHIC CONTRAST BETWEEN TEXT AND BACKGROUND, THIS PAGE DID NOT REPRODUCE WELL.

lucinogens, such as LSD. The great majority of drug-using children in the U.S. make their initial decision to try a drug between their 12th and 16th years — or between seventh and 10th grades.

When we consider that the metabolites of some commonly abused drugs, such as marijuana, remain active in the user's system for weeks, the implications for in-school behavior and performance grow ominous. In fact, in light of the figures for "recent heavy drinking" reported by the class of 1985 (45% of boys, 25% of girls), it seems statistically unlikely that on any given day there would be many American classrooms without *several* drug-altered students glassily meeting their teachers' expectant gazes.

Educationally and developmentally, this matters. It matters even more than whether students come to school underfed and underloved. For it is easier — much easier — to feed and to love and to teach a child than it is to reverse a pattern of drug abuse once it has begun. The most toxic effects of drug use have nothing to do with short-term stupefaction, nothing to do with "being high." The most toxic effects are not felt at all. The lodging of THC from marijuana in the fatty lining of a neuron is not felt by the user, nor is a teenager's passage from "experimental" drug use to "social" use, or from "social" use to chemical dependency.

Drugs are taken for the pleasurable feelings they produce — or are rumored to produce. A drug cannot create or alter feelings without chemically altering the functioning of the brain. Unfortunately, every external chemical known to produce changes in the nervous system also *damages* that system. There are no exceptions. There are no consequence-free drugs.

But while the brain is the principal organ affected by mind-altering drugs, it is an organ ill-equipped to register its own immediate impairment. The brain has no pain receptors. poke it, squeeze it, cut it, pound it, and it will not "hurt" (although the consequences will be otherwise dramatic). Because the brain doesn't hurt when it is injured, brain damage, whether caused by tumor growth, concussion, stroke, or drug abuse, often remains undetected until brain *function* is lost: speech, memory, movement, and so on. In the case of serious stroke, head trauma, or Alzheimer's disease, such losses are dramatic, but we should be no less attentive to losses caused by the use of alcohol and other drugs, even when those losses are subtler and are distributed over a longer period of time.

Most of us have observed a person in the process of getting drunk — a progressive pickling of the cortical functions. The subtlest and most elegant functions are the first to go: awareness of nuance, appraisal of consequences, responsiveness to time, place, and circumstance. A drink or two can reduce inhibitions. A few drinks in rapid succession knock out more basic functions: judgment, speech, motor coordination. Ultimately, consciousness itself is lost in the nervous system's last-ditch effort to preserve life. Occasionally, an impulsive or inexperienced drinker will take a fatal dose before losing consciousness. Yet, despite this progressive, easily observable impairment of brain function, the brain never once says ouch.

Herein, probably, lies the tenacity of the "drug problem." The impairment caused by many widely used drugs does not become obvious until an individual has become a confirmed user. Next to inhalable solvents, alcohol is probably the crudest of the nervous system depressants; its abuse is often followed by hangover — actually an indication of a healthy system working to expel poisons. But with more complex mind-altering drugs, such as marijuana, the hangover may be gradually distributed over days and weeks. The user may not link the uneasy, irritable feeling to marijuana at all, but rather to surrounding circumstances: family life, perhaps, or school.

Only when drug use has progressed to the point where a person's disposition and behavior are noticeably altered — to the "wasted" or "burned-out" condition — is it typically classified as a problem. And for more than a decade after the initial surge of illegal drug use in the Sixties, even the most dramatically and, as it happened, irreversibly "burned-out" individuals were often extolled for having *chosen* an alternative approach to life.

Tens of thousands of youthful chemical dependencies later, we know better — or we should know better. We should also know that, from an educational standpoint, the most abusive, dependent users are not the sole manifestation of the drug problem. The drug problem includes everything along the way. It includes the once-bright

suburban pot-smoker who, in an underchallenging high school program, is "doing fine." I have met, spoken with, and observed hundreds of such students in such unchallenging programs. I have seen high school juniors showing "no academic deficit" due to occasional marijuana use, as long as nothing new — nothing beyond a healthy seventh-grader's range — is required of them.

THE DESTRUCTIVE effects of student drug use on learning and on the conduct of schooling in general are by no means limited to the users themselves. Even a few drug-enervated students in a classroom will change the learning climate for everyone. Drug-altered children are largely impervious to classroom business: teachers are apt to see them as unprepared, preoccupied, hostile. Such students -- and again, it only takes a few — tend to shut teachers down and push them toward less-effective teaching. Teaching drugged children is like acting or singing in the presence of hecklers or hosting a party at which a few of the guests are bent on having a bad time.

A competent teacher who works hard trying to engage chemically impaired nervous systems is working against the grain. It is no coincidence that "teacher burnout" — the term itself is derived from the drug culture — should have surfaced as a national issue directly in the wake of epidemic student drug use. It is instructive that in the mid-Seventies, when the phenomenon of "teacher burnout" emerged so explosively, teachers' salaries (adjusted for inflation) were higher, class sizes and student loads were generally smaller, and school programs were overall less routinized and rigid than they were in the relatively drug-free years before the mid-Sixties.

Drugs change the people who use them, and when the users are students or teachers, drugs change schools. The use of drugs, including alcohol, is illegal for almost all school-age children. The use of drugs also violates school rules and most household policies. Drug use and exchange is therefore always a furtive business. As such, it is an inherently divisive force in school life. It divides straight groups from using groups, divides students from the faculty and the administration, divides strict from permissive faculty members. Especially in the aftermath of an embarrassing bust, a drunk-driving death, or the publication of poor scholastic performance, drug use causes people to point fingers of accusation. School boards find principals and faculty members lax. Teachers label whole classes or whole generations hopeless. Students find the new school drug policy or newly formed parent network reactionary and repressive.

At the heart of such divisions is illegal drug use. A nearby public high school

DUE TO A LACK OF

asked me to advise on a drug-related problem that had lowered student and faculty morale to the point that the continuation of the daily school program was in some doubt.

The basic problem in this school was as follows. Considerable community, school board, and administration concern had been raised about the extent of drug use and drug dealing taking place on school grounds during school hours. A student-conducted survey confirmed that more than 50% of the students used illegal drugs to some degree and that a majority of those who used drugs did so during school hours.

Administrators, counselors, and faculty members reflected on the problem and decided that the bulk of the drug traffic taking place during school hours was happening in unsupervised places, both on and off the school grounds. Thus it was decided that the school's relatively relaxed "open campus" policy, which allowed most students to study and socialize wherever they pleased — and even allowed some of them to leave campus during their unscheduled time — had to go. Supervised study halls were instituted, many of them housed in the student cafeteria and containing hundreds of students whose seats were assigned. Trips to the bathroom or to the library required a special pass. The students, as one might imagine, reacted angrily to what they perceived as "Gestapo" tactics. And the non-using students, who had enjoyed their former liberties without breaking the rules, were the angriest. In this way the new policy united the "straights" and the "heads" in anti-authoritarian indignation.

With hindsight, it is easy to see what went wrong. The "blanket" solution of enforced study halls might have been improved had the student government or an open student forum been asked to propose a solution that would 1) stop illicit drug use *and* 2) preserve appropriate student liberty. The school administration could have taken this step without in any way compromising its resolve to eliminate drug use. The students needed help in seeing that student drug use, not their repressive elders, had caused the curtailment of their liberties. And while students were rather more comfortable reviling the administration than confronting one another about drug use, it was the latter, less comfortable process that eventually improved the climate of the school.

Apart from its general effects on a school's tone and quality, drug use has particularly demoralizing effects on particular organizations and activities. Quite recently I was asked to appraise a new athletic policy being tried out by a football coach at a prestigious independent school. The coach had read about drug-related effects on student performance, had attended drug education conferences, had weighed his own recent experiences with drug-using students, and had decided that he would like to take the firmest possible stand against drugs. With approval from the administration and the athletic department, the coach explained his feelings to his players and announced the new policy: his players were to be drug-free. No compromises. Each player was to sign a pledge, indicating that he would not use alcohol or other drugs for the duration of the season and that he would remove himself, or consent to be removed, from the team if he did.

The policy sparked some controversy and also a good deal of interest and support. The coach was generally admired for his stand.

But by the time I visited the school and talked to the team, it was mid-season, and the players seemed troubled. When they were comfortable enough to speak confidentially, it was clear that the policy was not the problem, but what had happened to it. Because they liked the coach, the players had stuck to the pledge for the opening weeks of the season. Then parties and other tempting situations combined to break the resolve of some of the players. They waited to see what happened. And nothing happened. Before long, more than half of the team had broken the pledge. Students began calling the new policy a "farce." The coach himself suspected from his players' attitudes that they had broken the pledge, but he did not know for certain. Everyone was demoralized.

The coach's stand and the drug-free pledge were not the problems. The players' subsequent violations merely pointed up the real problem: the players drank and smoked pot. They either could not or would not stop — not for their coach, not for team solidarity, perhaps not for anything.

IN THE TWO decades that drug use has been a central factor in the lives of school-age children, the phenomenon has changed and "matured" in some particularly unattractive ways. Much wishful thinking and misguided editorial writing to the contrary, no healing "decline" in student drug use has taken place. But that statement needs some explaining.

Student use of illegal drugs increased steadily through the Sixties and Seventies and reached a peak for most categories of drugs in 1979-80. At that point, more than one in 10 high school students reported smoking marijuana *daily*. In the following five years, 1981 through 1985, the use of drugs by students gradually fell off — with the exception of cocaine, the use of which continues to rise.

But this recent decline should occasion only guarded optimism, at best. The real statistical story is that students in 1985 are using drugs (again, with the exception of cocaine) at about the same rate as in 1975. For example, 47% of the high school class of 1975 indicated that they had "ever used" pot; 54% of the class of 1985 indicated the same. The numbers reporting recent marijuana use (27% of the class of 1975, 26% of the class of 1985) have remained fairly constant over the past decade. It is hard to be encouraged by reported declines in drug use when the levels remain so high.

There are other general features of

TABLE 1.
Percentages of High School Seniors Saying They Had Ever Used Certain Drugs

	Ever Used										
	Class of										
	'75 %	'76 %	'77 %	'78 %	'79 %	'80 %	'81 %	'82 %	'83 %	'84 %	'85 %
Marijuana/Hashish	47	53	56	59	60	60	60	59	57	55	54
Inhalants	NA	NA	NA	NA	19	18	17	18	19	18	18
Amyl & Butyl Nitrites	NA	NA	NA	NA	11	11	10	10	8	8	8
Hallucinogens	NA	NA	NA	NA	19	16	16	15	15	13	12
LSD	11	11	10	10	10	9	10	10	9	8	8
PCP	NA	NA	NA	NA	10	10	8	6	6	5	5
Cocaine	9	10	11	13	15	16	17	16	16	16	17
Heroin	2	2	2	2	1	1	1	1	1	1	1
Other Opiates	9	10	10	10	10	10	10	10	9	10	10
Stimulants	NA	NA	NA	NA	NA	NA	NA	28	27	28	26
Sedatives	18	18	17	16	15	15	16	15	14	13	12
Barbiturates	17	16	16	14	12	11	11	10	10	10	9
Methaqualone	8	8	9	8	8	10	11	11	10	8	7
Tranquilizers	17	17	18	17	16	15	15	14	13	[illegible]	12
Alcohol	90	92	93	93	93	93	93	93	93	93	92
Cigarettes	74	75	76	75	74	71	71	70	71	70	69

Source: National Institute on Drug Abuse, Monitoring the Future Study, 1985

GRAPHIC CONTRAST
ROUND THIS PAGE

the drug epidemic that educators should note. One is a peculiar sort of Law of Unlimited Inclusion, according to which new drugs tend to be added to the illicit pharmacopoeia, but none is ever replaced. Thus pot and LSD, two of the most commonly used novelty drugs of the psychedelic Sixties, did not replace or even diminish the use of "established," legally available drugs, such as tobacco and alcohol. Nor has the more recent boom in the use of cocaine and "designer drugs" replaced pot or LSD.

This is not to say that, regionally and even nationally, the demand for particular drugs does not vary. It does. But the preference for individual drugs does not so much come and go, as it comes and goes and comes again. Two years ago streetwise kids in the city where I live were saying that "psychedelics" (read LSD) were out. But in the wake of a single sell-out Grateful Dead concert in the area, psychedelics have come back. This isn't a street rumor; this is the report of the families, schools, and treatment centers that have had to tend this newest crop of "Dead-heads."

None of this is meant to indict or belittle the efforts to fight drug abuse made by legislators, communities, schools, and parent organizations over the past decade. What declines have occurred in certain forms of drug use are almost certainly due to a growing consensus that drug use has no part to play in healthy child development. The consensus has expressed itself in a growing resolve to confront drug use, unpleasantness and all. The job, however, is barely begun.

II. HEALTHY CHILD DEVELOPMENT

TO THOSE with a vested interest in the physical, emotional, and intellectual development of children, the drug epidemic appears to have been designed with diabolical precision. Drugs block, retard, or distort the most crucial human capacities — perception, cognition, planning, physical coordination — and the loss of function is rewarded by surpassingly pleasurable sensations.

I noted above that American children are most likely to make their initial decision to try an intoxicating drug between the ages of 12 and 16, during the peak years of adolescent growth. During these years, every cell and tissue of the body is either altered or replaced altogether. Sexual potency, nearly all of one's adult skeletal stature, and the capacity for higher-order mental functions are produced during this developmental surge. The new mental attainments include the capacity to think abstractly, to interpret elaborate symbol systems (whether poetic or algebraic), and to decide the present behavior needed to achieve a variety of future possibilities. With the exception of the first 18 months of life, adolescence is the most accelerated period of human growth. Unlike preverbal infants, however, adolescents are conscious — indeed, acutely and exquisitely *self*-conscious — of the changes they are undergoing.

Adolescents regard their new size, new sensations, and new capacities with a good deal of positive anticipation, but these same developments are also occasions for unexpected awkwardness, worry, and loss of personal control. Both the drama and the awkwardness of adolescence are developmentally necessary. Adolescents must define a new relationship to younger children and come to see themselves as former children. They must forge new relationships with their parents and with other adults in authority. There must also be an intensified relationship with the opposite sex.

So many changes would be challenging enough to manage if the onset and rate of adolescent development were uniform and predictable. In reality, though, adolescent growth is a capriciously uneven process. The appearance — seemingly always too early or too late — of adult stature, a croaking voice, a beard, breasts, or body hair can be the source of devastating self-doubt. All such changes are unbidden, and some seem revolt-

The long-term answer is to prevent drug abuse before it begins. This means placing programs in elementary schools.

Building Drug-Free Schools

TO ADDRESS the need to bring together all the important elements of school-based drug prevention (policy, curriculum, and working with the community), the American Council for Drug Education has developed *Building Drug-Free Schools*. This four-part drug-prevention program for grades K-12 consists of three written guides and a film. It is designed to provide school administrators, teachers, counselors, parents, and other community members with detailed information and suggestions for developing a new school-based drug- and alcohol-prevention program or for augmenting an existing program. The four parts of the program are outlined below.

I. Policy. This part of the program details why drug and alcohol use is a serious detriment to education and spells out specifically which policies have proven effective in reducing drug use. It addresses curricular requirements, the role of law enforcement, and suspension, expulsion, and intervention procedures.

II. Curriculum. This part of the program provides a unique K-12 curriculum with easy-to-use and age-appropriate learning activities. It includes essential information for teachers, such as the effects of drugs on health, the "high-risk" child, and the developmental basis for a drug-prevention curriculum. The curriculum shows the importance of avoiding dangerous "responsible use" messages, and it integrates the cognitive and affective dimensions of learning.

III. Community. This part of the program outlines specific techniques for enlisting the support of parents, businesses, religious groups, the media, medical professionals, fraternal organizations, and other community groups in reinforcing the drug-free message.

IV. Three Schools: Drug-Free. This part of the program is the film that accompanies the written guides. It features the principals of three schools, who describe how a clear and consistently enforced policy, an age-appropriate curriculum, and the involvement of the community have enabled them to significantly reduce drug and alcohol problems in their schools. The 29-minute film demonstrates for administrators, teachers, counselors, school board members, parents, and other community members that the goal of a drug-free school can be achieved.

The three guides that make up *Building Drug-Free Schools* are available for $50 a set. The film is available for purchase at $275 (16mm) or $225 (videotape) or for rental at $35. For more information or to place an order, contact the American Council for Drug Education, Department K, 5820 Hubbard Dr., Rockville, MD 20852. Ph. 301/984-5700.

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ing new smells, regular eruptions of skin blemishes, oily hair, the onset of menstruation, the annoyance of irrelevant erections.

Developments that seem trivial from an adult perspective — for example, having the wrong kind of shoes — can imperil an adolescent's basic sense of well-being. Life itself has been known to hang on only slightly weightier issues: being in or out of the group, being on or off the team, being datable or not. Steering a survivable course through first love, first intimacy, finding oneself *adequate* — these are momentous challenges in adolescence. Each will arouse terrific stress, and the adaptive management of that stress is maturation. The only way out of adolescence is through it. Chemically anesthetizing oneself with drugs serves only to delay this maturation — or in some cases to replace it altogether — often with lifelong consequences.

ALONG WITH THE rapidly unfolding physical development in adolescence comes the capacity for new forms of thought. Measured on an electroencephalograph, an adolescent brain can put out faster, more "adult" brain waves than that of a preadolescent. Adolescents can perceive new gradations of color and musical pitch. They can see allegories in stories that were once understood only as literal narratives. Adolescents can understand whole systems (cellular systems, body systems, political systems, solar systems), make predictions about them, and draw inferences from them. Adolescents are able to pursue higher mathematics, advanced physics, and other sciences that proceed deductively from their own axioms; these theoretical disciplines need not bear any demonstrable relationship to observable reality.

The most profound capacity for moral thinking can emerge during adolescence. Cognitively, this amounts to projecting oneself imaginatively forward and backward in time, plotting hypothetical actions and their potential outcomes, referring the outcomes to feeling centers for evaluation, formulating plans, and then executing reasoned, purposeful actions.

All this staggering complexity and elegance comes into play only if adolescent development is healthy, not polluted and impaired by drugs. If we step back and take a long look, we can see child development as a continuous process in which 1) simple mental structures are superseded by complex ones; 2) exclusively self-directed motivation and behavior becomes, at least in part, other directed; and 3) utter dependence on nurturers develops into personal autonomy and one's own capacity for nurturing. Again, this is the direction of *healthy*, not necessarily typical, development.

Healthy maturation requires a capacity for managing pleasure. In other words, pleasure must be understood as a consequence of a good, not as an unqualified good in itself. The most reinforcing sensual pleasures — such as eating and sex — have evolved, I suspect, to promote such essential human purposes as survival, reproduction, and pair bonding. The non-sensual pleasures — such as pride, elation, and joy — have no doubt evolved to promote essential personal and social goods. But when pleasure is abstracted and pursued as an end in itself, people encounter such troubles of self-indulgence as obesity, promiscuity, emotional instability, and addiction.

Aristotle addressed the role of pleasure management in child development with remarkable clarity. His prescription has been revived intermittently through the centuries, most forcefully by Montessori and Dewey. Aristotle's point was that children must be "habituated" to desirable behavior — attending to tasks, sharing, telling the truth — before they can understand theoretically the benefit of doing so. By the time a developing child is able to understand why, theoretically, "honesty is the best policy," he or she may have internalized a pattern of truthfulness or deceit that is impervious to the more recently acquired, higher-order "theory." The standard educational rewards for desirable behavior are mastery, recognition, and praise. These rewards *follow* and thus reinforce the desired behavior.

Drug use inverts the healthy model. Complex thinking becomes simpler, distorted, even pathological — and not just while the user is high. Awareness of others and of the environment is replaced by euphoric, stupefied self-centeredness. Stress management is replaced by anesthetizing bad feelings or by chemically triggering good ones. Natural controls on pleasure are circumvented by chemicals that create rewarding sensations. In this way, essential developmental processes are not only reversed, but the *loss* is rewarded by indescribably compelling pleasure.

This is the real drug problem. It is also a disease and a sure sign of cultural deterioration. Because drug use runs so directly against the aims of education, school communities should not be reluctant to reestablish controls over the environment in which developing children make decisions. As current analysts have pointed out repeatedly, we are not enjoying a scholastic Golden Age.

III. HISTORICAL PERSPECTIVE

THE USE of alcohol and other intoxicating drugs in America extends back past the European settlement of the New World. Native Americans in the Southwest used naturally occurring hallucinogens in religious rites. The earliest dwellers in the high country of the Andes used coca leaves as a medicine and to achieve religious trances. The peoples of ancient China and India used cannabis (marijuana) for similar purposes. Down through the modern centuries, neither "white drugs" (those derived from opium) nor "brown drugs" (those derived from cannabis) made much of an impact on the culture of the West, where the preferred intoxicant was alcohol in either distilled or fermented form.

The opiates, cannabis, and after it was chemically extracted from the coca leaf in 1859, cocaine were contained in prescription and patent medicines in the 1800s. Cocaine was tried and found wanting as a local anesthetic. Freud initially used cocaine to relieve nervous disorders, but he later vilified the drug as a destroyer of health. It is also true that small amounts of cocaine were included in the original formula for Coca-Cola, but the drug was removed shortly after the turn of the century when cocaine was identified as a threat to health. The use of alcohol has also been intermittently accepted, regulated, deregulated, prohibited, and tolerated.

So drug use itself is not a late 20th-century novelty. The novelty is the *number* of people — especially young people — who are involved. There is no historical precedent for such phenomena as millions of school-age children using cannabis, cocaine, LSD, and other mind-altering drugs.

The reason the drug epidemic erupted in the mid-Sixties probably had less to do with the contemporary issues with which it is most often linked — protest over the Vietnam war, agitation for civil rights, and frustration with a repressively structured society — than it did with the fact that millions of baby boomers were coming of age at the same time. As the Sixties turned uneasily into the Seventies, for the

first time in American history there were more people under than over 25. An unprecedented proportion of them were clustered on college campuses, where adult presence was so minimal as to be unfelt, where a world of radical brotherhood and sisterhood was less rhetoric than daily reality.

A recurrent theme of the youth culture of the Sixties was a plea to sustain adolescence, not to complete the compromising passage into adulthood. In *Do It!*, his manifesto of the counter-culture, Jerry Rubin boldly stated the general aim: "When we're thirty-five, our ambition is to act like we're fifteen." In the Sixties, to act like a 15-year-old obliged one to defy standard conventions of dress, grooming, language, and public deportment. It also obliged one, perhaps most enduringly, to flout the conventional taboos against illicit drugs, especially pot and LSD. The older, pre-Sixties beats and hipsters became models for throngs of hippies, and within a year or two the long-standing barriers that had separated drug users from straight society had broken down.

> **Even the best programs can be subverted by the absence of strong, clear institutional policies forbidding drug use.**

From the standpoint of public health, the American drug epidemic has caused such severe problems because it had a decade's head start on any sustained, informed attempts to check it. Drugs were not merely used; they were extolled enthusiastically by the people and through music, the medium closest to the heart of the youth culture. The Beatles sang cheerily of "getting high with a little help from my friends," while the cast of *Hair* proclaimed the drug-lit profundity of "walking in space, explaining, 'in this way we rediscover sensation.'"

Meanwhile, in 1965 a team of Israeli scientists investigating the 420-plus chemicals composing marijuana isolated the one, delta-9 tetrahydrocannabinol (THC), that is most responsible for making users high. THC was further found to have some worrisome features. It lodged itself in fatty tissues all over the body, including the brain. It blocked healthy cell function and, over time, destroyed cells. It was a poison.

By the early Seventies, a federally funded project at the University of Mississippi was growing, under government supervision, a uniform grade of marijuana (about 2% THC) to be used in animal and human tests. With uniform marijuana available for tests, reliable, replicable studies could be made of the drug's effects on behavior and on cells, tissue, and vital human systems. Beginning in the mid-Seventies, improved and more persuasive studies were available, and important research is still under way.

But by the time the scientific and medical communities had begun to voice concerns about the health effects of marijuana and other drugs, patterns of drug use and supply were already deeply entrenched. Old, discredited research claiming the relative mildness or harmlessness of marijuana clashed with claims of its dangerous toxicity. Findings from casually conducted surveys were opposed to findings about cell metabolism. Small, dubious samples of ganja-smoking Jamaican cane farmers were used to suggest the relative safety of pot smoking among North American high school students. "Experts" appeared to disagree. Confusion reigned, and under the umbrella of so much confusion and controversy, drug use continued apace, reaching peak levels among high school students by 1980.

Slowly, however, a broadly based coalition of those opposed to illegal drug use began to make itself heard nationwide. The first people to organize and to articulate an anti-drug stand have been, appropriately, the ones among whom drug use has come inescapably to rest: families, schools, the staffs of drug treatment centers. National organizations, such as the Parents Resource Institute for Drug Education (PRIDE) and the National Federation of Parents (NFP), as well as regional movements, such as the Texans' War on Drugs, have made impressive progress in making freedom from drugs a goal for families, schools, and whole communities.

Yet even so agreeable-sounding a goal as "drug-free youth" is not as easy to sell as it may seem, particularly if "drug-free" is taken to mean "alcohol-free." There are handsomely printed books and curricular programs aimed not at "drug-free youth" but rather at the "responsible use" of drugs. Indeed, even as I write, the most widely distributed curricula for drug education in the country stress making considered responses to drugs. But these programs do not come out in favor of refusing to use drugs altogether.

LET ME PAUSE for a moment. For there is perhaps no greater indication of the inroads drug use has made on contemporary thinking than the fact that authoritative voices on the national education scene are endorsing *responsible levels* of criminal, not to mention health-endangering, activity. How does this reasoning translate into other areas of problem behavior for adolescents? Why not responsible levels of vandalism, assault, or reckless driving? Teenagers have problems with these behaviors, too, though they claim far fewer lives and sacrifice far fewer futures than drug abuse does.

Am I exaggerating? Readers who feel that I'm merely knocking down a straw man should consider the following. In Ruth Eng's 1979 book for teens, *Responsible Drug and Alcohol Use*, the chapter titled "Hints for the Responsible Use of Marijuana" cautions readers to smoke with friends, to sort the seeds out of their stash, to use clean smoking paraphernalia, and to avoid burning lips or carpets.

Andrew Weil, whose 1972 paean to drug-enhanced consciousness, *The Natural Mind*, was reissued last year, also collaborated with children's book author Winifred Rosen in 1983 to produce another drug book pitched to children: *Chocolate to Morphine: Understanding Mind-Active Drugs*. The first chapter, titled "Straight Talk," begins arrestingly: "Drugs are here to stay." The authors continue, "Drug education as it now exists is, at best, a thinly disguised attempt to scare people away from disapproved substances by greatly exaggerating the dangers of these substances." Young readers are advised to "question your parents about the drugs they use. Maybe they will agree to give up theirs if you will give up yours. If you can convince them that your

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gration into family, school, and community is not easy. Moreover, a newly described clinical syndrome, PDIS (Post-Dependence Impairment Syndrome), suggests that recovering dependents show abnormally high tendencies to chronic illness, injuries, learning difficulties, and depression.

The long-term answer is to prevent drug abuse before it begins. Schools are most likely to succeed in achieving this aim if they allot more and better instructional time to drug education *before* children confront the choice of whether or not to use a threshold drug. This means installing programs in elementary schools. Some exercises in such programs will be very basic and prescriptive: saying no. Some exercises will be affective: how to say no and how to avoid drug use and other harmful situations. Some lessons will be informational: what is safe and what is dangerous, what are the effects on the human system of various legal and illegal drugs. Special emphasis should be given to cigarettes, alcohol, marijuana, and inhalants, because these are the most prevalent threshold drugs.

However, even the best educational programs can be subverted by the absence of strong, clear institutional policies forbidding drug use. For the great majority of school-age children, adherence to the "rules" and observance of the law are the highest categories of ethical thought. Schools tend to stress the enforcement of those policies about which they care most strongly. Drug education must go hand in hand with an anti-drug policy.

Weary voices stating that "drug education" and "information" have proved ineffectual as ways of preventing drug abuse are misinformed and mistaken. A systematic prevention-based program of drug education has barely begun nationwide. The drug epidemic arose in the absence of such educational measures, not despite them.

• Changing the drug climate of a school begins with building a consensus among members of the faculty and staff. School staffs whose members are divided among themselves cannot stand firm against student drug use. They will be divided in the same way inconsistent parents are divided. Building a durable consensus is apt to require some learning on the part of faculty members about the biomedical effects of drugs and about their special effects on developing children. This learning may require some high-quality inservice training. The trainers and the materials they use should endorse the goal of a drug-free school. The entire faculty and staff (K-12) of a school system should be included in policy making and program building. Drug education is not the special business of health teachers and science teachers. The support of [illegible] and aides, especially [illegible]

• Faculty members and staff members must limit their own drug use to what is lawful and consistent with effective performance. Employee Assistance Programs (EAPs) for faculty and staff members with drinking and other drug problems are increasingly common in both public and private schools. Adults who have been treated through EAPs and who have remained in their posts tend to bolster rather than undermine the overall morale of a school. At the same time, their presence underscores the school's commitment to be drug-free.

• Drug-free means alcohol-free. Alcohol is the principal drug of abuse among U.S. schoolchildren. It is the preferred drug of the majority of chemical dependents, and its use is more likely than any other disease, accident, or activity to lead to the violent death of young people. School faculty members must be educated to respond to the standard defenses for and denials of underage drinking. How much harm is there in a little? I don't want my son or daughter going off to college inexperienced. Well, if they're going to drink, I at least want them to do it here where I can watch them. Hell, I used to throw back a few myself. At least it's only alcohol. At least it's only beer.

Alcohol is the problem, not the form in which it is taken. A can of beer, a typical glass of wine, and a Scotch and soda served at a bar each contains about an ounce of alcohol. Two consecutive ounces of alcohol consumed by a 5-year-old can kill the child. The same dose is highly toxic to a middle-schooler. Growing children are in the process of developing controls that might allow them to drink moderately as adults. Alcohol and other drugs *replace* these controls. The loss of performance, health, and life of young drinkers is well-documented and obvious. Against these losses, no positive benefits have been adduced. Camaraderie? Fellowship? Go *observe* the middle-schoolers in the basement rec room or the high school crowd at the rumored three-kegger at the home of a student whose parents are out of town. Observe, and perhaps clean up.

V. A PERSONAL NOTE

ALTHOUGH MY professional responsibilities are to direct a high school and my out-of-school preoccupations tend to be literary and musical, over the past 10 years I have done a good deal of writing, speaking, and conferring about drug-related issues. I never intended to do this, but, given my involvement with young people, I suppose an immersion in drug issues was inevitable. Sometimes I do wonder, though, whether I am coming to see this world through a drug-clouded lens. I have met some people who, it seems to me, have reduced all the world's problems to the drug abuse of American teenagers.

I don't want to become this way, and I try hard to maintain my balance. But I do read the paper. And on the morning that I wrote this paragraph, these were the headline stories in the *Cleveland Plain Dealer*.

The leading national news was the revelation that the crew members of the Conrail train that collided disastrously with an Amtrak passenger train were under the influence of marijuana. Locally, the dominant story was the continuing investigation of a convicted drug dealer and police informant who apparently received protection from the Cleveland police force to sell cocaine in the inner city, provided he turned the profits over to the department, which then used the funds to pay for the biggest drug bust in the city's history. A curious sort of ethic at work here.

The sports coverage was replete with Brian Bosworth's indignation that his use of steroids had barred him from NCAA football competition. He claimed that pot-smoking athletes got away with murder because their positive drug tests could be interpreted as "passive inhalation" of other people's smoke.

As I said, I was pressed for time and had to get moving, but I glanced at one more story, one that was given less prominence. It summarized a survey of internationally prominent education experts who were asked to appraise the relative effectiveness of the teaching in six nations of math, science, social studies, foreign language, and each nation's own language. Japan and West Germany were rated highest, the U.S. fared poorly. In math and science we were ranked second to last, and in the teaching of our own language we ranked last.

Hmm. Television? Affluence? Poverty? Permissiveness? Restrictiveness? Out-moded pedagogy and curricula? Existential ennui? Angst? Ask on. K

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drug use is responsible, you may be able to allay their anxiety."

Parents, too, are given counsel by Weil and Rosen. "Don't make your child feel it is wrong to get high," they argue, because "there are no bad drugs, only bad relationships with drugs." The authors look forward to the day when drug use will be woven comfortably and continuously into the fabric of ordinary life: "We have seen parents in good relationships with marijuana let their children take occasional puffs of joints in much the same way that some Jewish parents allow their children ceremonial sips of wine."

In 1986 Susan and David Cohen, another team of writers for teenagers, wrote an accessible guide to teen drinking called *A Six Pack and a Fake I.D.* The authors make some clear attempts at fair-mindedness, and they offer some informed cautions about alcohol abuse. But they couldn't quite bring themselves to advise their readers to obey drinking laws. Of drinking parties, they write:

> If you're planning a drinking party, and your parents accept the idea, then at least try to make your party a safe, pleasant, and interesting one, instead of a drunken bash. Don't overdo the amount of alcohol in the punch and don't let anyone else add to it.

If the party doesn't run too long and if provisions are made to get drunken guests home, "so far so good. You have behaved responsibly." In the book's final chapter, titled "Summing Up," there appears the incongruous caveat, "Adults who knowingly supply alcohol to minors may be liable to criminal penalties." (No doubt the publisher's legal counsel is responsible for this terse warning.)

There is a little craziness in these discussions of "responsible" law-breaking. I suspect that Weil would be both vocal and indignant if the teens (and their parents) in his neighborhood were exhorted to curtail his right of free speech or to threaten his person. Yet why, from the standpoint of those who genuinely feel that Weil is a social menace, should the laws respecting his welfare be taken more seriously than the drug laws he so energetically maligns?

It would be a mistake to dismiss the "do it anyway" drug message as a feeble cry of left-over voices from the Sixties. These books and similar school curricula continue to appear in the mid-Eighties. Nor are they the products of dingy underground presses. Macmillan brought out *Responsible Drug and Alcohol Use*, and Houghton Mifflin published both *The Natural Mind* and *Chocolate to Morphine*.

There is considerable optimism in drug education circles today about the anticipated gains to be made as a consequence of the Reagan Administration's Anti-Drug Abuse Act of 1986. If funded, this act is supposed to provide millions of dollars to schools for drug-related programs and materials.

But what materials? Very few comprehensive K-12 curricula come out clearly against the recreational use of drugs. Most of them aim to boost self-esteem and clarify values and decision making. Their stated goal is typically that students will learn to make informed, responsible choices about drugs. Most of them do not suggest that the informed, responsible thing for a child to do is to say no to drug use. In other words, there is nothing built into the new Anti-Drug Abuse Act to insure that existing patterns of drug use will not be reinforced by federal funds. It will take alert, informed school boards, principals, curriculum coordinators, and faculty members to prevent such a development.

IV. SCHOOL STRATEGIES THAT WORK

ONCE AGAIN I must stress that American education is not in the midst of a Golden Age. Schools are drug-ridden, and this is exacting an educational toll. Daunting though it may be, drug use by young people is a problem that can be beaten. Schools have been drug-free in the still-recollectable past; they can be again. Indeed, many have already begun.

Some prescriptions follow for changing the drug climate in the schools. Let me say at the outset that the policies I propose are my own passionate preferences, but they also happen to coincide with the positions of the American Council for Drug Education, the National Federation of Parents, the Parents Resource Institute for Drug Education, and the Texans' War on Drugs, among other national and regional organizations.

• The school's commitment must be

to become drug-free. This is a basic premise and a value-laden choice. It generates one kind of policy and program; other premises — to cut down on the levels of drug use or to help students make responsible drug choices — lead to different policies and programs. Robert DuPont, one of the clearest voices in the field of drug abuse prevention, likes to tell school faculties, "Every school will have precisely the amount of drug use that it tolerates."

It is only a sign of the times that the goal of maintaining drug-free schools is sometimes challenged as "unrealistic." The very mission of universal education requires a drug-free atmosphere for learning. Schools mobilize their energies and their money impressively to remove asbestos from the learning environment. And if the lives of a student or two were threatened by toxic shock, the suspected brand of tampons and the machines that vend them would be cleared out of the schools at once. But such threats will not take even a statistically measurable toll in student health and life. Drug use, by contrast, is taking a ghastly toll right now. Practically every reader of this article is acquainted personally with a casualty, if not a fatality, resulting from drug use. Allowing such a state of affairs to exist is inhumane — and "unrealistic."

• Leaders must endorse, articulate, and stand by a school's commitment to be drug-free. The responsibility for changing a school's drug climate should be widely shared, but it cannot be delegated. Especially in the early stages, a tough stand on drugs will involve confrontations, dispensing bad news, and taking criticism. If the "drug problem" becomes the special assignment of an assistant district superintendent or of a school's dean of students or of a special faculty task force, those people are likely to be seen as the district's or the school's drug fanatics, and school leaders will be asked to mitigate and temper drug policies that some may find uncomfortable. Maintaining a disinterested stance and keeping a reasonable distance from the problem by delegating the making of drug policy to others will seem the easier course to a school leader. But doing so is almost certain to impede the process of ridding the schools of drugs.

• Preventing drug abuse is easier, more educational, and more fun than remediating drug problems once they exist. Prevention, intervention, and treatment are all essential ingredients of anti-drug abuse policies, but prevention is by far the most promising approach. Unlike older, more stable drug abusers, adolescents pass from experimental drinking bouts to full-blown chemical dependencies in a matter of months. The news from the facilities that treat young drug dependents is frankly discouraging. The majority of those who have been treated lapse back into drug abuse. Even among those who persevere and remain drug-free, the reinte-

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Marijuana: Gateway to Drug Abuse

By Mark S. Gold, M.D.

This article was adapted from *The Facts About Drugs and Alcohol* published by Bantam Books and used by permission of the author.

Cannabis sativa, or marijuana (a.k.a. pot, dope, grass, marvjane, and a hundred other nicknames), grows wild throughout most of the tropical areas of the world. Historically, its seeds were used for animal feed, its stem as a tough fiber in hemp rope, and its oil as an ingredient in paint. But its biologically active ingredient, THC (delta-9-tetrahydrocannabinol), has made it a potent drug of abuse.

A general lack of credible evidence about marijuana's effects helped make it the number one illicit drug, tried by an estimated 35 to 60 million Americans, and used regularly by at least one-third of that number. Although 85 percent of high school seniors said they disapproved of regular marijuana use, and 71 percent attribute great risk to such use, 4 percent of users continued to do so on a daily basis in 1986.

The latest results show that long-term use of marijuana can be as hazardous as any other form of drug abuse. Its use is especially detrimental, both medically and psychiatrically, for the very group that uses it the most—adolescents.

How is Marijuana Used?

Marijuana is almost always smoked. The dried leaves are crumpled, cleansed of seeds, and rolled into the shape of a cigarette—the classic "reefer" or "joint." Pot also can be smoked in a water pipe, known as a "bong," for a stronger effect. Hashish, another by-product of the cannabis plant, is also smoked. Derived from the resinous secretions of the plant, "hash" is mainly produced in the Middle East. Its oils are collected, dried, and then pressed into balls or flat slabs for transport.

How Potent are the Different Forms?

The effects of the different strains of marijuana are directly related to the amount of THC present. On a scale of one to 10, marijuana imported from South America in the 1960s had a potency rating of one to two, while current forms of sensimilla grown here or in Asia (Thai sticks, for example) are ranked above seven. Smoking a marijuana cigarette today is like smoking three to seven 1960 "joints" at once!

Physiological Effects

The more marijuana you use, the more you need each time to recreate the high. This is because marijuana's active ingredients accumulate rapidly in the body, building tolerance. This causes a decrease in the effect with each repeated dose. Since the active amount of THC in marijuana is uncontrolled, unlike alcohol or pills, each dose is different. Thus, it is very hard to gauge exactly how much will cause tolerance and dependence. Some studies have demonstrated that tolerance can develop even after low doses.

THC is absorbed through the lungs into the bloodstream almost immediately after smoking. It clings to the fatty linings of the cells. It is then released back into the bloodstream over a period of time, usually a week or so. Some drugs are soluble in water, such as alcohol and cocaine, and are rapidly expelled from the body, but THC residue remains attached to fat cells, and unless no more marijuana is ingested before the system is cleared, there is a cumulative effect. Anyone smoking marijuana about once a week may actually never rid his body of the drug's effects.

What are the Adverse Physical Effects?

The downside effects of marijuana can occur after any amount of use. These can include: impairment of eye-hand coordination, making driving unsafe; infertility; increased heart rate leading to panic attacks; and distorted visual and time perceptions leading to anxiety, paranoia, and worst of all, drug dependence. Overdose of marijuana can also result in a trance-like state.

Three body systems—the endocrine system, the respiratory system, and the immune system—seem to bear the brunt of marijuana's effect with chronic use. Sore throats upper respiratory problems such as bronchitis are common. The tar contained in marijuana is five to 10 times greater than that in cigarettes, thus increasing the already dangerous risk of cancer for marijuana smokers who also smoke cigarettes.

The Marijuana-Cocaine Connection

- 98 percent of all people who have tried cocaine have used marijuana.
- 93 percent of all people who have tried cocaine used marijuana first.
- 84 percent of adolescent current cocaine users are also current marijuana users.
- 60 percent of marijuana users have their first experience between the sixth and ninth grades.
- 56 percent of 1986 cocaine users have used cocaine and marijuana together.

Source:
National High School Study
National Survey on Drug Abuse
1986

Cannabis' effect on the reproductive system is now certain. Marijuana diminishes both male and female reproductive hormones, which will cause a reduction in fertility by lowering sperm count and disrupting ovulation and the menstrual cycle. Marijuana is attached to high fat-containing areas in the body. The brain is one, but so are the ovaries and testicles.

Overall Psychological Effects

Does smoking marijuana make you stupid? This question is often asked by teenagers and adults alike, because it is one of the beliefs held by many high school students and researchers. There are certain patterns of behavior and memory among marijuana users, especially adolescents, that actually show a loss of intelligence.

Several studies have shown that marijuana *does* affect thought patterns, slows the formation of new learning, reduces the ability to remember simple things after a short period of time, and reduces concentration and the ability to handle complex intellectual tasks. As bad as this would be for an adult, it is far more serious in the adolescent, who is supposed to be retaining new information learned each day in school.

Is Marijuana Addicting?

Marijuana is an addicting drug, especially if addiction is defined by compulsive, repeated use in spite of adverse consequences. Marijuana's effects include tolerance leading to dependence, and then an inability to cease use. These properties are no different from any other drug whose patterns of use produce addictive disease.

The Gateway Effect

Marijuana use causes problems for the user in other ways: Marijuana is a gateway drug, a drug which predisposes adolescents to use additional illicit drugs. While the dependent user may believe he can stop smoking at any time, this is often not the case. Tolerance, withdrawal signs and symptoms are now being reported by patients. The heavy user, in particular, may experience distress (e.g., irritability, nausea, sleeplessness) when attempting to stop smoking, and this tends to perpetuate continued use. For example, five years after graduation from high school, only 15 percent of daily marijuana smokers had stopped, and more than half were still using the drug on a daily basis.

The use of drugs by adolescents is a progressive illness from adolescence through young adulthood. The exact sequence of substances involved is becoming more obvious. Adolescent drug use progresses from the use of at least one legal drug (alcohol and/or cigarettes) to marijuana and from marijuana to other illicit drugs, and/or to prescribed psychoactive drugs. This progression is the rule rather than the exception.

Gateway thinking can help clinicians, parents, and teachers. Family and school efforts to stop cigarette, alcohol and marijuana use appear to have the most promise. Early education, helping parents to give a coherent anti-drug message, and reducing the media's role in promoting drug solutions to life's problems are easy to write about and hard to implement. However, prevention is possible and has worked once a strategy is adopted and all efforts are coordinated.

Specific Effects on Adolescents

As young people go through puberty; a healthy balance of male and female hormones is essential to

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Mark S. Gold, M.D.

natural maturation. Marijuana disrupts this process in adolescents just as it affects the reproductive systems of adults.

Young boys must have a normal amount of testosterone—a male hormone—during adolescence to transform their bones, bodies, facial hair, genitals, and voices to those of men. Marijuana seems to decrease this hormone in teenage boys. On the other hand, it increases testosterone in young girls, which can affect the normal functioning of the menstrual cycle and can provoke skin problems.

Apart from the tragedies that result from teenagers overdosing or injuring themselves, adolescence is the worst time, from a developmental standpoint, to engage in drug use. Physiologically, marijuana can be very damaging to the natural growth cycles, and any departures from the norm in this area may be disastrous, just when a rapidly growing teenager needs the reassurance of being "normal." The physiological changes that take place in puberty are disruptive enough, without the added effects of drugs.

Psychologically, this is a period in life to develop self-awareness and a healthy sense of identity. A teenager who deals with the uncertainties of adolescence by "zonking out," simply avoids the whole process. If anxieties about intimacy or personal interactions exist and are avoided by use of marijuana, the teen fails to learn important life skills. And, even more fundamental, the adolescent will fail to attain a sound identity and fail to master the self-confidence that is essential as people slide into their twenties and early adulthood, where these qualities are needed for success.

But, the most dangerous psychological effect on teenagers is the so-called "amotivational syndrome," which has been linked to heavy use. The symptoms are sluggish mental response, slovenly appearance and attitude, and lack of ambition and motivation, accompanied by poor grades and poor school attendance.

A major problem in treatment of teenage marijuana smokers is that most teens don't recognize that the use of marijuana—and other drugs—is changing their behavior. Thus, while a teenager is smoking marijuana, it is almost impossible to correct the teen's behavior.

Needless to say, teenagers are at far more risk for traffic accidents, and a large percentage of all teen auto accidents involve both marijuana and alcohol. ★

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The Economist

Getting gangsters out of drugs

YOUNG men in the ghettoes and millionaires' daughters up at Oxford die horribly of it. Wherever it spreads, crime rates soar. Policemen are murdered for it, politicians suborned for it. Central Americans buy whole governments through it. Lebanese and Afghans nourish their feuds with it. The traffic in illegal drugs—partly in mildish marijuana and worse cocaine, but most dreadful in heroin— has become a main tragedy of this age. The trade was created in its present worst-possible form because democratic politicians fell into a well-meant confusion of policy 20 years ago.

Governments decided then to threaten long terms of imprisonment against the suppliers and pushers who were making your daughter a junkie, but to treat her possession of a little marijuana and cocaine as much less of an offence. Supply was made highly illegal, some demand was not—exactly as during America's prohibition of alcohol in the 1920s, and thus with the same results. Gangsters market the stuff to people who feel no guilt about buying from them. The expert criminal organisations that were so enriched by the attempts of earlier American governments to prohibit alcohol and gambling (another addictive practice) are applying Capone's old murderous skills to the international narcotics business.

Subsistence peasants in wretched places are glad to take cash for poppies and coca leaves which, after simple processing, are marked up by 5,000 times for sale to final consumers. This distributors' margin—turning $1m of raw material into $5 billion of revenue—makes drug smuggling the world's most profitable business. Drugs are very-high-price and light goods, easily transported in hand-baggage or even inside people. The most prudent smugglers get big organisations to launder the money and make unrefusable offers to politicians and policemen and rival salesmen in the way. A small group of criminals now probably launders tax-free sums of over $100 billion a year, more than the GNPs of 150 of the 170 nations of the world. If these huge mark-ups went to governments in tax, as a big slice of profits from drugs like alcohol and tobacco does, they would use it for better purposes, including reducing addiction. Is that the right way?

There have been escapes from tragedies as great as today's narcotics trade, significantly almost all along this same road. America's effective answer to Capone's bootleg gangs was not gang-busting but the legalised, taxed and regulated sale of quality-controlled liquor. The best enemy of the numbers racket is the state lottery and the off-course, licensed, taxed betting shop. The British coped similarly with the main drug scourge of the first industrial revolution. Gin Lane sold cheap rot-gut to the not-quite-destitute, who drank themselves out of misery into inefficiency. So the government brought the sale of spirits under local licensing courts, forced the distillers to sell only liquor of approved quality and strength, and raised prices by excise duties as high as the market would bear without driving drinkers to poisonous cheap intoxicants like methylated spirits. People got less drunk less damagingly, initially on untaxed beer (the brewers were delighted). The distillers, forced to sell better hooch, grew rich and respectable on exports of Scotch whisky and London and Plymouth gin.

Drugs are not a "disease of affluence", or any such glib slogan. Some big British companies founded their fortunes on the officially sponsored sale of Indian dope to the poorest people the world has ever known, the Victorian Chinese. Bhang and hashish and coca and kola-nuts and qat are the opiums of their respective poor peoples. None is good for them, but nor is alcohol for rich countries.

Legalise, control, discourage

Today there are four big recreational drugs on the market in most of the world's big cities. Two of them (alcohol and tobacco) are legal, two (marijuana and cocaine) illegal. People have been attacking their brains with the first of these poisonous chemicals since Noah had vines (Genesis ch 9, 20). Christianity uses alcohol in its central rite, as does most of mankind (outside the strict Muslim nations) in its social relations. Yet in countries like Britain lawful alcohol directly kills some 10,000 people a year, and is instrumental in about half of the country's violent crime. Cigarettes in Britain kill 100,000 a year. Marijuana, one of the illegals, has hardly killed anybody yet; but the toll from it will rise because it is a poison with the defects of both the legal drugs. Tobacco and marijuana give you lung cancer; alcohol and marijuana make you run over pedestrians in your car.

In the United States marijuana is now virtually tolerated, because tens of millions of Americans have smoked it or eaten it in cookies. They think it about as befuddling per dollar as alcohol, as bad for their health as cigarettes, and less habit-forming than either. The great extra worry about marijuana is that, while the addict gets his tobacco and whisky from a law-abiding and taxpaying publican, he gets his joint from a sinner who sometimes sells adulterated poison, pays no tax and—this is important—is often keen to lead his customers on to much more harmful drugs.

A sensible public policy might be to treat all three—alcohol, tobacco, marijuana— the same, with licensing, taxes and

quality control. Since all are bad for you, it may be right to plaster them with larger health warnings than those that are at last helping to cut smoking. Wary governments might stop the pub culture spreading to the communal joint culture by restricting marijuana sales to boringly uncongenial premises, like the glum state liquor-stores of Sweden or New Hampshire; or give monopolies to state shops like the post office, which has perfected the art of driving customers away. But a main weapon should be tax: high enough to deter consumption, and varied enough to move people from the worst drugs. Today's worst are possibly cocaine and certainly heroin.

Cocaine came back into high fashion only recently. It is more stimulating than alcohol, less addictive than tobacco. It may be worse for you than either, including being eventually more likely to poison you. What is certain is that it is causing more murders than any commodity ever before. Because it is newish and illegal, its supply is in the hands of the worst illegals. About 80% of American supply is channelled through one group of Colombian gangsters (see page 62) who kill the law-enforcers whom they cannot suborn. Cocaine most needs to be brought under the aegis of controlled and thus legal suppliers, either by treating it like alcohol, tobacco and marijuana (see above) or like heroin (see below), depending on how statistically awful it proves to be.

How present law hooks people on heroin

Heroin is different. It is more addictive than tobacco, and damages the health far more rapidly. It can enslave the mind, so addicts want more to satisfy a craving that obsesses them so that they cannot work. Without work, they have two ways of affording more: stealing or, more easily, dealing. Encouraged by their supplier, they buy a little more than they want, and sell it on at a profit by recruiting new users, whose supplier they become. The furtive illegality of this trade increases its danger, since by the time an addict realises that he needs help he is likely to have started supplying others, so that he cannot seek outside help without risking big trouble with the law. Illegality locks people into addiction.

Legislation pretends that heroin is not significantly more dangerous than marijuana or cocaine. Since dealing in all three is a crime, the same criminal gangs handle them all. Customers for the milder drugs are therefore exposed to salesmen of the really dangerous one. So marijuana (but not alcohol) gets blamed for leading its users on to hard stuff.

Recent developments in the market for heroin give c to how its use might eventually be curbed. Increased dem in the early 1980s led to increased production (in, am other places, lawless Burma and Afghanistan), just as the p licity about AIDS began to deter new users from experim with sticking filthy needles into themselves. Demand prices are falling. The evidence, scant as it is in this myster world, is that most long-term heroin users want to break t addiction, although probably then to destroy themselves w some other drug, usually alcohol. Since alcoholics do not cruit fresh heroin users, this is sadly to be encouraged.

So the best policy towards existing heroin users might to bring them within the law, allowing them to register for right to buy strictly limited doses. Taxes should be h enough to help deter consumption, but low enough to illicit dealers our of business. To get addicted to heroin have to be crazy, or weak-willed, or young and foolish. It problem of mental health, treated as one of crime and the fore made worse. If some extra stick is wanted, then in Am ica registered heroin and cocaine users could be disqualif from driving cars. They might then have an incentive to listed as cured.

Even if the present narcotics trade could be beaten, s destroyers will seek other ways to bend their minds. Calm pills from respected multinational companies produce dop up addicts when doctors prescribe them for non-medical such as poverty or unhappiness. Backroom chemists find a market new drugs. The LSD of the "psychedelic" 1960s w followed in the violent early 1980s by PCP, or angel-du There will be more nasty successors. But these drugs, chea produced close to their markets, do not spawn the sort of ternational racketeering that today's narcotics do. They through brief cycles of fashion, newspaper scares and obl ion. They are destructive teenage fashions, rather than soc menaces, which might also be reduced by discriminatory ta

If there were a lasting answer to drug abuse, it would beyond all this, in the chemists' dream of the good drug, t soma, driving out bad poisons by its controllable merits. may lie close in the future, if research for it can be broug into the open. That is another reason why the worst policy the present one of making the supply of noxious drugs illeg so that only dreadful illegals engage in their supply.

Jackson power

Jesse Jackson's success mainly reflects the narrowing base of the Democratic party

ANDREW JACKSON occupied the White House from 1829 to 1837, and conventional wisdom says he is the only man Americans will refer to as President Jackson for a long time to come. The Rev Jesse Jackson does not believe in conventional wisdom. Nor do the blacks who have been voting for him in large numbers in Democratic primary elections and caucuses across America this year, most recently in Michigan on March 26th. They think he can be president. Few whites do, but some have been voting for him because th like what he says, and the way he says it. As a result, with mo than half the delegates to the Democratic convention n selected, Mr Jackson has about as many as Mr Michael Duk kis, hitherto the front-runner. Mr Dukakis has yet to win in large industrial state. And the Democratic party faces t choice of either giving Mr Jackson his due, and thus losing t presidential election in November, or denying him his du

Forests go to pot

EUREKA, CALIFORNIA

THANKS to the efforts of the Drug Enforcement Administration, the marijuana flow from Mexico and South America is not what it was. With cheer and alacrity, American growers are stepping into the breach. But rather than grow marijuana on their own land, which runs the risk of confiscation, they are planting it on other people's. The Forest Service admits that nearly 1m acres of the 191m it administers has been taken over by marijuana growers. The land has been closed and pronounced "unmanageable", mostly because the Forest Service cannot protect the public from armed marijuana growers. Timber cutting and mining permits are being denied; signs keep walkers away.

Although marijuana is grown in national forests in North and South Carolina, Arkansas, Oregon and Florida, the heartland of the enterprise is California, in particular the "Emerald Triangle", a 10,000-square-mile stretch of national forest lying in Humboldt, Trinity and Mendocino counties in the northern part of the state. Californian growers specialise in sinsemilla, a premium, seedless marijuana noted for its potency.

Methods of cultivation vary. Some pot-patches have 5,000 plants; some have two. Some growers stick a few seeds in the ground and come back occasionally to look at them; others pamper their plants with fertiliser and complicated irrigation systems. A healthy plant, it is said, can produce up to a pound of sinsemilla, worth between $2,000 and $7,000. Small wonder that marijuana, rather than oranges, cotton, lettuce, wheat or almonds, is California's leading cash crop.

The precious plants are fiercely protected. Pot farmers have been known to use land mines, hand grenades, AK-47 assault rifles, machineguns, guard dogs and pits set with sharpened sticks to deter intruders. Local officials cannot offer much of a response. Until recently the average Forest Service employee was not allowed to carry firearms. Now, under recent legislation, they are allowed to carry guns. The Forest Service has also been allowed to train 850 agents to carry out full-scale investigations into the marijuana industry alongside the Drug Enforcement Administration, which can investigate the drug barons in the cities.

California's leading cash crop

The new laws also give more power to controversial paramilitary marijuana-eradication teams. One such is the Campaign Against Marijuana Planting (CAMP), which is run jointly by the Forest Service and 102 other local, state and federal agencies. CAMP sprang out of the frustrations of local police forces, which had too few men to deal with the marijuana growers. It has been going for six years, and has spent $10m of public money to destroy 650,000 plants worth around $1.6 billion. After complaints in 1985, a retired judge was appointed to monitor CAMP's raids. One of the most common grievances was the buzzing of property with helicopters. They are now obliged to fly at least 500 feet above the ground.

Local people are often reluctant to help clean out the growers. Despite the hazards that mass marijuana cultivation creates, the revenues help to offset low returns from timber. The growers, too, are becoming more discreet. Drug-related violence is down, at least locally (there were 13 drug-related deaths in Humboldt County in 1981, perhaps none in 1987), and land mines and booby traps have become rarer. Some "gardeners" are moving out to less well patrolled places, such as Oregon. Those who remain in California are increasingly using indoor gardens, camouflage netting and plants in movable sacks in order to avoid detection. In the words of a weary sheriff in Humboldt County, "We still have a big problem."

IRS itself. Nonetheless, transition difficulties aside, the professionals are reporting that many of their clients now have far more complex returns than before.

Not everyone. Tax reform took several million low-income taxpayers off the income-tax rolls altogether: simplification at its utmost. Millions of others, particularly those earning $15,000-20,000 a year, have found that they are no longer allowed to deduct many of the expenses they once could (sales tax, for example) and that they now do better opting for the increased standard deduction. For them, filling out the "short form" is simpler.

The hair-pulling begins with the richer taxpayers. They are finding a series of new complications. Many of the deductions they took before are still allowed (professional dues, subscriptions and so on), but only on amounts greater than 2% of their adjusted gross income. Some, but not all, interest paid on loans remains deductible, in some instances, depending on what the loan is used for. Some of the interest that is deductible (that paid to credit-card companies, for example) is being phased out over a number of years, meaning that the proportion that may be deducted this year is not the same as that allowed next year. Better records must be kept to prove that the deductions are legitimate. Businesses face as many as five different depreciation rules and a set of new inventory regulations.

The government is apparently adding to the confusion. The General Accounting Office reported in February that the IRS (which expects 26m telephone calls asking for help) was answering 39% of the questions posed to it about the new tax law incorrectly (the agency's own estimate of inaccuracy is lower). And it was not until February 22nd that the Treasury released its 266-page guide on how to deal with "passive income", income arising from limited partnerships, rental property and so on. As for Congress, it still has not passed legislation dealing with the 500-odd technical errors that have come to light in the 1986 law.

Tax accountants say they are overworked and getting little official guidance. They complain too much. Most of them are paid by the hour, so a 10-50% increase in the time they take to fill out their clients' tax returns means a 10-50% increase in their charges. The rub is that for most taxpayers the cost is no longer deductible.

Food stamps

Not for strikers

THE wives and children of men who are on strike lost one of their rights on March 23rd, when the Supreme Court upheld, by five votes to three, Congress's decision in 1981 that they could be denied food stamps. These are vouchers which enable poor people to obtain food in the shops; 20m Americans benefit from them. A fed-

MARIJUANA MORE POTENT -- STILL HARMFUL

Advanced growing techniques and marijuana hybrids are now yielding not only a more potent form of pot, but also new types of the drug that can produce specific effects on the user. The National Institute on Drug Abuse (NIDA) has been monitoring the Tetrahydrocannabionl (THC) content of marijuana through the School of Pharmacology, University of Mississippi, and have found contemporary marijuana to be four times the strength of pot available in the mid 1970's.

In 1976 the monitoring project showed an average THC content of 1%. The potency of marijuana then climbed steadily to an average of 5.5% in 1985. Some of the more specific marijuana types such as Sensimilla averaged a higher TCH content, ranging from 6 to 7%. Some of the Sensimilla samples tested out as high as 14%.

Marijuana has become a more socially acceptable drug of use over the years, particularly with adolescents and young adults. Comedian, George Carlin, said, "Grass doesn't make you sick, your breath doesn't stink, and you don't puke on your shoes." Unfortunately, the high level of social acceptance ignores the inherent problems found in any mood-altering drug usage. Like alcohol, marijuana use can cause multiple problems for the user and those around him/her. With more potent marijuana available it might be accurate to assume the problems experienced by the marijuana user will also be compounded.

Community Update, November 1987
New Connection Programs, Inc.
73 Leech Street
St. Paul, MN 55102

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Youth who begin using drugs before age 18 are more likely to develop severe drug abuse or dependence than those who start later, according to Dr. Lee Robbins, a researcher. As first drug use was delayed, the risk of developing a drug problem decreased, she noted. Her study found that sex, race and education were less significant predictors of drug problems in later life than was the age at first drug use, although there were slightly higher rates for males, whites, and inner-city residents. Dr. Robbins found that the leading predictors of drug use problems are early drunkenness, school discipline problems, depression, stealing, vandalism, and truancy.

--Communique, March 1987

Marijuana Legalization Flouts U.N. Treaty

By Gabriel G. Nahas

Next month, the people of Oregon will vote on an initiative that would legalize the cultivation and possession of marijuana for personal use by anyone over age 17. While polls show the initiative is likely to lose, Americans also should be aware of the national and international implications of the vote. The Oregon initiative runs counter to a major treaty signed by the U.S. that attempts to control the traffic of illicit dependence-producing drugs: The Single Convention of the United Nations.

In 1975, the Oregon legislature eliminated criminal penalties for possession of marijuana for personal use. Within a few years similar "decriminalization" measures were adopted by 12 additional states. This trend was slowed and then halted by a mounting pile of scientific and medical evidence that marijuana is a serious health hazard.

This message has not seemed to have had sufficient impact in Oregon, which is a major domestic marijuana producer. With the help of the National Organization for the Reform of Marijuana Laws (NORML), over 87,000 signatures were collected to place a marijuana-legalization initiative on the November ballot. Because of the treaty commitments mentioned earlier, its passage would be a major international embarrassment for the U.S.

Twenty-five years ago, acting on the recommendation of a World Health Organization expert committee, the U.N. recommended that member nations adopt a single convention that would supersede all of the multilateral treaties negotiated since the turn of the century to control the illicit traffic of dependence-producing drugs (mainly opium, cocaine and cannabis). These conventions included the First Opium Conference of The Hague, called in 1913 at the initiative of Theodore Roosevelt, and the Second Opium Conference of Geneva of the League of Nations, held in 1924. These conferences had been organized by enlightened statesmen who were convinced that the gradual suppression of drugs that enslave the mind and body of men would be beneficial to mankind.

The Single Convention on Narcotic Drugs of the United Nations was drafted and approved by 500 delegates from 74 nations, all of whom assembled in New York in 1961. It obligates the parties to "limit exclusively to medical and scientific purposes, the production, manufacture, export, import, distribution of, trade in, use and possession of drugs covered by the Convention." These drugs include, in addition to opium, coca leaves, and all of their known derivatives, "the flowering or fruiting tops of the cannabis plant, marijuana, excluding the seeds and leaves when not accompanied by the tops, from which the resin has not been extracted, by whatever name they may be designated."

The leaves of the plant were excluded from the convention as a compromise gesture to the delegates from India and Pakistan, where bhang, a concoction made of cannabis leaves, was still widely used. However, in order to limit the use of cannabis leaves, the following article was added: "The parties shall adopt such measures as may be necessary to prevent the misuse of, and illicit traffic in, the leaves of the Cannabis plant."

Finally, the convention recognized the need for transitional reservations in countries where cannabis preparations had been used for centuries. "The use of Cannabis for other than medical and scientific purposes must be discontinued as soon as possible, but in any case within 25 years from the coming into force of this Convention." However, countries where cannabis had never been cultivated for its intoxicating properties were requested to make a special pledge: "Whenever the prevailing conditions in the country or a territory of a Party render the prohibition of the cultivation of opium poppy, the coca bush or the cannabis plant, the most suitable measure in its opinion for protecting the public health and welfare and preventing the diversion of drugs into the illicit traffic, the Party concerned shall prohibit cultivation." This convention, ratified by the U.S. in 1967, has become the law of the land.

Approval of the Oregon initiative would not only violate the Single Convention but also hinder the efforts of the U.S. to curtail the traffic of illicit drugs entering the U.S. from abroad. The U.S. has frequently requested that producing countries comply with the terms of the Single Convention and prohibit the growing of the opium poppy, coca bush or the cannabis plant. U.S. support for the marijuana-eradication programs carried out by Jamaica, Colombia and Mexico could hardly be justified if a U.S. state voted for the legalization of marijuana.

Approval of the Oregon initiative would also impede efforts to limit the social acceptance of "recreational" intoxication through the use of marijuana and other dependence-producing drugs. It also would be more difficult for parents to persuade their children to say "no to drugs," a message endorsed by President and Mrs. Reagan in a recent television address.

Whatever the fate of the Oregon initiative, it is indicative of the cultural revolution that has swept the U.S. since World War II—a revolution that has set self-gratification as its primary goal. It is time to turn back that revolution, beginning in Oregon. Surely we all should be committed to the American dream of building a country in which children may grow up in a drug-free environment.

Dr. Nahas is a professor of anesthesiology at Columbia University. He is also a consultant to the United Nations Commission on Narcotics.

The initiative failed.

Check on vote

Marijuana . . .

infectious disease or cancer. If there were significant damage, we might expect to find a higher rate of these diseases among young people beginning in the 1960s, when marijuana first became popular. There is no evidence of that.

The effects of marijuana on the reproductive system are a more complicated issue. In men, a single dose of THC lowers sperm count and the level of testosterone and other hormones. Tolerance to this effect apparently develops; in the Costa Rican study, marijuana smokers and controls had the same testosterone levels. Although the smokers in that study began using marijuana at an average age of 15, it had not affected their masculine development. There is no evidence that the changes in sperm count and testosterone produced by marijuana affect sexual performance or fertility.

In animal experiments THC has also been reported to lower levels of female hormones and disturb the menstrual cycle. When monkeys, rats, and mice are exposed during pregnancy to amounts of THC equivalent to a heavy human smoker's dose, stillbirths and decreased birth weight are sometimes reported in their offspring. There are also reports of low birth weight, prematurity, and even a condition resembling the fetal alcohol syndrome in some children of women who smoke marijuana heavily during pregnancy. The significance of these reports is unclear because controls are lacking and other circumstances make it hard to attribute causes. To be safe, pregnant and nursing women should follow the standard conservative recommendation to avoid all drugs, including cannabis, that are not absolutely necessary.

A well-confirmed danger of long-term heavy marijuana use is its effect on the lungs. Smoking narrows and inflames air passages and reduces breathing capacity; damage to bronchial cells has been observed in hashish smokers. Possible harmful effects include bronchitis, emphysema, and lung cancer. Marijuana smoke contains the same carcinogens as tobacco smoke, usually in somewhat higher concentrations. Marijuana is also inhaled more deeply and held in the lungs longer, which increases the danger. On the other hand, almost no one smokes 20 marijuana cigarettes a day. Higher THC content in marijuana may reduce the danger of respiratory damage, because less smoking is required for the desired effect. This is true only as long as no significant tolerance develops, and as long as users do not try to get a proportionately more intense effect from a stronger form of the drug.

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Assessing Allegations of Child Sexual Abuse

By Diane H. Schetky, MD and Elissa P. Benedek, MD

Heightened public and professional concern has led to overreporting of suspected child sexual abuse. According to the American Humane Association, 60 percent of such reports are unsubstantiated. Some of these are probably valid cases dropped for lack of evidence or because a child is too young to testify. Since sexual abuse of very young children usually does not involve penetration of orifices, physical evidence is often lacking, and it may also be difficult for a young child to describe such experiences accurately and repeatedly. Other cases are not prosecuted because the law chooses to disregard evidence obtained by highly coercive or suggestive techniques. In perhaps 5 to 30 percent of cases, however, unsubstantiated allegations occur because malicious or well-meaning persons have misinterpreted physical symptoms or behavior that has other causes.

Types of Unfounded Allegations

1. Charges of abuse sometimes arise in divorce cases when there are disputes about custody or visitation rights. The mother may anxiously misinterpret things the father has done while physically caring for their child. Less often a mother vindictively fabricates allegations to punish her former husband or exclude him from the child's life. Children who hear such charges repeated often enough may come to believe them and doubt their own perceptions.

2. A child occasionally makes a false allegation. In rare cases a child's fantasizing about sexual rela-

constantly thinking about the drug, or intoxicated, or recovering from its effects. The habit impairs their mental and physical health and hurts their work, family life, and friendships. They often know that they are using too much and repeatedly make unsuccessful attempts to cut down or stop. These problems seem to afflict proportionately fewer marijuana smokers than users of alcohol, tobacco, heroin, or cocaine. Even heavy users in places like Jamaica and Costa Rica do not seem to be dependent in this damaging sense.

Cause or Effect

It is often difficult to distinguish between drug use as a cause of problems and drug use as an effect; this is especially true in the case of marijuana. Most people who develop a dependency on marijuana would also be likely to develop other dependencies because of anxiety, depression, or feelings of inadequacy. The original condition is likely to matter more than the attempt to relieve it by means of the drug. The troubled teenager who smokes cannabis throughout the school day certainly has a problem, and excessive use of marijuana may be one of its symptoms.

The idea has persisted that in the long run smoking marijuana causes some sort of mental or emotional deterioration. In three major studies conducted in Jamaica, Costa Rica, and Greece, researchers have compared heavy long-term cannabis users with non-users and found no evidence of intellectual or neurological damage, no changes in personality, and no loss of the will to work or participate in society. The Costa Rican study showed no difference between heavy users (seven or more marijuana cigarettes a day) and lighter users (six or fewer cigarettes a day). Experiments in the United States show no effects of fairly heavy marijuana use on learning, perception, or motivation over periods as long as a year.

On the other side are clinical reports of a personality change called the amotivational syndrome. Its symptoms are said to be passivity, aimlessness, apathy, uncommunicativeness, and lack of ambition. Some proposed explanations are hormone changes, brain damage, sedation, and depression. Since the amotivational syndrome does not seem to occur in Greek or Caribbean farm laborers, some writers suggest that it affects only skilled and educated people who need to do more complex thinking.

...m of distinguishing causes from symp- ...s particularly acute here. Heavy drug users in our society are often bored, depressed, and listless, or alienated, cynical, and rebellious. Sometimes the drugs cause these states of mind and sometimes they result from personality characteristics that lead to drug abuse. Drug abuse can be an excuse for failure or a form of self-medication. Because of these complications and ... sence of confirmation from controlled studi... existence of an amotivational syndrome caused by cannabis use has to be regarded as unproven.

Stepping Stone Hypothesis

Much attention has also been devoted to the idea that marijuana smoking leads to the use of opiates and other illicit drugs: the stepping stone hypothesis. In this country, almost everyone who uses any other illicit drug has smoked marijuana first, just as almost everyone who smokes marijuana has drunk alcohol first. Anyone who uses any given drug is more likely to be interested in others, for some of the same reasons. People who use illicit drugs, in particular, are somewhat more likely to find themselves in company where other illicit drugs are available. None of this proves that using one drug leads to or causes the use of another. Most marijuana smokers do not use heroin or cocaine, just as most alcohol drinkers do not use marijuana. The metaphor of a stepping stone suggests that if no one smoked marijuana it would be more difficult for anyone to develop an interest in opiates or cocaine. There is no convincing evidence for or against this. What is clear is that at many times and places marijuana has been used without these drugs, or these drugs have been used without marijuana.

It is hard to generalize about abuse or define specific treatments, because the problems associated with marijuana are so vague, and cause and effect so hard to determine. Marijuana smokers may be using the drug to demonstrate rebelliousness, cope with anxiety, or medicate themselves for early symptoms of mental illness. People with serious problems who have been smoking marijuana heavily should be persuaded to stop so that their problems can be more effectively dealt with by psychotherapy or other means.

Health Hazards

Most recent research on the health hazards of marijuana concerns its long-term effects on the body. Studies have examined the brain, the immune system, the reproductive system, and the lungs. Suggestions of long-term damage come almost exclusively from animal experiments and other laboratory work. Observations of marijuana users and the Caribbean, Greek, and other studies reveal little disease or organic pathology associated with the drug.

For example, there are several reports of damaged brain cells and changes in brain-wave readings in monkeys smoking marijuana, but neurological and neuropsychological tests in Greece, Jamaica, and Costa Rica found no evidence of functional brain damage. Damage to white blood cells has also been observed in the laboratory, but again, its practical importance is unclear. Whatever temporary changes marijuana may produce in the immune system, they have not been found to increase the danger of

Continued on next page

Marijuana . . .

could be a problem for people with cardiovascular disease, dangerous physical reactions to marijuana are almost unknown. Like many other drugs, it produces a toxic delirium when taken at very high doses, especially by mouth. The symptoms are confusion, agitation, disorientation, loss of coordination, and often hallucinations; the delirium ends when the drug passes out of the body. No human being is known to have died of an overdose. By extrapolation from animal experiments, the ratio of lethal to effective (intoxicating) dose is estimated to be on the order of thousands to one.

Anxiety Reactions

The most common disturbing reaction to marijuana is acute anxiety, sometimes accompanied by paranoid thoughts. The user becomes fearful of dying or going insane, and may read hostility or ridicule into the gestures and words of companions. Mounting anxiety may lead to panic. The most likely victim of this reaction is an inexperienced user inadvertently taking a high dose in an unpleasant or unfamiliar setting. The best way to handle the anxiety and paranoia is calming support and reassurance. The reaction is not a psychosis; there are no hallucinations, and reassurance would not be effective without an ability to test the reality of thoughts and perceptions. Some authorities also refer to a cannabis delusional disorder with feelings of persecution or jealousy. Whether or not this is distinguishable from the anxiety reaction, the treatment is the same—reassurance and waiting for the drug effect to fade.

The anxiety reaction or delusional disorder is a milder version of the frightening LSD experience known as a bad trip. A truly nightmarish experience is rare under the influence of cannabis, because it is less potent than hallucinogenic or psychedelic drugs and the user is better able to control its effects. Use of LSD and other psychedelic drugs is often followed by flashbacks—the recurrence of emotions and perceptions originally experienced under the influence of the drug. They usually last only a few seconds and are not necessarily disturbing, but sometimes they become a persistent problem, which has been labelled post-hallucinogen perception disorder. Marijuana smoking may precipitate flashbacks in psychedelic drug users; a few reports suggest that marijuana flashbacks also occur without the previous use of psychedelic drugs.

Some observers, mainly in India and North Africa, have reported a cannabis psychosis caused mainly by long-term heavy use of the drug. It is described as a prolonged psychotic reaction with symptoms that include delusions, hallucinations, inappropriate emotions, and disordered thinking. In the descriptions, this psychosis is usually difficult to distinguish from acute schizophrenia, manic states, panic reactions, and other conditions. The reaction is rarely reported in the United States. Given the many millions of marijuana smokers in this country, the evidence for it would probably be less equivocal if it occurred with any regularity. Some people may suffer a psychotic reaction to cannabis because they are vulnerable to psychosis under any stress or after any change in consciousness or body image. For example, marijuana smoking probably increases the danger of relapse in schizophrenic patients (although any effect of this kind must be distinguished from a desperate attempt at self-medication because symptoms of schizophrenia are already returning).

Long-Term Effects

In recent years the psychological and physical effects of long-term use have caused the most concern. Studies are often conflicting and permit various views of marijuana's possible harmfulness. This complicates the task of presenting an objective statement about the issue.

One of the first questions asked about any drug is whether it is addictive or produces dependence. This question is hard to answer because the terms 'addiction' and 'dependence' have no agreed-upon definitions. Two recognized signs of addiction are tolerance and withdrawal symptoms; these are rarely a serious problem for marijuana users. In the early stages, they actually become more sensitive to the desired effects. After continued heavy use, some tolerance to both physiological and psychological effects develops, although it seems to vary considerably among individuals. Almost no one reports an urgent need to increase the dose to recapture the original sensation. What is called behavioral tolerance may be partly a matter of learning to compensate for the effects of high doses, and may explain why farm workers in some Third World countries are able to do heavy physical labor while smoking a great deal of marijuana.

A mild withdrawal reaction also occurs in animal experiments and apparently in some human beings who take high doses for a long time. The symptoms are anxiety, insomnia, tremors, and chills, lasting for a day or two. It is unclear how common this reaction is; in a Jamaican study, heavy ganja (marijuana) users did not report abstinence symptoms when withdrawn from the drug. In any case, there is little evidence that the withdrawal reaction ordinarily presents serious problems to marijuana users or causes them to go on taking the drug.

In a more important sense, dependence means an unhealthy and often unwanted preoccupation with a drug to the exclusion of most other things. People suffering from drug dependence find that they are

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Marijuana

The present generation of young people cannot remember when marijuana was an exotic weed with an aura of mythical power and mysterious danger. Although still illegal, it has become a commonplace part of the American social scene, used regularly by millions and occasionally by millions more. A realistic view of this drug is now both more important and easier to achieve.

The use of marijuana reached a high point in the late 1970s and early 1980s, and has been declining ever since. In a 1978 survey, 37 percent of high school seniors said they had smoked marijuana in the last 30 days, and 11 percent said they used it daily. By 1986 the number who said they had smoked it in the last 30 days had fallen to 23 percent—lower than in 1975—and the proportion of daily users had dropped steadily to 4 percent. The trend among people aged 18 to 25 is similar. On the other hand, more people over 25 may be using marijuana occasionally, and young people are still experimenting with it. In 1969, 20 percent of high school seniors had used marijuana at least once; in 1979, 60 percent had; and in 1985, 54 percent. The attitudes expressed in surveys show why habitual marijuana use is in decline. In 1978, 65 percent of high school students said they disapproved of it; in 1985, 85 percent disapproved. In 1978, 35 percent said it was very risky, and in 1985, 70 percent said it was.

The main active ingredient of marijuana is delta-9-tetrahydrocannabinol (THC), one of more than 60 related chemicals found in the resin that covers the flowers and top leaves of the cannabis (hemp) plant. The leaves and flowers can be ground up in drinks or food, but more often they are dried and smoked in a cigarette or pipe. The pure resin, known as hashish, can also be smoked, eaten, or drunk. New breeding and cultivation techniques have raised the THC content of marijuana smoked in the United States as much as ten times over the last 20 years, from an average of 0.4 percent to 4 percent. Some varieties now contain as much as 10 percent.

The effects last two to four hours when marijuana is smoked and five to twelve hours when it is taken by mouth. Although the intoxication varies with psychological set and social setting, the most common response is a calm, mildly euphoric state in which time slows and sensitivity to sights, sounds, and touch is enhanced. The smoker may feel exhilaration or hilarity and notice a rapid flow of ideas with a reduction in short-term memory. Images sometimes appear before closed eyes; visual perception and body image may undergo subtle changes. It is dangerous to operate complex machinery, including automobiles, under the influence of marijuana, because it slows reaction time and impairs attention and coordination. This impairment persists for at least several hours after the feeling of intoxication has passed.

The main physiological effects of cannabis are increased appetite, a faster heartbeat, and slightly bloodshot eyes. Although the increased heart rate

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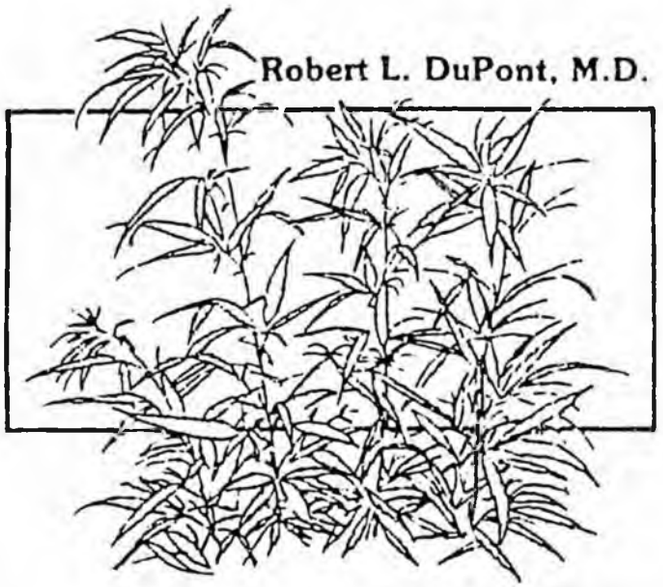
MARIJUANA SMOKING— A NATIONAL EPIDEMIC

Robert L. DuPont, M.D.



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MARIJUANA SMOKING constitutes the greatest single new threat to the health of our lungs in the United States. In the next ten years, the potential exists for an enormous worsening of the respiratory health of Americans, unless we do something about it now.

Marijuana is a new problem in American society. Twenty years ago, virtually no one used it. As recently as 1962, only 1% of American youth aged 12 to 17 and 4% of Americans aged 18 to 25 had ever tried marijuana. By 1979, these figures had risen to 31% and 68%.

A national epidemic

Today, marijuana smoking is a national epidemic. Fifty-five million Americans have smoked it at least once. Twenty-three million Americans are currently regular smokers of the weed. Four million young people of 17 years and under are at present smokers. Among the nation's ninth graders, the percentage of students who have smoked it jumped from 16% in 1975 to over 32% in 1979. Among high school seniors, slightly less than 11% smoke it every day, and the average number of joints smoked by those seniors is 3½% a day.

Substances used most commonly on a daily basis by high school seniors are tobacco, marijuana, and alcohol. Among high school seniors, 29% use tobacco daily, roughly 11% use marijuana every day, and 6% use alcohol daily. Those percentages of daily tobacco and alcohol users have remained the same since 1975, while the proportion of daily marijuana users has doubled in that period. There is certainly no other illegal drug that compares with marijuana in terms of frequence of usage.

The extent of marijuana usage in the United States comes more clearly into focus when you compare it with the experience of other countries with the habit. Most people are aware that marijuana has been smoked around the world for a long time. However, you may not know that American young people are literally the only population in the history of the world in which large numbers of an entire generation have smoked marijuana; experience with the cannabis product (it comes from the cannabis sativa plant) is restricted in other parts of the world. The use of marijuana in other countries does not involve an entire society; generally, its use is limited to either religious groups or social classes that are relatively isolated and generally looked down on in the society.

How we got into the mess

Something new and dramatic has happened that may affect the growing acceptance of marijuana in the United States: Scientists have identified some of the hazardous effects of marijuana smoke on the body.

Before I discuss those new findings, let me talk about how we got into the mess we are in with marijuana; it will reveal some of the challenges that we must meet

©American Lung Association of California, 1981

The first thing to realize about the drug is that it does work — it produces powerful effects. The major psychoactive agent is THC (delta-9-tetrahydrocannabinol). Ten years ago, the average THC content in a marijuana cigarette was 2/10 of a percent. Today, it's more like 4% or 5%. That's an increase of 20 to 25 times in the last six or seven years.

The second point is that marijuana is unique in that it has been a potent symbol. It has been a symbol of youth, a symbol of anti-authority positions, a symbol of modernity.

There has also been a unique tendency to trivialize the marijuana experience, and this is truly frightening to people who are aware of the effects of marijuana on the body. As one high school student said to me a year or so ago, "Marijuana is not a drug. It's part of the scene, like blue jeans." This remark represents the evolution of an attitude from the days ten years ago when marijuana was a meaningful symbol to its present status as "part of the scene."

Reasons why it has been accepted

Now, one might ask why there are 23 million people regularly smoking a new substance which society would ordinarily resist. I want to outline some of the reasons for this. First, there is a history of exaggerations in the past about the harmfulness of marijuana, based on little or no data. This has been captured by pro-marijuana lobbyists with a 1930's film called "Reefer Madness." The message is putdown for anyone who has anything bad to say about marijuana.

Second, the decriminalization of marijuana use has led to greater acceptance. Over half of the public attention devoted to the issue in recent years has focused on the criminal sanctions for possession. Much of the debate is symbolic: If you are for decriminalization, you are for marijuana. If you're against decriminalization, you're against marijuana use.

The reality is that virtually no one in the United States is sent to jail for possession of the product any more. There are still about 400,000 arrests for marijuana possession a year, but the offenders are rarely prosecuted. The concept that we need to reform our laws to deal with the marijuana possessor is unreasonable when viewed against the realities of the present enforcement attitude.

The third reason why marijuana has been accepted lies in the charge of parental or adult hypocrisy. The idea is that, because adults smoke cigarettes or drink alcohol, kids ought to be able to smoke marijuana. Therefore, if adults condemn marijuana smoking, they are being hypocritical.

The answers to the parental or adult hypocrisy charge is that decisions about the use of a psychoactive substance — whether it be marijuana, alcohol or tobacco — should be made by adults and not by children. Even Keith Stroup of the national marijuana lobbying organization opposes the use of cannabis, as well as tobacco and alcohol, by people under the age of 18.

The therapeutic use argument, another red herring

The fourth red herring that has been drawn across the path of anyone trying to do something about the marijuana epidemic is the therapeutic-use argument. Twenty state legislatures in the past year have been bamboozled into passing laws to legalize the use of marijuana as a medicine. The legislation is unnecessary, there are federal statutes that make marijuana available as a medication, if it were ever to pass muster as a clinically effective agent for any specific ailment. In my opinion, that possibility is extremely unlikely.

Marijuana is not a chemical; it is a vegetable plant product. It contains over 400 separate chemicals, 60 of them unique to the cannabis sativa plant and known as cannabinoids. When marijuana is smoked, it emits more than 4,000 separate, identifiable chemical substances. The idea of treating any disease with something so complex is unmedical and unscientific. It is a little like saying, "We'll have people eat bread mold to treat pneumococcal pneumonia instead of using penicillin."

At the same time, some of the components of marijuana — and particulary THC — may have some therapeutic use. I certainly favor the investigation of those components, but we do not need any new laws for that. My point is that if marijuana is treated as a helpful medicine, it will gain acceptability in terms of public perception. That is why marijuana lobbyists are so vigorously promoting the use of marijuana for glaucoma sufferers and those who are undergoing chemotherapy for cancer. They don't want doctors to use purified chemicals such as THC, because they lose their symbolic argument.

Marijuana and the lungs

So much for the past. Let me review quickly some of the basic outlines of the case against marijuana in relation to the lungs. Marijuana smoke is much like tobacco smoke, with two exceptions: It has THC in it, and it does not contain nicotine. If you switch those two compounds, putting nicotine in the marijuana and THC in the tobacco, they are similar in their biological effects and their chemical constituents. Although nicotine is clearly a toxic substance, the effects of THC are possibly even more devastating because of the intoxicating qualities of cannabis.

Another aspect of marijuana is that it is at least as serious a respiratory irritant as tobacco, and probably more so.

The manner in which marijuana is smoked is a key factor in irritating the lungs. Most modern tobacco smokers are concerned about their lungs and tend to inhale relatively lightly. In contrast, the marijuana smoker inhales deeply and holds his breath to sustain the exposure for maximum absorption of the fumes. Too, the cigarette smoker is likely to buy a filtered cigarette nowadays and will not puff it all the way

.. the ethos of the marijuana smoker is to burn the entire joint. A "roach clip" enables the marijuana user to smoke until there is nothing left except the part that is just touching the lips, maximizing the exposure to tar and other respiratory irritants.

Still another aspect of marijuana smoke is that it contains well-recognized carcinogens. When the smoke is condensed and painted on the skins of laboratory mice, it produces a metaplasia of the sebaceous glands, a cancerous change. The effects of tobacco smoke are not so marked.

So we have evidence that marijuana contains more tar and known carcinogens than tobacco. Moreover, when human and animal lung tissue are exposed to marijuana smoke in a laboratory setting, the resulting cancerous changes are analogous to those produced by tobacco smoke and, in some cases, more frequent. Finding evidence on the development of human lung cancer from marijuana smoke is, I think, just a matter of time.

The evidence piles up

There is yet more evidence that indicates harmful respiratory complications from marijuana use. Some studies have shown severe inflammation of the small airways. Others have demonstrated that the alveolar macrophages, the primary defense against alien bodies in the lungs, are less able to dispose of bacteria and foreign materials when exposed to marijuana smoke.

In addition, there is a rise in the carboxyhemoglobin level in the blood — an increase in the ratio of carbon monoxide to oxygen. One study found that a single marijuana cigarette smoked for 15 minutes produced as high a level of carboxyhemoglobin as ten to twenty tobacco cigarettes smoked in the course of a day. I think the likeliest reason for this difference is the way marijuana is smoked.

So, the evidence suggests that smoking marijuana is harmful to the lungs. Furthermore, everything we now know about the effects of tobacco smoking is applicable to marijuana use in terms of what it does to the lungs — at least, one ought to begin with that assumption until there is evidence to the contrary. We obviously need broad-based epidemiological studies before the final "i" is dotted in this indictment, but I don't know how anyone can believe that marijuana is harmless to lungs in the light of the available data.

Effects of the drug on other parts of the body

Let me cover very briefly the effects of marijuana on other organs of the body. It is important to know that the intoxicating effect of marijuana is profound. The consequences are in some ways like those of alcohol, being of several hours' duration. However, alcohol is soluble in water, and because of this, the water based waste disposal system of blood and urine works quite well to get rid of it. THC, not being water-soluble, tends to be retained in the body, particularly in the brain and the reproductive organs.

A person who smokes one marijuana cigarette has half of the THC in his body five to seven days, later, and measurable quantities are present after a month. This means that if a person smokes as infrequently as once a month, the THC accumulates, and the brain and reproductive organs are continously exposed. There is good evidence that there are profound effects both on brain function and reproductive function from marijuana use.

Hard to reverse the tide

It has proved difficult, even with all the data available in recent years on the health hazards of tobacco smoking, to convince Americans — and especially young people — to quit the cigarette habit or never start it.

Those of us in the marijuana field have found it even harder to turn the tide of the marijuana epidemic because of the perceived lack of sufficient scientific evidence on the dangers of marijuana. This information is just beginning to come to light. As a result, many young people — who make up the majority of marijuana users — have seen no reason not to smoke pot.

Among American high school seniors, about 60% perceive that there is a great health risk in cigarette smoking. Only 35% see the similar peril of cannabis sativa. It is that disparity which is contributing to the explosive growth of marijuana smoking.

The most bizarre thing that strikes me about young people is that so many are concerned about pollution, worried about the environment, believers in eating natural foods, crusaders against the problems of nuclear energy — and yet they continue to smoke marijuana cigarettes. The idea that smoking pot may be hazardous to your health just hasn't cut through all the controversy and the politics surrounding the weed. There is a growing body of information about health risks, and we need to get that across.

I would add that scientific data on the health effects of any drug or product is not, in itself, sufficient to solve the public health problem. However, it is a necessary condition for public health mobilization.

It is actually within only the past year or two that some initial findings on the changes in the body produced by marijuana smoking have been developed. I am convinced that if marijuana smoking were to be taken up as a priority by the American Lung Association, we would take a giant step forward in the education of the public about cannabis.

Smoke is bad for the lungs, whether it's industrial smoke, tobacco smoke or marijuana smoke. We need your help in stemming the marijuana epidemic.

ROBERT L. DUPONT, M.D., is president of the American Council on Marijuana and a former director of the National Institute on Drug Abuse. A practicing psychiatrist, he heads Washington, D.C.'s first phobia treatment program and writes on health topics for local and national television, radio, magazines, and newspapers. He is also president of the non-profit Institute for Behavior and Health, which conducts research and demonstration programs aimed at preventing drug and alcohol abuse.

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PULMONARY HAZARDS OF SMOKING MARIJUANA AS COMPARED WITH TOBACCO

TZU-CHIN WU, M.D., DONALD P. TASHKIN, M.D., BEHNAM DJAHED, M.D., AND JED E. ROSE, PH.D.

Abstract To compare the pulmonary hazards of smoking marijuana and tobacco we quantified the relative burden to the lung of insoluble particulates (tar) and carbon monoxide from the smoke of similar quantities of marijuana and tobacco. The 15 subjects, all men, had smoked both marijuana and tobacco habitually for at least five years. We measured each subject's blood carboxyhemoglobin level before and after smoking and the amount of tar inhaled and deposited in the respiratory tract from the smoke of single filter-tipped tobacco cigarettes (900 to 1200 mg) and marijuana cigarettes (741 to 985 mg) containing 0.004 percent or 1.24 percent Δ^9-tetrahydrocannabinol.

As compared with smoking tobacco, smoking marijuana was associated with a nearly fivefold greater increment in the blood carboxyhemoglobin level, an approximately threefold increase in the amount of tar inhaled, and retention in the respiratory tract of one third more inhaled tar ($P<0.001$). Significant differences were also noted in the dynamics of smoking marijuana and tobacco, among them an approximately two-thirds larger puff volume, a one-third greater depth of inhalation, and a fourfold longer breath-holding time with marijuana than with tobacco ($P<0.01$). Smoking dynamics and the delivery of tar during marijuana smoking were only slightly influenced by the percentage of tetrahydrocannabinol.

We conclude that smoking marijuana, regardless of tetrahydrocannabinol content, results in a substantially greater respiratory burden of carbon monoxide and tar than smoking a similar quantity of tobacco. (N Engl J Med 1988; 318:347-51.)

WE have previously shown that the habitual smoking of 3 or 4 marijuana cigarettes a day is associated with the same frequency of the symptoms of acute and chronic bronchitis[1] and the same type and extent of epithelial damage in the central airways[2] as the regular smoking of more than 20 tobacco cigarettes a day. A possible explanation for these findings is that a greater quantity of smoke particulates and noxious gases is delivered to and deposited or absorbed in the lungs by marijuana than by a similar amount of tobacco, possibly as a result of differences in the way each type of cigarette is smoked. To investigate this possibility, we examined the dynamics of smoking a marijuana or a tobacco cigarette and measured the particulates delivered to the smoker's mouth during the smoking of a single cigarette of each type.

METHODS

We studied fifteen men who were habitual smokers (mean age [±SD], 31.5±7.1 years), each of whom smoked both tobacco and marijuana. The subjects smoked an average of 29.9±16.7 tobacco cigarettes per day and had smoked an average of 16.1±12.2 pack-years of tobacco (one pack-year equals one pack of tobacco cigarettes per day times the number of years of smoking); they smoked an average of 16.5±17.1 marijuana cigarettes per week, and had smoked an average of 54.8±34.8 joint-years of marijuana (one joint-year equals one cigarette [joint] of marijuana per day times the number of years of smoking). All were in good general health and had normal or nearly normal values for forced vital capacity (101±8.7 percent of predicted values[3]) and forced expiratory volume in one second (96±14 percent of predicted values[3]). None reported intravenous drug abuse or smoking other illicit substances besides marijuana.

Each subject was studied on a single day after refraining from smoking tobacco for at least one hour and marijuana for at least six hours. During the study session, each subject smoked his own brand of filter-tipped tobacco cigarette, followed, in single-blind fashion, first by a placebo marijuana cigarette (from which nearly all Δ^9-tetrahydrocannabinol [Δ^9-THC] had been extracted, so that the concentration was 0.004 percent) and next by a marijuana cigarette of similar weight containing 1.24±0.06 percent Δ^9-THC. An interval of approximately 30 minutes separated the smoking of each two cigarettes. The tobacco cigarettes weighed 900 to 1120 mg and had a tar yield of 4.6 to 23.1 mg (mean, 12.0±5.7 mg) and a nicotine yield of 0.4 to 1.4 mg (mean, 0.84±0.32 mg) by Federal Trade Commission analysis. The placebo marijuana cigarettes weighed 741 to 940 mg (mean, 840 mg) and those containing 1.24 percent Δ^9-THC weighed 849 to 985 mg (mean, 907 mg); both were supplied by the National Institute on Drug Abuse, were stored at 4°C to minimize chemical degradation, and were maintained in a humidifier at 60 percent humidity and 21°C for 24 hours before the study, to reduce harshness.

The subjects were asked to smoke both the tobacco cigarette and the two marijuana cigarettes in a manner as similar as possible to their usual pattern of smoking tobacco and marijuana. Peripheral venous blood was withdrawn anaerobically immediately before and two minutes after the first two cigarettes were smoked for measurement of the percentage of carboxyhemoglobin saturation, with use of a carbon monoxide–oximeter (Model 282, Instrumentation Laboratory, Lexington, Mass.). After smoking each of the marijuana cigarettes, the subjects were asked to rate their level of intoxication on a scale of 0 to 100 percent, with 100 percent representing the greatest "high" they had ever experienced.

The volume, duration, and number of puffs and the intervals between puffs were measured with a 00 Fleisch pneumotachygraph (linear from 5 to 100 ml per second) connected through a differential pressure transducer (Model MP54-3, Validyne, Northridge, Calif.) (range, ±2 cm of water) to an oscilloscopic recorder with a differential integrator–computer and a rapid photographic writer (Model VR6, Electronics for Medicine, Pleasantville, N.Y.). To prevent the pneumotachygraph screen from becoming clogged by smoke particles,[4] the pneumotachygraph was connected through wide-bore Tygon tubing (length, 70 cm; internal diameter, 1 cm) to the distal end of a glass cylinder (length, 12 cm; diameter, 5 cm) that contained two ventilation ports (each 1 cm in diameter) and was sealed at its proximal end by a rubber stopper. The tobacco or marijuana cigarette was held in a small plastic holder inserted through the rubber stopper. The ventilation ports were left open between puffs to prevent either the extinction of the lighted cigarette or the excessive accumulation of carbon monoxide. During a puff, the smoker covered the ventilation holes with his index and middle fingers so that the entire volume of air drawn through the cigarette could be measured by the pneumotachygraph. The resistance of the pneumotachygraph (0.0068 cm of water per milliliter per second) was considerably lower than that of the cigarette (0.51 cm of water per milliliter per second for tobacco; 0.17 cm of water per milliliter per second for marijuana); therefore, the pneumotachygraph itself was

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not likely to have a substantial effect on smoking dynamics. The duration of a puff was timed from the pneumotachygraphic flow tracing. The interval between puffs was defined as the period between the end of one puff and the start of the next.

To measure "wash-in" volume (the volume of air inhaled), inductive plethysmographic coils (Respitrace Ambulatory Monitoring Systems, Ardsley, N.Y.) were placed around each subject's rib cage and abdomen.[5,6] A demodulator converted changes in electrical inductance in the coils during respiratory movements into voltage signals proportional to changes in the volume enclosed by the coils. Changes in the volume of the respiratory system were calculated from the weighted sums of the signals from the rib cage and abdomen; the weights were determined by the least-squares calibration method.[7] The accuracy of the calibration was confirmed by comparing the inhaled volumes calculated from respiratory inductive plethysmography with spirometric values; the measurements obtained by spirometry and inductive plethysmography agreed within ±10 percent. The amount of time the inhaled smoke was retained in the lungs (smoke-retention time) was calculated as the interval between the times corresponding to one third of the maximum inhaled volume and two thirds of the maximum volume exhaled following breath holding (Fig. 1). The no-smoking interval was timed from the end of the smoke-retention time to the start of the next puff.

A previously described proportional smoke-trapping device[8] was connected to the apparatus for measuring the volume of puffs in order to measure the amount of smoke particulates delivered to the smoker's mouth. This device consisted of a plastic cigarette holder through which the mainstream smoke was diverted into two parallel pathways, one containing one capillary tube (pathway A) and the other seven parallel capillary tubes (pathway B). A Cambridge filter pad trapped the smoke that passed through pathway A. The tar trapped by the filter was extracted with methanol and analyzed by means of a spectrophotometer (wavelength, 400 nm). A constant fraction of the tar (12.5±0.53 percent) was retained in the filter over a wide range of puff volumes (30 to 60 ml), puff durations (1 to 4 sec), and puff flow rates (20 to 100 ml per second).[8] This apparatus, therefore, permitted the actual quantity of smoke particulates delivered to the mouth to be calculated by multiplying the amount of particulates trapped in the Cambridge filter pad in pathway A by seven. At the end of the period of breath holding after each puff, the subjects turned their heads slightly to one side and exhaled the smoke into the large end (diameter, 26 cm) of an adjacent megaphone device, the distal end (diameter, 4.5 cm) of which was fitted with a high-efficiency filter attached to a vacuum system as described by Hinds et al.[9] After the tar was extracted from the filter with methanol, the exhaled particulates were measured with a spectrophotometer. The amount of smoke retained (deposited) in the respiratory tract was expressed as a percentage of the amount inhaled: percentage deposited = [1 − (amount of exhaled particulates/amount of inhaled particulates)] × 100.

Each subject's measurements were averaged for each cigarette smoked. These mean values, as well as the number of puffs, the quantity of particulates inhaled, the percentage of inhaled particulates deposited, and the increment in carboxyhemoglobin saturation per cigarette, were averaged for all 15 subjects for each type of cigarette smoked. The subjects' ratings of their degree of intoxication after marijuana smoking were also averaged for all subjects for each type of marijuana cigarette (placebo and 1.24 percent Δ^9-THC). Two-way analysis of variance (for subject and type of cigarette) was used to determine the significance of differences in smoking patterns, the delivery and deposition of particulates, and the increase in carboxyhemoglobin saturation among types of cigarette.[10] Pairwise comparisons were then performed using testing for least significant differences[11]; differences were considered significant if P values were <0.05.

Results

Descriptive data about smoking in the group of 15 subjects are shown in Table 1. Placebo marijuana and marijuana containing approximately 1.24 percent Δ^9-THC were smoked in a similar manner. However,

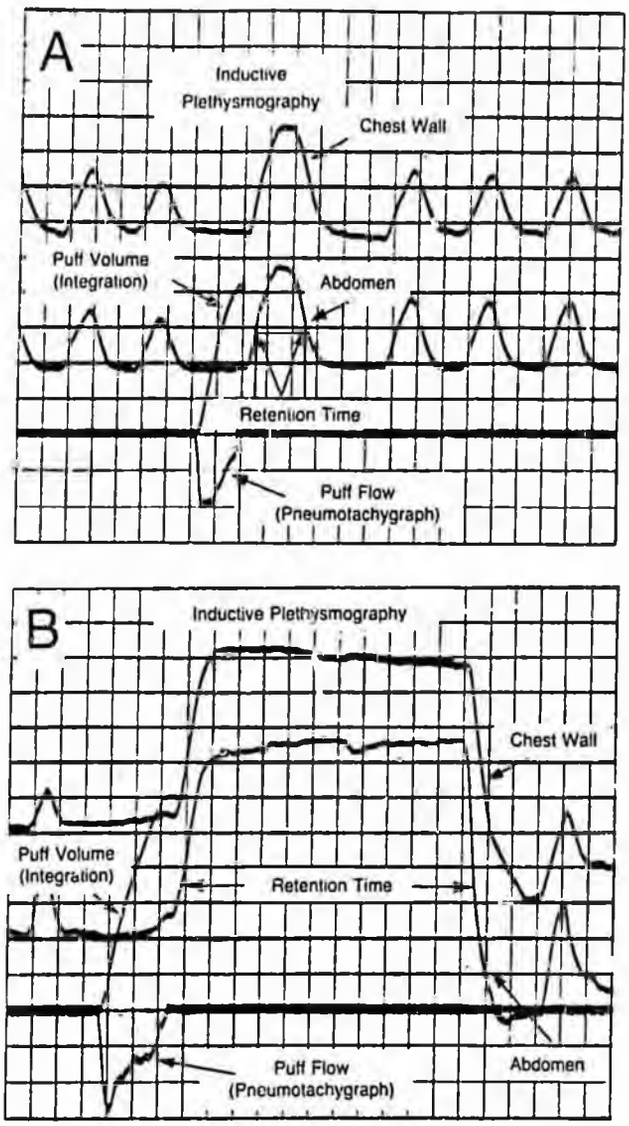

Figure 1. Analogue Tracings of Voltage Signals from Inductive Plethysmographic Coils around the Chest Wall and Abdomen of a Representative Subject and Simultaneous Flow and Integrated Volume Signals from a Pneumotachygraph Incorporated into a Puff-Volume Measuring Device during the Smoking of a Tobacco Cigarette (A) and a Marijuana Cigarette (B).

Note that during marijuana smoking, there is greater amplitude of the voltage signals representing puff volume (measured by the pneumotachygraph) and inhaled volume (measured by the inductive plethysmograph) than during tobacco smoking.

the average volume of puffs was about 70 percent larger (P<0.001) and the duration of puffs about 60 percent longer (P<0.01) during the smoking of marijuana than the smoking of tobacco, regardless of whether the marijuana contained 1.24 or 0.004 percent Δ^9-THC; significantly more puffs were taken from the tobacco cigarette than from either the placebo marijuana cigarette or that containing 1.24 percent Δ^9-THC (P<0.001). Although the interval between puffs was less for tobacco than for marijuana smoking (P<0.05), the no-smoking interval, which did not include the breath-holding time after

Table 1. Characteristics of 15 Subjects' Smoking of Tobacco, Placebo Marijuana (0.004 Percent Δ^9-THC), and Marijuana Containing 1.24 Percent Δ^9-THC.*

Index	Tobacco	Marijuana		P Value†
		0.004% Δ^9-THC	1.24% Δ^9-THC	
	mean ±SD			
Puff volume (ml)	49.4±15.2	88.3±24.8	78.0±22.8	<0.001
Puff duration (sec)	±1.1	3.8±1.9	4.0±2.2	<0.01
No. of puffs	13.5±4.0	7.5±2.3	8.5±3.1	<0.001
Interval between puffs (sec)	27.0±8.2	35.3±12.2	37.6±14.5	<0.05
Inhaled volume (liter)	1.31±0.22	1.82±0.66	1.75±0.52	<0.002
Smoke-retention time (sec)	3.5±1.3	13.8±9.2	14.7±10.2	<0.001
No-smoking interval (sec)	23.5±8.5	21.5±6.4	23.0±8.8	NS

*All subjects were habitual smokers of both tobacco and marijuana. They smoked their own brands of tobacco cigarettes. Δ^9-THC denotes Δ^9-tetrahydrocannabinol; NS denotes not significant.

†P values indicate the significance of comparisons between tobacco and each strength of marijuana; none of the comparisons between the two different strengths of marijuana (0.004 percent vs. 1.24 percent Δ^9-THC) was statistically significant.

smoke was inhaled, was similar for both substances. The mean inhaled volume was 36 percent greater ($P<0.002$) and the smoke-retention time was four times longer ($P<0.001$) during marijuana smoking than tobacco smoking.

The volume of the portion of the proportional smoke-trapping device through which smoke was delivered was approximately 13 ml. After the first puff, this volume was filled with smoke that was delivered in subsequent puffs; thus, after the first puff, no additional volume of air not containing smoke was included in the measurement of puff volume. When the pneumotachygraph was disassembled from the proportional smoke-trapping device and used to measure puff volume, the difference in the mean volume was negligible (4.2±2.0 ml lower without the smoke-trapping device). Similarly, inhaled volumes determined directly from the cigarette by the inductive plethysmograph, without the attachment of either the pneumotachygraph or the proportional smoke-trapping device, were similar to (within 50 ml) the inhaled volume determined when the subjects smoked through these devices.

The amounts of particulates inhaled, the percentage of inhaled particulates deposited in the respiratory tract, and the differences between the carboxyhemoglobin levels before and after smoking each type of cigarette are shown in Table 2. The major significant difference between smoking marijuana cigarettes containing 0.004 percent Δ^9-THC (placebo) and smoking cigarettes containing 1.24 percent Δ^9-THC was that the latter caused a greater degree of intoxication. In addition, the amount of particulates inhaled from marijuana containing 1.24 percent Δ^9-THC was slightly but significantly greater (20 percent) than that delivered from placebo marijuana ($P<0.05$). In contrast, smoking either type of marijuana was associated with the inhalation of 2.8 to 3.3 times more insoluble particulates (tar) and with the deposition of 32 to 35 percent more of these inhaled particulates than smoking the subject's own brand of tobacco ($P<0.001$). Consequently, marijuana smoking resulted in a tar burden to the respiratory tract that was 3.5 to 4.5 times greater than that produced by tobacco smoking in the same subjects. Furthermore, smoking a single marijuana cigarette caused a fourfold greater increment in carboxyhemoglobin saturation ($P<0.001$) than did smoking a single tobacco cigarette.

Discussion

Long-term adverse pulmonary consequences of tobacco smoking have been shown to be related to dose.[12] For example, the incidence of chronic obstructive pulmonary disease or bronchogenic carcinoma in smokers of fewer than 5 to 10 tobacco cigarettes a day is substantially less than in habitual smokers of more than 20 tobacco cigarettes a day.[13] Although regular tobacco smokers consume more than 15 tobacco cigarettes a day, most current smokers of marijuana smoke less than 1 marijuana cigarette a day.[12] Even among the estimated 6 million daily smokers of marijuana in the United States,[14] smoking more than five marijuana cigarettes a day is unusual. In view of the many similarities in the smoke contents of marijuana and tobacco,[15,16] it has been argued that habitually smoking only a few marijuana cigarettes a day may have a proportionately less harmful long-term effect on the lungs than regularly smoking several times more tobacco cigarettes. This argument assumes that the number of cigarettes smoked is directly proportional to the dose of smoke contents inhaled; however, this assumption ignores the ways in which the characteristics of smoking may influence the delivery of the combustion products of cigarettes.[17,18]

Table 2. Inhalation and Deposition of Particulates, Increases in Blood Carboxyhemoglobin Saturation, and Levels of Intoxication Associated with the Smoking of Tobacco and Marijuana in 15 Smokers of Both Substances.*

Index	Tobacco	Marijuana	
		0.004% Δ^9-THC	1.24% Δ^9-THC
	mean ±SD		
Inhaled particulates (optical density)	4.9±2.0	13.5±6.0†	16.3±6.3†‡
Percentage of particulates deposited	64.0±8.9	84.4±6.9†	86.1±6.7†
Increase in carboxyhemoglobin saturation (%)	0.60±0.52	2.99±1.51†	—§
Degree of intoxication (maximum "high" = 100%)	—	15.3±16.9	63.9±18.3‡

*Δ^9-THC denotes Δ^9-tetrahydrocannabinol.

†Significantly greater than values for tobacco ($P<0.001$ by analysis of variance and testing for least significant difference).

‡Significantly greater than values for marijuana containing 0.004 percent Δ^9-THC ($P<0.05$ by analysis of variance and testing for least significant difference).

§Not measured.

Few studies have been carried out in which the actual dose of smoke contents delivered to and retained in the respiratory tract during natural smoking has been measured. In our study, both the amount of particulate matter that was inhaled and the amount that was deposited in the respiratory tract were quantified during tobacco and marijuana smoking by means of a simple, new, noninvasive device.[8] These measurements allowed us to compare the actual dose to the smoker of particulate matter from the smoke of marijuana with that from tobacco. At the same time, the characteristics of smoking were determined in order to ascertain the relation between behavioral variables in smoking and the delivery and retention of smoke contents in the respiratory tract for each type of cigarette. The proportional smoke-trapping device had little measurable influence on smoking dynamics.

Findings from the present study indicate that approximately three times as much particulate matter is delivered to the smoker's mouth during the smoking of a single marijuana cigarette than during the smoking of a single tobacco cigarette of the smoker's own brand. These results are similar to those obtained in studies that used smoking machines to simulate conditions thought to be representative of marijuana and tobacco smoking.[19,20] Our results also revealed that approximately one third more of the particulates inhaled from the smoke of marijuana are retained in the respiratory tract than is the case when tobacco is smoked. Consequently, the net respiratory burden of particulates was approximately four times greater during marijuana smoking than tobacco smoking.

Several explanations are possible for the greater burden of particulates to the lungs from marijuana than from a similar quantity of tobacco. First, in all 15 cases, the tobacco cigarettes were more densely packed than the marijuana cigarettes and, unlike the marijuana cigarettes, were filter-tipped; therefore, the filtration efficiency of the tobacco cigarettes was greater. Second, the average residual length of the marijuana cigarettes (23±13 mm) was smaller than that of the tobacco cigarettes (37±12 mm), thereby further reducing the filtration efficiency of the marijuana cigarette. However, because the tobacco cigarettes were initially longer and because the filter tip was included in the tobacco butt, the actual quantities of tobacco and marijuana consumed were similar. Third, the subjects' patterns of inhalation in smoking the two types of cigarettes were markedly different; marijuana was smoked with a puff volume that was more than two thirds larger, an inhaled volume one third greater, and a retention time four times longer than the values for tobacco. Although the larger puff volumes for marijuana were partially offset by a smaller number of puffs, this factor may still have contributed to the greater mass of smoke particulates delivered to the mouth in marijuana smoking. The deeper inhaled volumes and, in particular, the severalfold longer retention times during marijuana smoking than during tobacco smoking may have accounted for the greater percentage of the inhaled particulates from marijuana smoke deposited in the respiratory tract.

The four-to-five-times-greater increments in carboxyhemoglobin saturation during marijuana smoking than tobacco smoking were probably due mainly to differences in how the cigarettes were smoked rather than in the amount of carbon monoxide produced, since syringe-simulated puffs of similar volumes and durations from lit cigarettes yielded approximately 25 percent lower concentrations of carbon monoxide from marijuana than from tobacco. This finding is consistent with the more complete combustion of the more loosely packed marijuana. On the other hand, the subjects' deeper inhalations and, in particular, their considerably longer retention of smoke in the lungs during marijuana smoking than during tobacco smoking made possible a greater uptake of carbon monoxide by the pulmonary microcirculation by means of passive diffusion. We measured the increment in blood carboxyhemoglobin after placebo marijuana (from which the cannabinoids had been extracted), and not after marijuana containing Δ^9-THC. However, we would not expect appreciable differences between the effects of real marijuana and those of placebo marijuana on blood carboxyhemoglobin levels, since the smoking dynamics and the carbon monoxide delivery of the two types of marijuana cigarettes were similar. The expected physiologic consequences of the markedly greater boost in carboxyhemoglobin levels from a single marijuana cigarette are a higher degree of impairment in oxygen transfer in the lung,[21] a reduction in the oxygen-carrying capacity of the blood, and impairment in the release of oxygen from hemoglobin in the tissues.[22] Moreover, the Δ^9-THC in marijuana causes dose-related increases in heart rate[23,24] and thus in cardiac work and myocardial oxygen requirements. Therefore, in persons with underlying coronary artery disease who smoke marijuana, the combined effects of a marked rise in the level of carboxyhemoglobin and the cardioacceleration induced by Δ^9-THC could lead to a critical imbalance between reduced myocardial oxygen supply and increased demand.

Interestingly, no significant differences in smoking dynamics were noted between placebo marijuana and marijuana containing 1.24 percent Δ^9-THC, despite marked differences in the subjects' perceived level of intoxication. These findings differ from previous observations in tobacco smokers that puff volume increases when low-nicotine cigarettes are smoked.[25] Our results in marijuana smokers are consistent with data from other studies,[26,27] however, and suggest that the pattern of smoking marijuana is not immediately adjusted to alter the inhaled dose of Δ^9-THC but, instead, probably represents a learned technique based on previous experiences and interactions.

In conclusion, our findings demonstrate that smoking behavior differs markedly between marijuana and tobacco smoking and that these differences are associ-

ated with a respiratory burden of smoke particulates and absorption of carbon monoxide that are approximately four times greater in the case of marijuana smoking. These results may account for previous findings that smoking only a few marijuana cigarettes a day (without tobacco) has the same effect on the prevalence of acute and chronic respiratory symptoms[1] and the extent of tracheobronchial epithelial histopathology[2] as smoking more than 20 tobacco cigarettes a day (without marijuana). These observations justify concern about the potential long-term pulmonary consequences of the habitual smoking of only a few marijuana cigarettes a day.

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Now, striking evidence of short- and long-term consequences

How the lungs are affected by marijuana smoking

ABSTRACT: Short-term use of marijuana causes bronchodilation, an alteration in ventilatory control, and a substantial increase in end-expired carbon monoxide. Long-term use produces tachyphylaxis and airflow obstruction, and potentiates tobacco in causing airway hyperreactivity. Marijuana smoking appears to have its major impact on the large airways, in contrast to tobacco smoking, which primarily affects the peripheral airways and alveolated regions. Bronchoscopic studies of the mucosa of marijuana smokers have revealed abnormalities such as loss of cilia, basal cell and goblet cell hyperplasia, squamous metaplasia, and inflammation. (*J Respir Dis* 1987;8(11):87-107)

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Marijuana has been used for centuries for its mind-altering effects. Yet careful studies of the biologic properties of marijuana in humans and animals have been conducted only recently because Δ^9-tetrahydrocannabinol (THC)— the psychoactive component of marijuana—and related cannabinoid compounds were not identified and synthesized until the 1960s. Further, despite its ancient history in some cultures, marijuana acquired widespread popularity as a smoked substance in our society only within the last 25 years.

Smoking marijuana in the form of cigarettes ("joints") or in pipes (bongs or water pipes) increased dramatically during the 1970s and peaked in 1979. Since then, self-reported use has gradually declined. Nevertheless, according to the most recent nationwide survey, as many as 18.2 million Americans, mostly persons 25 years and younger, admit to smoking marijuana within the past month. Of these current users, about 6 million reportedly smoke marijuana one or more times daily.

In view of the widespread, habitual use of marijuana, there is concern about the risk of long-term pulmonary consequences, based on the well-known effects of regular tobacco smoking on the lung. However, because of the relative recency of the marijuana "epidemic" in countries where health is carefully monitored, the extent of lung damage due to heavy, habitual marijuana use may not yet be clinically evident.

In this article, we briefly review

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Marijuana smoking

Now, striking evidence of short- and long-term consequences

the results of studies evaluating the effects of marijuana smoke on the lungs of animals. We then discuss human studies dealing with the possible short- and long-term respiratory effects of marijuana smoke, and compare these effects with those of tobacco smoke.

ANIMAL STUDIES

Research with animals has revealed that both histologic and functional pulmonary abnormalities develop after exposure to marijuana smoke.

Histologic changes

Chronic marijuana inhalation in controlled animal studies results in histologic abnormalities in both the airways and lung parenchyma. During a 365-day exposure to marijuana smoke, rats demonstrated a dose-related spectrum of histopathologic lesions in the alveoli and the interstitium—including granulomatous inflammation; accumulations of alveolar macrophages, neutrophils, and mononuclear inflammatory cells; and focal pneumonitis. These abnormalities did not reverse following a 30-day recovery period.

Tracheotomized dogs exposed to the smoke from four standardized marijuana cigarettes daily for 30 months had a significantly higher incidence of bronchiolitis and squamous metaplasia in the trachea than unexposed control animals. Detailed morphometric analysis of the tracheal epithelium in rats exposed to marijuana smoke for only 31 consecutive days showed a 30% decrease (relative to control animals) in secretory cell density but significant increases in the number of secretory cells and glycoprotein volume per cell staining positive with Alcian Blue and with periodic acid-Schiff stains. Further, the epithelial thickness was increased in these animals.

These histopathologic changes are similar to those noted following experimental exposures to tobacco smoke and other inhaled irritants. However, the effects of chronic marijuana smoke inhalation on respiratory epithelial function, such as mucociliary transport, are as yet unknown.

Functional effects

Marijuana smoke has deleterious effects on the cellular defense functions of the lung. Alveolar macrophages obtained from normal rats by bronchoalveolar lavage exhibited dose-dependent depression of bactericidal activity against *Staphylococcus albus* when incubated with different amounts of marijuana smoke. This in vitro finding was confirmed by in vivo evidence from a study in which rats were first exposed to marijuana smoke and then submitted to an aerosolized challenge with *Staphylococcus aureus*. The impairment of macrophage antibacterial defense mechanisms may be related to a water-soluble, gas-phase cytotoxin in marijuana smoke.

Studies of mouse, hamster, and human lung explants exposed to marijuana smoke have shown abnormalities in mitosis, deoxyribonucleic acid content, and number of chromosomes. These abnormalities were more marked than those noted in cultured lung cells exposed to tobacco smoke. Tobacco or marijuana smoke alone caused irregular growth and accelerated malignant cell transformation of cultured hamster lung cells within three to six months of exposure. These findings underscore the carcinogenic potential of habitual marijuana smoking.

HUMAN STUDIES

The pulmonary physiologic, clinical, and histopathologic findings in persons who smoke marijuana are summarized in Tables 1, 2, and 3.

Short-term effects

Initial studies addressed the short-term effects of marijuana smoking on lung function.

Table 1—Pulmonary physiologic effects of smoked marijuana

Short-term

- Bronchodilation (pharmacologic effect of Δ^9-tetrahydrocannabinol (THC) dose-dependent mechanism undefined)
- Decreased maximal oxygen consumption during exercise (possibly due to cardioaccelerator effect of THC with premature achievement of maximal heart rate)
- Increased resting oxygen consumption
- Increased or decreased central ventilatory drive (conflicting experimental data)
- Marked boost in end-expired carbon monoxide and carboxyhemoglobin following a single "joint" (more than three times greater than the increase noted after a single tobacco cigarette)

Long-term (in frequent, habitual smokers)

- Tachyphylaxis to acute bronchodilator effect of THC
- Airflow obstruction (mainly affecting large airways, probably due to chronic irritation leading to structural changes)
- Nonspecific airway hyperreactivity (noted in smokers of both marijuana and tobacco; suggestive evidence of interaction between effects of both substances)

• *Bronchodilation:* Marijuana smoke caused moderate but statistically significant bronchodilation both in healthy volunteers and subjects with mild asthma and even reversed artificially induced bronchospasm in persons with asthma. These results were in marked contrast to the mild transient bronchoconstrictor effect of tobacco smoke.

Marijuana-induced bronchodilation was noted immediately after smoking and lasted for at least two hours; it was not observed after smoking marijuana from which the cannabinoids had been extracted with methanol. That marijuana-related bronchodilation is a pharmacologic response specific to THC was confirmed by experiments demonstrating that synthetic oral THC produced dose-dependent bronchodilation.

Efforts to explore the therapeutic potential of the bronchodilator properties of THC have not succeeded for several reasons: Only slight bronchodilation was achieved with oral THC, and unacceptable side effects resulted when THC was given systemically. When THC was administered as an aerosol, it had an irritating effect on the tracheobronchial tree, and it provoked bronchospasm in some patients with asthma. Further, synthetic analogues of this substance appear to have only negligible bronchodilator properties.

Although bronchodilation is an immediate response to THC, administration of this compound by smoking marijuana is not an appropriate therapeutic strategy for bronchospastic disease because of the many irritating gases and particulates in the smoke that are likely to have an adverse long-term impact on the airways. In addition, tachyphylaxis to the acute bronchodilator effect of THC has been demonstrated after long-term regular use.

Table 2—Clinical findings in marijuana smokers

Increased prevalence of chronic cough, sputum, and wheezing; increased frequency of acute bronchitic episodes in heavy, habitual smokers
Pneumothorax and/or pneumomediastinum (isolated reports)
Cough and hemoptysis temporally related to smoking paraquat-contaminated marijuana
Bronchopulmonary allergic aspergillosis (case report)
Aspergillus pneumonitis in immunocompromised smoker (case report)

The mechanism of THC-induced bronchodilation remains unclear. The bronchodilator effect is not caused by stimulation of β-adrenergic receptors or blockade of muscarinic receptors because it is not inhibited by β-adrenergic blockade and THC does not prevent bronchospasm provoked by a cholinergic agonist. Attempts to elucidate the mechanism of bronchodilation produced by THC have been hampered by failure to elicit a bronchodilator response in experimental animals. Although it has been suggested that marijuana-induced relaxation of airway smooth muscle could be mediated by the effects of THC on the central nervous system (CNS), the observation that aerosolized THC causes bronchodilation without any significant CNS intoxication casts doubt on this possibility.

Table 3—Bronchoscopic findings in heavy, habitual marijuana smokers*

Endoscopic visualization
Acute tracheobronchitis indicated by hyperemia or erythema
Increased secretions
Vocal cord inflammation
Tracheobronchial histopathology
Squamous metaplasia
Hyperplasia of basal and goblet cells
Cellular disorganization of epithelium
Cellular atypia with hyperchromatic nuclei and increased frequency of mitosis
Basement membrane thickening
Chronic cellular inflammation
Bronchoalveolar lavage cells
Increased numbers of alveolar macrophages and polymorphonuclear neutrophils
Impaired killing of *Candida* by alveolar macrophages
Numerous, large complex cytoplasmic inclusions in alveolar macrophages

*With or without concomitant tobacco smoking

• *Maximal oxygen consumption during exercise:* After smoking a single marijuana cigarette containing 10 mg of THC, maximal oxygen consumption was measured during an exercise protocol that employed a multistage, rapidly incremented workload. When this marijuana cigarette was smoked, oxygen consumption was slightly but significantly less than when placebo marijuana (containing a negligible amount of THC) was smoked. Maximum heart rate was similar. The mechanism of this impairment in maximal exercise performance may be secondary to premature achievement of maximal heart rate caused by the cardioaccelerator effect of THC.

• *Ventilatory drive and resting oxygen consumption:* Results of studies of the effects of smoked marijuana on respiratory control in small numbers of experienced users have yielded conflicting results. One group of researchers noted an

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Bronchodilator

Tablets 10 and 20 mg	Metered Dose Inhaler 15 ml*	Syrup 10 mg/5 ml	Inhalant Solution 5% 10 ml, 30 ml	Inhalant Solution Unit Dose Vials 0.4% and 0.6%

*15 mg/ml (approx. 0.65 mg delivered with each metered dose)

Brief Summary of Prescribing Information

CONTRAINDICATIONS Use in patients with cardiac arrhythmias associated with tachycardia is contraindicated

Although rare, immediate hypersensitivity reactions can occur. Therefore Alupent® (metaproterenol sulfate USP) is contraindicated in patients with a history of hypersensitivity to any of its components

WARNINGS Excessive use of adrenergic aerosols is potentially dangerous. Fatalities have been reported following excessive use of Alupent® (metaproterenol sulfate USP) as with other sympathomimetic inhalation preparations, and the exact cause is unknown. Cardiac arrest was noted in several cases. Paradoxical bronchoconstriction with repeated excessive administration has been reported with sympathomimetic agents. Therefore, it is possible that this phenomenon could occur with Alupent.

Patients should be advised to contact their physician in the event that they do not respond to their usual dose of a sympathomimetic amine aerosol.

PRECAUTIONS Because Alupent® (metaproterenol sulfate USP) is a sympathomimetic drug, it should be used with great caution in patients with hypertension, coronary artery disease, congestive heart failure, hyperthyroidism or diabetes, or when there is sensitivity to sympathomimetic amines.

Information for Patients Extreme care must be exercised with respect to the administration of additional sympathomimetic agents. A sufficient interval of time should elapse prior to administration of another sympathomimetic agent.

Carcinogenesis Long-term studies in mice and rats to evaluate the oral carcinogenic potential of metaproterenol sulfate have not been completed. Studies of metaproterenol sulfate have not been conducted to determine mutagenic potential or effect on fertility.

Pregnancy *Teratogenic Effects. Pregnancy Category C.* Alupent has been shown to be teratogenic and embryocidal in rabbits when given orally in doses 620 times the human inhalation dose and 62 times the human oral dose. There are no adequate and well-controlled studies in pregnant women. Alupent should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Oral reproduction studies in mice, rats and rabbits showed no teratogenic or embryocidal effects at 50 mg/kg, corresponding to 310 times the human inhalation dose and 31 times the human oral dose. Teratogenic effects in the rabbit (malformations, skeletal abnormalities, and fetal resorptions) were seen at [illegible]

Nursing Mothers It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Alupent is administered to a nursing woman.

Pediatric Use Consult package insert for age limit.

ADVERSE REACTIONS Adverse reactions are similar to those noted with other sympathomimetic agents. Adverse reactions such as tachycardia, hypertension, palpitations, nervousness, tremor, nausea and vomiting have been reported.

The most frequent adverse reactions to Alupent Inhalant Solution (metaproterenol sulfate USP) are nervousness and tachycardia which occur in about 1 in 7 patients, tremor which occurs in about 1 in 20 patients and nausea which occurs in about 1 in 50 patients. Less frequent adverse reactions are hypertension, palpitations, vomiting and bad taste which occur in approximately 1 in 100 patients.

HOW SUPPLIED ***Metered Dose Inhaler:*** Each Alupent® Metered Dose Inhaler contains 225 mg of metaproterenol sulfate as a micronized powder in inert propellants. Alupent Metered Dose Inhaler with mouthpiece (15 ml). Alupent Metered Dose Inhaler refill (15 ml).

Store below 77°F (25°C). Avoid excessive humidity.

Inhalant Solution: Alupent Inhalant Solution is supplied as a 5% solution in bottles of 10 ml or 30 ml with accompanying calibrated dropper.

Store below 77°F (25°C). Protect from light. Do not use the solution if it is brown or has a precipitate.

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Tablets: Alupent is supplied in two dosage strengths as scored, round white tablets in bottles of 100 tablets of 10 mg coded BI/74, tablets of 20 mg coded BI/72.

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Storage for blister samples: Store below 77°F (25°C). Protect from light.

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AL-3806

acute depressant effect on ventilation from smoking marijuana containing 19.8 mg of THC. Other investigators observed significant ventilatory stimulation and an increase in resting oxygen consumption during the hour after a marijuana cigarette containing 11 mg of THC was smoked.

It is unclear whether this discrepancy resulted from differences in the methodology used by these two groups of investigators when measuring ventilatory responses, individual variations in ventilatory response to marijuana, or a dose-dependent bimodal effect of marijuana on ventilatory control.

Long-term effects

In India and Jamaica, the prevalence of chronic bronchitis has been noted to be greater among habitual marijuana smokers than among nonsmokers, but these conclusions were based largely on uncontrolled observations. In contrast, a few small-scale studies in Costa Rica, Jamaica, and Greece failed to find evidence of a higher frequency of pulmonary disease or clinically significant physiologic abnormalities in habitual smokers of marijuana compared with control tobacco smokers.

These studies, however, were flawed by the small size and nonrepresentative nature of the samples of subjects examined, and were insufficiently controlled with regard to tobacco smoking. In addition, the cross-sectional design of these studies may not have been sensitive to the detection of long-term consequences of habitual marijuana smoking within individual subjects.

Tennant reported a high prevalence of respiratory symptoms and tracheal histopathologic findings in young, heavy smokers of hashish. (Hashish, which is derived

Deconamine® SR
capsules SUSTAINED-RELEASE

Before prescribing, please see full prescribing information. A brief summary follows.

Description: Each sustained-release blue and yellow capsule contains:

chlorpheniramine maleate	8 mg
d-pseudoephedrine hydrochloride	120 mg

Each DECONAMINE® SR Capsule also contains the following inactive ingredients: coloring agents, gelatin, starch, and sucrose.

Each DECONAMINE® SR Capsule may also contain one or more of the following inactive ingredients: butyl paraben, methyl paraben, propyl paraben, titanium dioxide and other ingredient(s).

The capsules are designed to provide prolonged release of medication.

Clinical Pharmacology: Chlorpheniramine maleate antagonizes the physiological action of histamine by acting as an H_1 receptor blocking agent.

Pseudoephedrine is an orally active sympathomimetic amine and exerts a decongestant action on the nasal mucosa. It does this by vasoconstriction which results in reduction of tissue hyperemia, edema, nasal congestion and an increase in nasal airway patency. The vasoconstriction action of pseudoephedrine is similar to that of ephedrine. In the usual dose it has minimal vasopressor effects.

Indications: For relief of nasal congestion associated with the common cold, hay fever and other allergies, sinusitis, eustachian tube blockage, and vasomotor and allergic rhinitis.

Contraindications: Patients with severe hypertension, severe coronary artery disease and patients on MAO inhibitor therapy. DECONAMINE® medications are also contraindicated in patients sensitive to antihistamines or sympathomimetic agents.

Warnings: Chlorpheniramine maleate should be used with extreme caution in patients with narrow angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction, symptomatic prostatic hypertrophy, or bladder neck obstruction. Due to its mild atropine-like action, chlorpheniramine maleate should be used cautiously in patients with bronchial asthma.

Sympathomimetic amines should be used with caution in patients with hypertension, ischemic heart disease, diabetes mellitus, increased intraocular pressure, hyperthyroidism and prostatic hypertrophy. Sympathomimetics may produce central nervous system stimulation with convulsions or cardiovascular collapse with accompanying hypotension.

Precautions: *Information for patients.* Antihistamines may impair mental and physical abilities required for the performance of potentially hazardous tasks, such as driving a vehicle or operating machinery. Patients should also be warned about possible additive effects with alcohol and other central nervous system depressants (hypnotics, sedatives, tranquilizers). *Drug interactions.* Pseudoephedrine containing drugs should not be given to patients treated with monoamine oxidase (MAO) inhibitors because of the possibility of precipitating a hypertensive crisis. MAO inhibitors also prolong and intensify the anticholinergic effects of antihistamines. Sympathomimetics may reduce the antihypertensive effect of methyldopa, reserpine, veratrum alkaloids and mecamylamine.

Alcohol and other sedative drugs will potentiate the sedative effects of chlorpheniramine.

Care should be taken in administering DECONAMINE® medications concomitantly with other sympathomimetic amines, since their combined effects on the cardiovascular system may be harmful to the patient.

Pregnancy. Pregnancy Category C. Animal reproduction studies have not been conducted with DECONAMINE® medications. It is also not known whether DECONAMINE® medications can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. DECONAMINE® medications should be given to a pregnant woman only if clearly needed.

Nursing Mothers. Due to the possible passage of pseudoephedrine and chlorpheniramine into breast milk, and because of the higher than usual risk for infants from sympathomimetic amines and antihistamines, the benefit to the mother vs. the potential risk should be considered and a decision should be made whether to discontinue nursing or to discontinue the drug. *Pediatric Use.* DECONAMINE® Capsules or Tablets should not be given to children under 12 years of age.

Adverse Reactions: Chlorpheniramine maleate. Slight to moderate drowsiness may occur and is the most frequent side effect.

Other possible side effects of antihistamines in general include: *General:* urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills, dryness of mouth, nose and throat. *Cardiovascular:* hypotension, headache, palpitation, tachycardia, extrasystoles. *Hematological:* hemolytic anemia, thrombocytopenia, agranulocytosis. *CNS:* sedation, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesia, blurred vision, diplopia, vertigo, tinnitus, hysteria, neuritis, convulsion. *Gastrointestinal:* epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation. *Genitourinary:* urinary frequency, difficult urination, urinary retention, early menses. *Respiratory:* thickening of bronchial secretions, tightness of chest, wheezing and nasal stuffiness.

Pseudoephedrine hydrochloride. Pseudoephedrine may cause mild central nervous system stimulation, especially in those patients who are hypersensitive to sympathomimetic drugs. Nervousness, excitability, restlessness, dizziness, weakness and insomnia may also occur. Headache and drowsiness have also been reported. Large doses may cause lightheadedness, nausea and/or vomiting. Sympathomimetic drugs have also been associated with certain untoward reactions including fear, anxiety, tenseness, restlessness, tremor, weakness, pallor, respiratory difficulty, dysuria, insomnia, hallucination, convulsion, CNS depression, arrhythmias and cardiovascular collapse with hypotension.

Overdosage: Acute overdosage may produce clinical signs of CNS stimulation and variable cardiovascular effects. Pressor amines should be used with great caution in the presence of pseudoephedrine. Patients with signs of stimulation should be treated conservatively.

Dosage and Administration: Adults and children over 12 years, 1 capsule every 12 hours. Children under 12 years, DECONAMINE® Syrup is recommended.

DECONAMINE® SR Capsules are manufactured for
BERLEX Laboratories, Inc., Wayne, New Jersey 07470

References: 1. von Maur K: *Ann Allergy* 1985;55:458-462. 2. Crutcher JE, Kaniner TR: *J Clin Pharmacol* 1981;21:9-15. 3. Hamilton LH, Chobanian SL, Cato A, et al: *Ann Allergy* 1982; 48:87-92. 4. Empey DW, Medder KT: *Drugs* 1981;21:438-443.

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181-74 September 1987

Marijuana smoking

Now, striking evidence of short- and long-term consequences

from the resin scraped off the top leaves of the cannabis plant, has a much higher THC content than marijuana, which is usually prepared from the whole leaf.) Tennant studied 200 patients who reported to a military medical facility in West Germany with complaints of pharyngitis (75%), rhinitis (13%), bronchitis (10%), and/or asthma (2%), which were temporally related to hashish smoking.

Of this group, six patients with bronchitis who smoked 50 g or more of hashish a month (as well as one pack of tobacco cigarettes a day) underwent bronchoscopy and tracheal biopsies. The mucosa appeared congested in all six, and random biopsy specimens of tracheal epithelium showed multiple abnormalities, including loss of cilia, epithelial cell hyperplasia, and atypical cells with hyperchromatic nuclei. Squamous metaplasia was present in one patient, while basement membrane thickening and chronic inflammatory cells were noted in all six patients. The fact that over 90% of the 200 hashish smokers also smoked tobacco may have biased these results.

A subsequent three- to 24-month study found that respiratory symptoms were less frequent in seven smokers of only hashish than in 23 smokers of both hashish and tobacco, although both groups had a similar prevalence (greater than 70%) of rhonchi, rales, or wheezes. Bronchoscopic results revealed that the smokers of hashish alone did not have erythema or congestion, which were present in smokers of both hashish and tobacco. Histopathologic lesions were also fewer in the hashish smokers (two of seven subjects) than in the smokers of both hashish and tobacco (23 of 23 subjects). However, the symptomatic nature of the patients, the method of recruitment, and the small numbers of patients examined may have skewed the results of the study.

An intermediate-term prospective study of 29 regular smokers of marijuana who markedly increased their consumption of marijuana from about one joint a day to an average of five joints a day for six to eight weeks showed a modest but significant worsening of several indices of airway function during the period of increased marijuana use. These changes reverted to baseline within 14 weeks of cessation of the increased use.

Extrapolation of the marijuana-related decreases in lung function in these subjects results in a yearly decline in forced expiratory volume in one second about 20 times greater than the expected rate in nonsmokers (about 30 mL/yr). This markedly accelerated decline in pulmonary function predicts the development of respiratory disability within a few short years. Since such an outcome should be obvious clinically, it is likely that these observations represent an initial steep decline in pulmonary function that would not have progressed at the same accelerated rate even if the subjects had continued to smoke marijuana more heavily than usual. Prospective studies are needed to ascertain the real rate of decline of lung function in smokers of marijuana compared with that of nonsmokers, while considering the effect of concomitant tobacco smoking.

A prospective, longitudinal study of heavy, habitual smokers of marijuana (more than two joints a day for more than five years), either alone or with tobacco, smokers of tobacco alone, and nonsmokers is currently under way at the University of California, Los Angeles. A cross-sectional comparison of 144 smokers of marijua-

na alone, 135 smokers of marijuana plus tobacco, 70 smokers of tobacco only, and 97 nonsmokers conducted from 1982 to 1985 yielded the following results:

- Smokers of marijuana alone, tobacco alone, and marijuana plus tobacco had similar incidences of acute and chronic bronchitis, which were significantly higher than those of nonsmokers.
- Habitual smokers of marijuana, either alone or with tobacco, had a significantly higher frequency of abnormalities in tests of large-airway function (airway resistance, specific airway conductance) than nonsmokers.
- Regular smokers of tobacco, irrespective of concomitant marijuana use, had a significantly higher frequency of abnormalities in tests of small-airway function and diffusing capacity than nonsmokers.
- Habitual smokers of both marijuana and tobacco, but not smokers of either substance alone, had a significantly higher frequency of nonspecific airway hyperreactivity than nonsmokers.

From a functional standpoint, therefore, habitual marijuana smoking appears to have its major impact on the large airways, while tobacco primarily affects the peripheral airways and alveolated regions of the lungs.

Why might marijuana be more harmful than tobacco?

Daily smoking of only a few marijuana joints appears to be comparable with smoking over 20 tobacco cigarettes a day in its effects on the prevalence of acute and chronic respiratory symptoms, tracheobronchial histopathologic findings, and the number of alveolar macrophages recovered in bronchoalveolar lavage fluid.

One explanation may be that the components of marijuana smoke are more irritating to the lungs than those of tobacco smoke. Comparison of the smoke contents of one joint of marijuana with those of one unfiltered tobacco cigarette of the same weight reveals many similarities, both qualitative and quantitative, as well as a number of differences. While nicotine is present in tobacco but not in marijuana, Δ^9-tetrahydrocannabinol (THC)—itself a respiratory irritant—and more than 60 additional cannabinoid compounds are present in marijuana but not in tobacco. In addition, marijuana smoke contains greater than 50% more of the carcinogenic polynuclear aromatic hydrocarbons benzanthracene and benzpyrene than is found in tobacco smoke, indicating the potential for malignant changes in the airways of frequent users.

Another possibility is that more particulates and irritating gases per cigarette are deposited and retained in the lungs of marijuana smokers than in the lungs of tobacco smokers, possibly because of the manner in which each type of cigarette is smoked. To investigate the latter possibility, we assessed smoking dynamics, the amount of smoke particulates delivered to the respiratory tract, and the change in the amount of end-expired carbon monoxide while a single marijuana or tobacco cigarette was smoked.

The results indicate that marijuana smokers took nearly twofold larger puffs, inhaled the smoke into their lungs 40% to 50% more deeply, and retained the smoke in their lungs three to five times longer than did tobacco smokers. Moreover, these differences were associated with a more than three times greater increase in end-expired carbon monoxide and a three to four times greater delivery and respiratory deposition of smoke particulates from a single cigarette of marijuana compared with that of tobacco.

Bronchoscopic findings

The previously mentioned findings of chronic respiratory symptoms and functional abnormalities in a relatively high proportion of habitual, heavy marijuana smokers were complemented by bronchoscopic biopsy results in a subset of subjects from the same cross-sectional study.

We found airway hyperemia in 88% of 16 smokers of only marijuana, 92% of 13 smokers of both marijuana and tobacco, 100% of six smokers of only tobacco, and 25% of four nonsmokers (Figure 1). Light and scanning electron microscopic evaluation of proximal airway biopsy specimens showed two or more histopathologic abnormalities in all smokers (Figures 2 and 3). Squamous metaplasia was observed in all smokers of both marijuana and tobacco and in approximately 50% of the smokers of marijuana or tobacco alone.

Hyperplasia of basal and goblet cells was more prevalent in the marijuana smokers (80%) than in the combined smokers (50% to 67%) or the nonsmokers (0%). Further, cellular disorganization was more prevalent in the marijuana smokers (53%) than in the other groups.

These results indicate that relatively young, habitual, heavy marijuana smokers have a high inci-

Analysis of the mainstream smoke of a single marijuana cigarette and a single tobacco cigarette*

	Marijuana	Tobacco
Gas phase		
Carbon monoxide		
Volume %	3.99	4.58
mg	17.6	20.2
Carbon dioxide		
Volume %	8.27	9.38
mg	57.3	65
Ammonia (μg)	228	198
Hydrocyanic acid (μg)	532	498
Isoprene (μg)	83	310
Acetaldehyde (μg)	1,200	980
Acetone	443	578
Acrolein (μg)	92	85
Acetonitrile (μg)	132	123
Benzene (μg)	76	67
Toluene (μg)	112	108
Dimethylnitrosamine (ng)	75	84
Methylethylnitrosamine (ng)	27	30

	Marijuana	Tobacco
Particulate phase		
Total particulate matter, dry (mg)**	22.7	39.0
Phenol (μg)	76.8	138.5
o-Cresol (μg)	17.9	24
m- and *p*-Cresol (μg)	54.4	65
2,4- and 2,5-Dimethylphenol (μg)	6.8	14.4
Cannabidiol (μg)	190	—
Δ^9-Tetrahydrocannabinol (μg)	820	—
Cannabinol (μg)	400	—
Nicotine (μg)	—	2,850
Naphthalene (ng)	3,000	1,200
1-Methylnaphthalene (ng)	6,100	3,650
2-Methylnaphthalene (ng)	3,600	1,400
Benz[a]anthracene (ng)	75	43
Benzo[a]pyrene (ng)	31	22.1

*The reference marijuana cigarette is 85 mm and 1.115 mg; the reference tobacco cigarette is 85 mm and 1,100 mg.

**There is 40.7 mg of dry particulate matter in sidestream marijuana smoke and 57.3 mg in sidestream tobacco smoke.

Reproduced from Cohen S, Tashkin DP (eds): *Marijuana Smoking and Its Effects on the Lung*. New York, The American Council on Marijuana and Other Psychoactive Drugs, Inc, 1981.

dence of abnormal airway appearance and tracheobronchial histopathologic findings, irrespective of concomitant tobacco smoking, justifying the concern about potential long-term clinical sequelae, such as the development of chronic airway disease and lung cancer. Moreover, the combined habit of marijuana and tobacco smoking could have additive or possibly synergistic effects on the airways.

Additional studies using bronchoscopy have also provided important information about the effects of habitual marijuana smoking on bronchoalveolar cell populations: The total number of cells and the number of alveolar macrophages recovered in bronchoalveolar lavage (BAL) fluid are significantly increased in smokers of marijuana and/or tobacco. The number of neutrophils from BAL fluid is significantly higher in smokers of both marijuana and tobacco and smokers of tobacco only than in nonsmokers. Preliminary ultrastructural evaluation of alveolar macrophages from marijuana smokers indicates a greater variety of large, complex, frequently multilayered cytoplasmic inclusions than is seen in macrophages of nonsmokers or tobacco smokers. With respect to function, the mac-

Figure 1 – *Increased hyperemia of the tracheobronchial wall is a common bronchoscopic finding in heavy, habitual marijuana smokers.*

rophages from marijuana or tobacco smokers exhibit decreased killing of *Candida albicans;* the clinical significance of this microbicidal defect is as yet unknown.

Other potential complications

• *Barotrauma:* Isolated occurrences of pneumothorax and/or pneumomediastinum have been reported in association with marijuana smoking. In these instances, the barotrauma was believed to be caused by an increase in intrathoracic pressure from Valsalva's maneuver during breath-holding after deep inhalation of the smoke.

• *Effects on plasma theophylline clearance:* Hydrocarbon components of marijuana (and tobacco) smoke can induce hepatic microsomal enzymes to speed up the metabolic breakdown of theophylline. As a result, plasma theophylline clearance is increased and serum theophylline half-life is shortened in habitual marijuana (and tobacco) smokers who are taking theophylline. In patients treated with theophylline, therefore, it is important to inquire about a history of regular marijuana smoking, as well as tobacco smoking, because such practices can influence dosing requirements.

• *Pulmonary effects of marijuana contaminants:* Government efforts to control marijuana use have included spraying of marijuana fields with paraquat, a herbicide that can cause severe oxidative lung injury if swallowed in a concentrated solution. When instilled into the lungs of experimental animals paraquat causes pulmonary edema, eventually leading to lung fibrosis. However, since paraquat is largely destroyed by the heat of combustion, only a minute fraction of this compound is released in the smoke of paraquat-contaminated marijuana. Moreover, since paraquat is highly water-soluble, the small fraction that does survive pyrolysis is likely to be largely removed by absorption in the moisture of the upper airways.

Paraquat, when pyrolyzed, is degraded to a bipyridine, a respiratory irritant. Therefore, the cough and hemoptysis that have been reported after paraquat-contaminated marijuana was smoked are most likely caused by respiratory tract irritation from bipyridine or other combustion products in marijuana smoke, rather than from paraquat itself. However, the possibility of chronic pulmonary fibrosis developing after repeated exposure to even minute quantities of paraquat by heavy, habitual users of contaminated marijuana cannot be completely discounted.

Contamination of marijuana with *Aspergillus fumigatus* can cause lung disease in humans, as illustrated by two case reports—one of a patient with allergic bronchopulmonary aspergillosis and another of *Aspergillus* pneumonitis in a young patient with impaired immunity that developed after smoking several pipesful of marijuana contaminated with the fungus. In addition to fungal contaminants, potentially pathogenic gram-negative bacteria have also been found frequently as contaminants of marijuana.

Marijuana is sometimes smoked by cancer patients to prevent chemotherapy-induced nausea. However, unless the marijuana cigarettes are sterilized before use to eliminate potential pathogens, serious pulmonary infection could ensue because these patients already have impaired lung antimicrobial defenses due to malignancy and immunosuppressive drug therapy. Marijuana smoke may also have a direct effect on the ability of alveolar macrophages to phagocytize and kill potential pathogens which could further predispose patients receiving chemotherapy to lung infections.

FUTURE STUDIES

The nature, extent, and clinical significance of the pulmonary conse-

quences of habitual marijuana smoking have not yet been adequately defined. Further studies are needed to assess the long-range impact of habitual marijuana smoking on respiratory symptoms, lung dysfunction, tracheobronchial histopathologic findings, and alveolar macrophage structure and function. The long-term effects of marijuana smoking on immunologic and nonimmunologic defenses against lung injury also need further evaluation.

Additional research is needed to evaluate the interactive effects of tobacco and marijuana on the lungs and to determine the extent to which marijuana-related abnormalities in lung structure and function can be reversed with cessation of smoking.

In recent years, smoking of cocaine "freebase," including dealer-

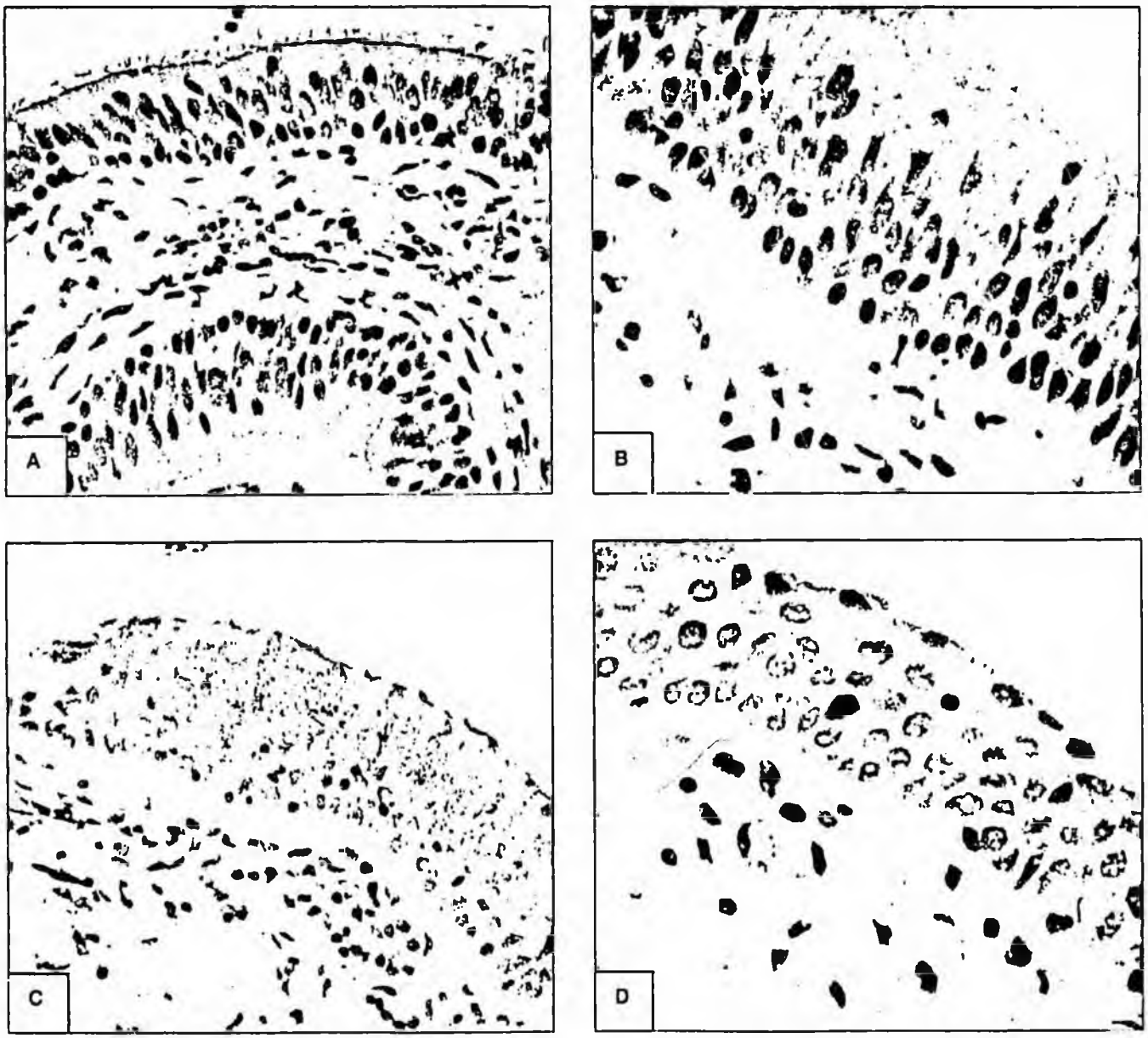

Figure 2 – *Occasional goblet cells and numerous ciliated epithelial cells are the normal findings of light microscopic evaluation of a bronchial biopsy specimen from a healthy nonsmoker (A) (× 130). In contrast, basal and goblet cell hyperplasia, intraepithelial inflammation, and numerous mucus-filled goblet cells are evident in the bronchial biopsy specimen from a marijuana smoker (B and C) (× 250).*

The bronchial mucosa specimen from a marijuana plus tobacco smoker reveals loss of normal ciliated epithelial covering and replacement by squamous epithelium, indicating squamous metaplasia. Note the mitotic figure present in the center of the mucosa (D) (× 250).

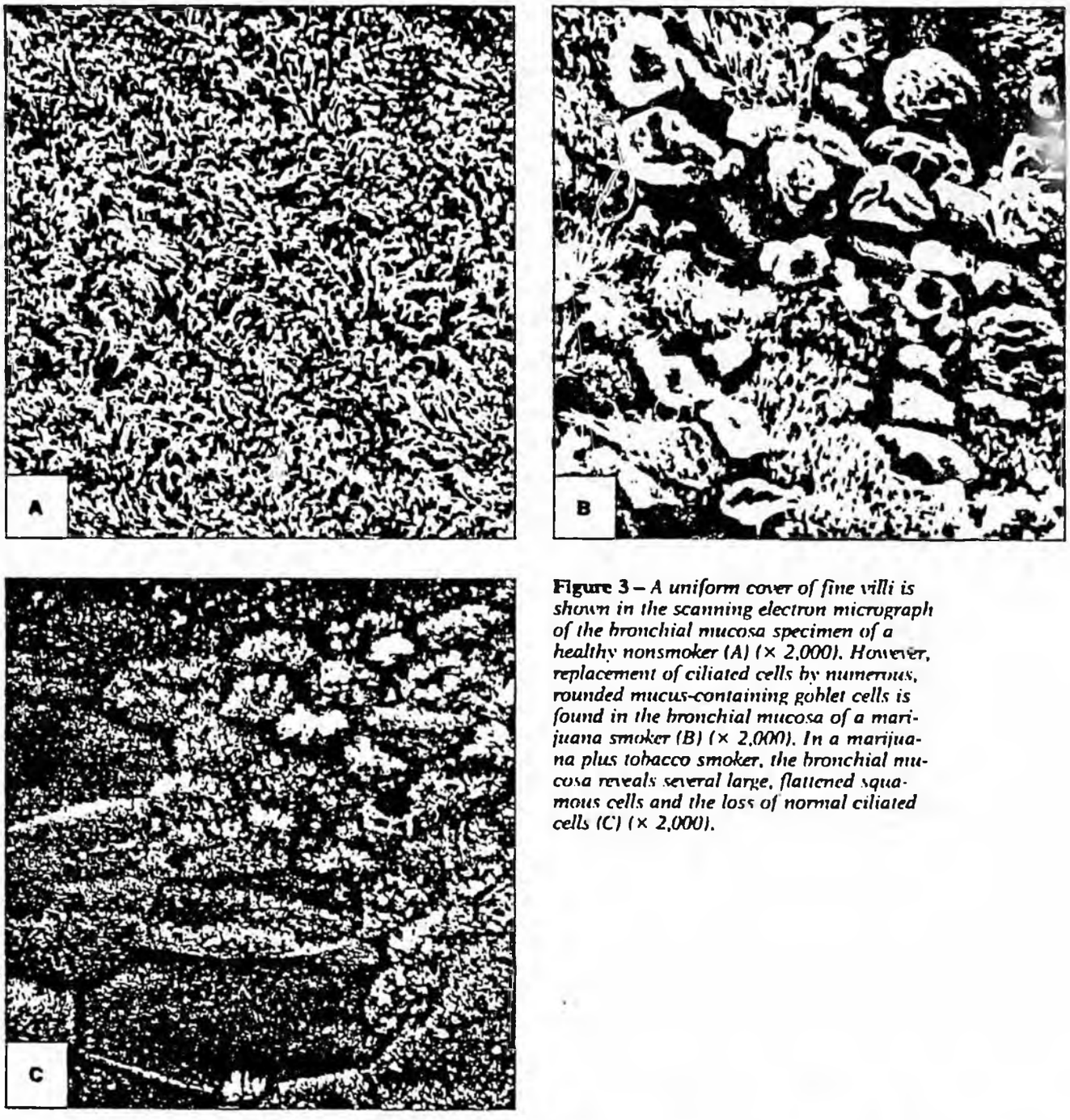

Figure 3 – *A uniform cover of fine villi is shown in the scanning electron micrograph of the bronchial mucosa specimen of a healthy nonsmoker (A) (× 2,000). However, replacement of ciliated cells by numerous, rounded mucus-containing goblet cells is found in the bronchial mucosa of a marijuana smoker (B) (× 2,000). In a marijuana plus tobacco smoker, the bronchial mucosa reveals several large, flattened squamous cells and the loss of normal ciliated cells (C) (× 2,000).*

prepared alkaloidal cocaine ("crack"), has become increasingly prevalent in our society, especially among habitual smokers of marijuana. Therefore, future studies also need to address the independent and interactive effects of smoking cocaine and marijuana on various aspects of pulmonary structure and function.

WHAT YOU CAN DO

Since habitual marijuana smoking has significant effects on health, it is important for us to ascertain, through nonjudgmental history taking, whether and to what extent our patients smoke marijuana. This information can be clinically useful in several ways.

- Symptoms of bronchitis can be due to marijuana smoking and should resolve following cessation of marijuana use. ▶

ZANTAC® 150 Tablets **BRIEF SUMMARY**
(ranitidine hydrochloride)
ZANTAC® 300 Tablets
(ranitidine hydrochloride)

The following is a brief summary only. Before prescribing, see complete prescribing information in ZANTAC® product labeling.

INDICATIONS AND USAGE: ZANTAC® is indicated in:
1. Short-term treatment of **active duodenal ulcer**. Most patients heal within four weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (eg, Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer**. Most patients heal within six weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease** (GERD). Symptomatic relief commonly occurs within one or two weeks after starting therapy. Therapy for longer than six weeks has not been studied.

In active duodenal ulcer, active, benign gastric ulcer, hypersecretory states, and GERD, concomitant antacids should be given as needed for relief of pain.

CONTRAINDICATIONS: ZANTAC® is contraindicated for patients known to have hypersensitivity to the drug.

PRECAUTIONS: General: 1. Symptomatic response to ZANTAC® therapy does not preclude the presence of gastric malignancy.

2. Since ZANTAC is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see **DOSAGE AND ADMINISTRATION**). Caution should be observed in patients with hepatic dysfunction since ZANTAC is metabolized in the liver.

Laboratory Tests: False-positive tests for urine protein with Multistix® may occur during ZANTAC therapy and therefore testing with sulfosalicylic acid is recommended.

Drug Interactions: Although ZANTAC has been reported to bind weakly to cytochrome P-450 in vitro, recommended doses of the drug do not inhibit the action of the cytochrome P-450 linked oxygenase enzymes in the liver. However, there have been isolated reports of drug interactions which suggest that ZANTAC may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg, a pH-dependent effect on absorption or a change in volume of distribution).

Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no indication of tumorigenic or carcinogenic effects in lifespan studies in mice and rats at doses up to 2 000 mg/kg/day.

Ranitidine was not mutagenic in standard bacterial tests (*Salmonella / E. coli*) for mutagenicity at concentrations up to the maximum recommended for these assays.

In a dominant lethal assay, a single oral dose of 1,000 mg/kg/day to male rats was without effect on the outcome of two matings per week for the next nine weeks.

Pregnancy: Teratogenic Effects: Pregnancy Category B: Reproduction studies have been performed in rats and rabbits at doses up to 160 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to ZANTAC. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: ZANTAC is secreted in human milk. Caution should be exercised when ZANTAC is administered to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Use in Elderly Patients: Ulcer healing rates in elderly patients (65 to 87 years of age) were no different from those in younger age groups. The incidence rates for adverse events and laboratory abnormalities were also not different from those seen in other age groups.

ADVERSE REACTIONS: The following have been reported as events in clinical trials or in the routine management of patients treated with oral ZANTAC®. The relationship to ZANTAC therapy has been unclear in many cases. Headache, sometimes severe, seems to be related to ZANTAC administration.

Central Nervous System: Rarely, malaise, dizziness, somnolence, insomnia, and vertigo. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients. Rare cases of reversible blurred vision suggestive of a change in accommodation have been reported.

Cardiovascular: Rare reports of tachycardia, bradycardia, and premature ventricular beats.

Gastrointestinal: Constipation, diarrhea, nausea/vomiting, and abdominal discomfort/pain.

Hepatic: In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid IV for seven days, and in 4 of 24 subjects receiving 50 mg qid IV for five days. With oral administration there have been occasional reports of reversible hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice.

Musculoskeletal: Rare reports of arthralgias.

Hematologic: Reversible blood count changes (leukopenia, granulocytopenia, thrombocytopenia) have occurred in a few patients. Rare cases of agranulocytosis or of pancytopenia, sometimes with marrow hypoplasia, have been reported.

Endocrine: Controlled studies in animals and man have shown no stimulation of any pituitary hormone by ZANTAC (ranitidine hydrochloride) and no antiandrogenic activity, and cimetidine-induced gynecomastia and impotence in hypersecretory patients have resolved when ZANTAC has been substituted. However, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving ZANTAC, but the incidence did not differ from that in the general population.

Integumentary: Rash, including rare cases suggestive of mild erythema multiforme, and rarely alopecia.

Other: Rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia) and small increases in serum creatinine.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: Active Duodenal Ulcer: The current recommended adult oral dosage is 150 mg twice daily. An alternate dosage of 300 mg once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.

Maintenance Therapy: The current recommended adult oral dosage is 150 mg at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison syndrome): The current recommended adult oral dosage is 150 mg twice a day. In some patients it may be necessary to administer ZANTAC® 150-mg doses more frequently. Doses should be adjusted to individual patient needs, and should continue as long as clinically indicated. Doses up to 6 g/day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg twice a day.

GERD: The current recommended adult oral dosage is 150 mg twice a day.

Dosage Adjustment for Patients with Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with ZANTAC, the recommended dosage in patients with a creatinine clearance less than 50 ml/min is 150 mg every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosage schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

HOW SUPPLIED: ZANTAC® 300 Tablets (ranitidine hydrochloride equivalent to 300 mg of ranitidine) are yellow, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) and unit dose packs of 100 tablets (NDC 0173-0393-47).

ZANTAC® 150 Tablets (ranitidine hydrochloride equivalent to 150 mg of ranitidine) are white tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 tablets (NDC 0173-0344-42) and unit dose packs of 100 tablets (NDC 0173-0344-47).

Store between 15° and 30°C (59° and 86°F) in a dry place. Protect from light. Replace cap securely after each opening.

August 1987

Glaxo

Glaxo Inc
Research Triangle Park, NC 27709

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- A history of marijuana smoking is occasionally associated with otherwise unexplained hemoptysis or pneumothorax.
- Marijuana use could predispose to pulmonary infection, especially in patients with preexisting impairment in immunity.
- In patients receiving therapy with theophylline, inadequate serum levels could result from the enhancement of hepatic clearance of theophylline by components in marijuana smoke.
- Several lines of evidence strongly suggest that habitual marijuana smoking may be a causative factor in the development of bronchogenic carcinoma.

The latter possibility is further supported by the several-fold greater deposition in the lower respiratory tract of tar particulates from the smoke of one marijuana joint compared with that from one tobacco cigarette. However, there is a long lag period between initiation of daily exposure to tobacco tar and the development of frank neoplasia. Moreover, smoking-related pulmonary malignancy will develop in only a small, albeit significant, percentage of smokers.

For these reasons, it will be difficult to document empirically a link between heavy, habitual marijuana smoking and lung cancer. In the case of tobacco smoking, this link was established by autopsy and epidemiologic studies. To permit pathologists and epidemiologists to ascertain an analogous association for marijuana, we need to ask patients about their marijuana smoking habits and to include this information in the medical record.

A strong physician message to patients informing them of what we do know about the harmful effects of marijuana on the lung and other organs may persuade some of them, especially those with man-

juana-related symptoms, to quit smoking.

Patients and parents of children who smoke marijuana who want further advice and assistance can contact the following organizations: PRIDE (Parent Resource Institute for Drug Education), Atlanta; National Federation of Parents for Drug-Free Youth, Silver Springs, Maryland; The American Council for Drug Education, Rockville, Maryland; or their local chapter of the American Lung Association. □

SUGGESTED READINGS

The authors recommend these references for physicians seeking further information:

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REPORT OF THE COUNCIL ON SCIENTIFIC AFFAIRS

Proceedings American Medical Association
House of Delegates
December, 1980

Report: B
(I-60)

Subject: Marijuana in the '80s

Presented by: Rogers J. Smith, M. D., Chairman

Referred to: Reference Committee E
(Grant V. Rodkey, M.D., Chairman)

It is perhaps ironic that concomitant with emerging therapeutic possibilities for cannabis and its constituents, new evidence has appeared that marijuana is hazardous to health.

On the one hand, we are at the threshold of providing symptomatic relief to some patients who suffer extreme nausea from cancer chemotherapy and for whom existing anti-emetic agents are ineffective. On the other hand, we face the growing prospect of an appreciable number of marijuana users incurring physiological and psychological impairment.

Marijuana is the drug of the young. More than two-thirds of 18 to 25 year old persons in the United States have tried it on at least one occasion.(1) Some have been chronic users. For the children, adolescents and young adults who do smoke marijuana regularly there is considerable risk ahead. The risk for them, and for society, is of a nature and magnitude that belies the characterization of marijuana as a "soft drug." It can be hard on its user, and inflict a great deal of harm.

The Council on Scientific Affairs has on two previous occasions called attention to the health aspects of marijuana use. In a report adopted by the House of Delegates in December 1977 (Report D: I-77), the Council expressed concern over evidence of a range of adverse effects that had been appearing in the scientific literature.(2) Two years later, in December 1979 (Report I: I-79), the Council reaffirmed its concern to the House, and emphasized in particular the dangers of pulmonary involvement and possible carcinogenesis.(3) The Council also took cognizance of investigations into possible medical applications of marijuana, and urged that research be more rigorously designed and conducted in the future.

In adopting the second Council report, the House asked the Council to prepare a subsequent report on "(1) increased regular use of marijuana by youth, (2) the proliferation of the paraphernalia industry and so-called 'headshops,' and (3) the subverting of FDA laws and regulations by state laws that legalize marijuana use for medical purposes."

This report was developed for the Council on Scientific Affairs by a special panel on drug abuse consisting of Joseph H. Skom, M. D., Chicago, chairman; Henry Brill, M. D., Brentwood, Long Island; Sidney Cohen, M. D., Los Angeles; David E. Smith, M. D., San Francisco; and Jokichi Takamine, M. D., Los Angeles. Rogers J. Smith, M. D., Portland, Oregon, chairman of the Council, participated as an ex-officio member of the panel.

Past House Action: A-80:212; I-79:178-181; I-77:188-193

Then, in July 1980, the House referred to the Council Resolution 3, introduced by the Wisconsin delegation, proposing that, in view of growing evidence of health hazards, the AMA "officially declare marijuana to be a dangerous drug."

This report, which constitutes a response to these requests, comes in the wake of three documents released earlier this year by the National Institute on Drug Abuse (NIDA): Marijuana and Health: 1980,(4) HEW's eighth annual report to Congress; A Drug Retrospect: 1962 to 1980;(5) and The National Survey on Drug Abuse: 1979(1) Taken together, these publications paint a disquieting picture of a growing proportion of young people exposing themselves to dangers that no longer are in the area of tenuous speculation.

Use of Marijuana by Youth

NIDA's latest national survey reflected significant changes in marijuana usage from 1971 to 1979.(1)

In 1971, one of 10 adolescents aged 14 and 15 reported ever using the drug. By 1979, the rate for this age group had tripled, climbing to 32 per cent. In the same period life time prevalence for 16 and 17 year olds had risen from 27 per cent to 51 per cent.

Looking at the 12 to 17 year olds who said in 1979 that they smoked marijuana on a fairly regular basis, the survey showed that 8.4 per cent reported using the drug on five or more days during the previous month. Over 22 per cent of young adults (18 to 25 years old) reported this frequency of usage. These figures, based as they are on a survey of households, undoubtedly are conservative; it can be assumed that a sizable number of chronic users detach themselves from family settings, and that students living away from home -- who were not interviewed -- might include a proportionately larger number of regular users than the surveyed population.

Although the NIDA survey indicated that only 8 per cent of 12 and 13 year old children in 1979 had ever tried marijuana, this figure is a third larger than the percentage of children of that age in 1971 who said they had ever used it. Moreover, other surveys conducted in two states found a greater proportion of children than this who used marijuana. In 1978, one in five 8th graders questioned in Maryland said they were currently smoking marijuana, and one in 11 said they were doing so daily or several times a week.(6) In Maine the same year, 56 per cent of 13 to 15 year olds who were sampled said they had used the drug at least once, and 42 per cent reported being regular users.(7)

As pointed out in the two previous Council reports on marijuana, regular use can constitute a hazard for anyone; especially vulnerable, however, are children and adolescents, who are in crucial phases of psychological and physiological development. Additional findings of adverse effects of marijuana use in animals and humans, coupled with evidence of substantial regular use by young people, therefore have serious implications for the health of a new generation.

Some of the major recent findings as summarized in the 1980 Marijuana and Health report [4] that have particular relevance to youth can be grouped under the headings of brain function, psychomotor effects, reproductive function, pulmonary involvement, and psychopathology.

It should be emphasized that most deleterious effects are related to chronic or consistent, as opposed to episodic, use of marijuana. Metabolites of delta-9-tetrahydrocannabinol (THC) can be found in fatty tissue for up to eight days following intake, so that a cumulative build-up takes place with regular use. (THC is the most prominent psychoactive component of marijuana.) The quality of the marijuana is also significant; in this regard, it is noteworthy that cannabis preparations in use today are as much as five times as potent in THC content as those available five years ago.

Brain Function

Conclusive evidence of macroscopic brain damage is lacking. Microscopic cellular changes, however, have been found in brains of rhesus monkeys who received the equivalent of one marijuana cigarette daily for six months.[8] Similar measurements have not been made in humans.

Yet, the possibility that such changes, which may or may not be reversible, can take place in man as well as in another primate cannot be dismissed out of hand. Moreover, damage does not necessarily have to be visible to result in impaired mental functioning.

In that regard, there are abundant anecdotal reports, if not controlled studies, on the lack of academic drive on the part of students who regularly use high doses of marijuana. Long-term sedative and other effects from chronic intake may combine with acute intoxication effects to initiate or to reinforce inattention to schoolwork or the wish to drop out.

The NIDA report[4] alludes to "dozens of experimental studies" which consistently have shown adverse acute effects of marijuana use on cognition and immediate memory; so that for "substantial numbers of high school students (who) are using marijuana during the course of the school day...a detrimental effect on their classroom functioning and knowledge acquisition" is likely.

Psychomotor Effects

The Council in its 1977 report on marijuana singled out motor vehicle crashes as potentially the most serious consequence of psychomotor impairment resulting from acute intoxication. Subsequent studies have indicated that as many as eight of ten marijuana users sometimes drive when they are "high."[4] NIDA predicts that "as use becomes increasingly common and socially acceptable and as the risk of arrest for simple possession decreases, more users are likely to risk driving while high."[4]

A recent study in California, involving blood samples of 1,800 motorists arrested for driving while intoxicated, detected marijuana in 16 per cent of the cases, nearly all of them in conjunction with the presence of alcohol.[9]

The concomitant use of marijuana and alcohol, which is quite common, has its greatest implications in the area of highway safety. Reduction in reaction time, poor cognition and impaired coordination that have been observed with the use of either substance alone are markedly amplified when the two drugs are taken in combination.(10)

Reproductive Function

Possible disturbances in endocrine function of adolescents and young adults are of greatest interest insofar as they adversely affect sexuality and reproduction. In 1977, the evidence for such effects was sparse. Now, although inconclusive and often preliminary, there is a growing body of data from studies of chronic heavy use in animals and humans that point to diminished fertility and that substantiate danger to the fetus.

For males, there is conflicting evidence regarding the lowering of testosterone levels, especially as to whether such effects are long-term and attendant upon chronic use, or transitory as a result of acute administration. In either case, interesting research questions can be raised concerning aphrodisiac qualities of marijuana that have been alleged by some users. Reduced sperm counts, which were found in one controlled study, probably are not as significant for decreased fertility as are abnormalities in structure and impaired motility, also detected in sperm in this study.(11)

For females, chronic marijuana use may cause abnormal menstruation, including failure to ovulate, and fetal damage. Menstrual problems were evident in a controlled study of street users in St. Louis,(12) although concomitant use of alcohol by some of the subjects could have had some influence on the results. Experiments with rhesus monkeys have implicated THC as a disruptive influence on the reproductive system, with effects apparently mediated through inhibition of pituitary gonadotropin secretion, and also possibly through direct action on reproductive tissues.(13) In another study, female monkeys treated with THC over a period of three to five years at levels comparable to daily human consumption of one or two marijuana cigarettes, suffered four times the incidence of fetal deaths, abortions and resorptions as did drug-free controls.(14) Although demonstrable fetal effects have been largely embryocidal, the possibility of abnormal fetal development as a result of the mother smoking marijuana during pregnancy cannot be ruled out.

Pulmonary Involvement

The two previous Council reports cited evidence of bronchial impairment and lung damage, including carcinogenic risks, associated with chronic and heavy marijuana smoking, and with combined marijuana and tobacco use. Additional supporting data come from a study done with rats who inhaled marijuana smoke daily for a period of one-eighth to one-half their life spans and suffered degenerative changes in their lungs more severe than those caused by cigarette tobacco.(15).

Although the degree of comparability of marijuana and tobacco smoke in pulmonary effects is still debatable, one study of bronchoconstriction found

that smoking less than one marijuana cigarette per day diminished vital capacity of the lungs as much as smoking 16 tobacco cigarettes.(16) Because smoking several marijuana "joints" daily is not unusual among young people, their risk of incurring pulmonary problems may be far greater than that of heavy users of tobacco. The combination of tobacco and marijuana smoking, a common practice, is probably additive in its pulmonary side effects.

The 1979 Council report also dealt with the issue of spraying marijuana crops with paraquat, a herbicide found to have possible toxic pulmonary effects, although no evidence of paraquat toxicity in humans from smoked marijuana has been noted. This spraying reportedly has been discontinued; nevertheless, it would be advisable, in any future consideration of applying herbicides to marijuana plants, to determine and evaluate the health hazards of the chemicals involved before actually putting them into use.

Psychopathology

It has been known for some time that marijuana use can produce panic reactions, flashbacks and other emotional disturbances, and that children and adolescents are at high risk psychiatrically when they abuse psychoactive substances.

It is now also clear that persons with a history of schizophrenia or other major mental disorders place themselves in jeopardy by using marijuana, because even acute use has been shown to precipitate psychiatric symptoms in such individuals.(17)

The fact that the marijuana being smoked today is far more potent than that used just a few years ago may bring an increasing number of psychiatric casualties into emergency rooms, crisis centers, and physician's offices. It might also produce confirming evidence of the "cannabis psychosis" reported in other countries where typical dose levels and drug potency have been higher than those heretofore found in the United States.

Implications of the Research

Marijuana is a dangerous drug. A growing body of evidence from both animal and human studies and from clinical observations attests to its deleterious effects on behavior, performance, and functioning of various organ systems. There undoubtedly must be improvement in research design and techniques before definitive incontrovertible data can be secured in certain areas. But that is no reason to hesitate in calling attention to the potentialities for harm as they become clearer and more widespread.

In view of the evidence of possible adverse effects of marijuana use, the sale of, or other trafficking in, marijuana should be subject to stringent penalties and vigorous prosecution.

The AMA has long opposed excessive and unrealistic penalties for possession of small amounts of this drug for personal use. Nevertheless, legislative action that is designed to moderate penalties for possession should be of

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Behavioral, Psychosocial, and Academic Correlates of Marijuana Usage in Adolescence

A Study of a Cohort Under Treatment

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In 1985 approximately 120,000 American high school seniors smoked marijuana daily. We interviewed 35 middle-class, cannabis-dependent adolescents with a mean age of 16 years who were patients in a drug treatment program. The patients also completed a lengthy self-assessment questionnaire designed to elicit information on drug-related problems. Our results show that family harmony, school attendance, and school achievement deteriorated once these young people began to use marijuana at least 4 days a week. The following behaviors were noted: remaining away from home without permission or parental knowledge for at least 7 consecutive days (29%), a D or F grade average on the last report card before they entered the drug treatment program (43%), involvement in a motor vehicle accident when the driver was under the influence of marijuana (26%), suicide attempts (20%), and convincing a "marijuana-naive" younger sibling to smoke the drug (20%). Despite such seemingly apparent signs of possible drug use by these 35 adolescents, a mean time of 12 months elapsed before parents suspected their children of marijuana abuse. In many cases mental health professionals consulted by a number of the children when they were using drugs were likewise unaware of the marijuana abuse.

THE PROPORTION of high school seniors who admit to smoking marijuana daily has declined from a peak of 10.8 percent in 1978 to five percent in 1985.[1] Thus, 120,000 seniors in American high schools intoxicate themselves daily by smoking marijuana. The average age of first-time users of marijuana is currently between 13 and 14 years. Of all young people who smoke marijuana even once, an estimated 10 percent will progress to daily use of the drug.[1]

Previous claims that marijuana is not injurious to health were based in large measure on the results of studying the effects of relatively low-potency *Cannabis* smoked by large numbers of young adults between 1960 and 1975. Today, ordinary marijuana, at 3.6% Δ9-tetrahydrocannabinol (THC), has four times the potency of the marijuana generally smoked during the 1970s.[2] Indeed, marijuana is now a bit more potent in Δ9-THC than hashish, at least in the United States.[2] Sinsemilla (seedless marijuana), which adolescent "aficionados" prefer and use almost exclusively when available, contains an average of 7% Δ9-(THC).[3] This is approximately six times the concentration of most marijuana smoked in 1975 and twice the concentration of Δ9-THC in hashish.

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Inhibition of Cellular Mediated Immunity in Marihuana Smokers

Abstract. *The cellular mediated immunity of 51 young chronic marihuana smokers, as evaluated by the lymphocyte response in vitro to allogeneic cells and to phytohemagglutinin, was significantly decreased and similar to that of patients in whom impairment of T (thymus derived) cell immunity is known to occur. This inhibition of blastogenesis might be related to an impairment of DNA synthesis.*

It has been previously reported (*1*) that delta-9-tetrahydrocannabinol (Δ^9-THC), a psychoactive substance of *cannabis*, when administered to rodents alters their cellular mediated immune responsiveness, and it was suggested that similar changes might also occur in man. In our study the mixed lymphocyte culture (MLC) and phytohemagglutinin (PHA) responsiveness of 51 marihuana smokers, 16 to 35 years old (median age 22), were studied. Only subjects who had used *Cannabis* products (at the exclusion of other drugs) at least once a week (average four times a week) for at least 1 year (average 4 years) were selected for this investigation.

Eighty-one healthy volunteers, 20 to 72 years of age (median age 44) were used as controls. Purified lymphocyte suspensions were prepared from fresh samples of venous blood by the Ficoll-Isopaque density gradient method (*2*). A microculture system was used for screening of cellular responsiveness (*3*). For the MLC test, 1×10^5 responding cells were incubated, per well, with 2×10^5 stimulating cells pooled from a panel of ten donors, phenotypically different (allogeneic cells in which 25 different HL-A specificities were represented (*4*)).

For the PHA test, 2×10^5 responding cells were incubated per well with 1 μg of purified PHA. The medium used was RPMI 1640 with penicillin, streptomycin, and glutamine, to which 25 percent autologous serum was added.

Results are summarized in Table 2 and compared with data obtained in 60 patients with cancer, 20 patients with uremia, and 24 renal allograft recipients with iatrogenically induced immunosuppression. The mean values registered in the group of marihuana users were significantly lower than those of the normal, but much older, [illegible] relation exists between cellular immunity, as reflected by in vitro lymphocyte blastogenesis and aging (*5*), results obtained in the group of marihuana smokers may be interpreted as being indicative of cellular hyporesponsiveness. Supporting this conclusion is the close similarity between the depressed MLC and PHA responsiveness of marihuana users and that of cancer (*6*), uremia (*7*), and immunosuppressed transplant patients in whom impairment of T (thymus derived) cell immunity is known to occur. Furthermore, we observed that in vitro inhibition of PHA-induced blastogenesis of normal human lymphocytes started with 1.6 μM THC and was complete with 20 μM.

The major psychologically active constituent of *Cannabis sativa* is Δ^9-THC. This substance, as well as its metabolites, is insoluble in H_2O, but is very fat soluble, and has a half-life of several days in tissues where it might exert a cumulative and pharmacological effect (*8*). Such an effect might be related in a still unknown way to the depressed cellular immune response in vitro of chronic marihuana smokers. The effect of THC on adrenergic receptors (*9*) might also play a role in its immunosuppressive activity, as was suggested for other drugs administered continuously over a long period (*10*).

This inhibition of blastogenesis might result from an impairment of DNA synthesis. One of us (A.M.) sampled lymphocytes from four marihuana smokers, cultivated the cells for 72 hours, and then observed a decreased number of cells during the period of DNA synthesis (S period of the cell cycle). There was also an increased incidence of chromosomal breakages.

Table 1. Comparative cellular mediated immunity of normal subjects, marihuana smokers, and patients with impairment of T cell immunity. The in vitro blastogenic response of lymphocytes was studied by the MLC and the PHA tests. The incorporation rate of [^{3}H]thymidine of the T lymphocytes is given in counts per minute ± the standard error.

Subjects	MLC		PHA	
	No. tested	[^{3}H]Thymidine incorporated (count/min)	No. tested	[^{3}H]Thymidine incorporated (count/min)
Normal controls	81	26400 ± 200	81	23250 ± 210
Cancer patients				
Primary tumors	16	14894 ± 792	16	17501 ± 124
Regional spread	23	15816 ± 420	23	13345 ± 530
Distant spread	21	8968 ± 459	21	10516 ± 580
Uremic patients	26	12001 ± 272		
Transplant patients*	24	12307 ± 357		
Marihuana smokers†	34	15679 ± 499	51	13779 ± 169

* After 1 to 4 years of immunosuppressive therapy. † At least 1 year, at least once a week; no other drug taken.

Black American Manual - 1985 Edition

MARIJUANA

What is marijuana?

Marijuana ("grass", "pot", or "weed"),comes from a common plant with the botanical name Cannabis Sativa. It is not a single substance, but a crude drug -- a "complex chemical factory" which contains at least 421 different chemicals. The main psychoactive ingredient in marijuana is delta-9-tetrahydrocannabinol, or THC. This, and 60 other cannabinoids, are chemicals which are found only in the marijuana plant. Because of the complexity of marijuana's chemical composition, its instability, and its wide variation in potency due to different varieties, climates, and growing conditions, no two batches of marijuana will be the same. And, as with any other street drug, people who buy marijuana can never be certain what else it may be mixed with, or if it even is marijuana.

What is THC?

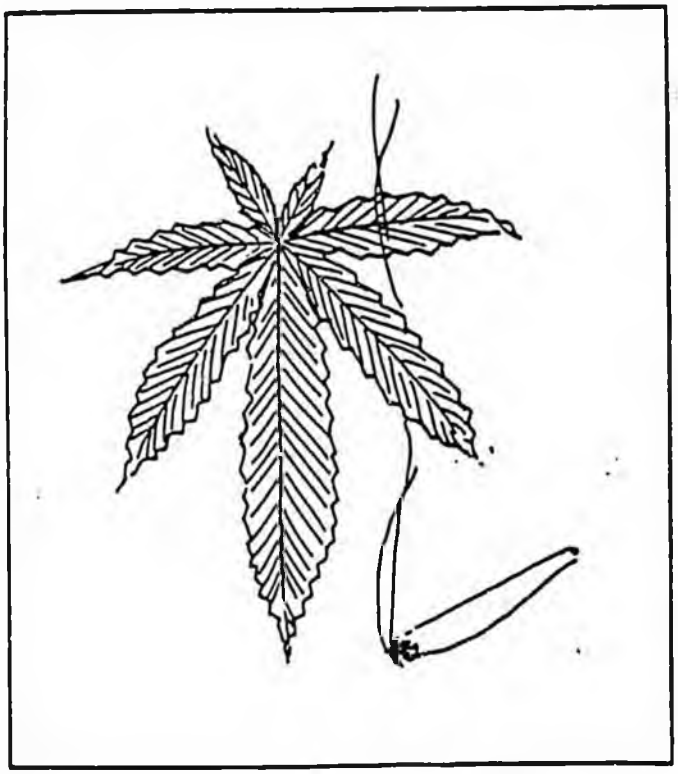
THC Is the chemical in pot that produces the "high". It is the THC content of marijuana that determines its potency.

THC is toxic. (Toxic means "poison".) It is an intoxicant.

THC actually stands for delta-9-tetrahydrocannabinol. THC is the best-known of the 61 cannabinoids in marijuana. All cannabinoids are fat-soluble chemicals. They accumulate in the fatty lining of the cells in the body and brain and are cleared from the body very slowly.

What is hash?

Hashish or "hash" is a dark brown resin from the tops of the marijuana plant. The resinous secretions of the plant are collected, dried, and then compressed into "bricks." The Middle East is the main source of hash used in the United States. In the past, hash was stronger than marijuana, but with the increasing potency of pot, hash is often a weaker drug, averaging about two percent THC content.



What is hash oil?

Hash oil is a tarlike substance smoked in small amounts on tobacco or marijuana or in small glass pipes. It is distilled from the marijuana plant and is extremely potent, with a THC content from five to 40 percent or more. It is so potent that one drop of high potency oil could produce an hallucinogenic effect. Hash oil is produced in a manner similar to percolation of coffee.

How potent is today's marijuana?

Marijuana is a far more powerful drug today than it was 10 years ago when the average THC content was only about .5 percent. Marijuana being smoked today is often from Colombia and contains four to six percent THC. U.S.-grown Sinsemilla is especially cultivated to have a THC content of up to 11 percent or higher.

Wouldn't it be better to sell marijuana legally so the potency could be controlled?

The idea that people will one day be able to buy "joints" in a grocery store in packages with a label describing the THC content is a fantasy, because marijuana is such an unstable drug. Even after a joint is made, the chemical composition of the THC and other chemicals changes. The strength of marijuana varies according to the length of time it's stored, the place it is is stored in, the temperature it is stored at, and a variety of other factors.

Are other drugs sometimes added to pot?

PCP ("angel dust"), LSD, hash oil, and other chemicals are often added to marijuana -- often without the knowledge of the purchaser.

KIDS: STAY AWAY FROM POT

DEAR ABBY: I was glad to see your warning about angel dust. Everything you said about it was true. It makes you violent and can really mess up your head. I know. I was in high school, ready to graduate, when I smoked that dust. I didn't even know it. I smoked some pot that had been laced with angel dust. I didn't get high. I just went crazy.

I was sent to a mental hospital where I spent three months. I put my poor parents through hell. I'm out now, but I have to see a social worker every week. I'm still on medication, and my head still hurts. But at least I can dress myself and comb my own hair. My biggest fear is that one day I will go completely crazy again and end up back in the hospital. I saw kids there who'd had that experience.

My God, what a terrible price to pay for wanting to get high. Abby, please keep telling kids to stay away from pot. You never know what's in it. I am signing my name and address just to prove this letter is not a phony, but if you print it, sign me...

PAID A BIG PRICE
Nonpareil
July 6, 1982

Besides other dangerous drugs, are there other impurities found in marijuana?

Dried oregano looks like marijuana; dried parsley looks like marijuana; dried cow manure looks like marijuana. All these substances are candidates for filler in marijuana. All have been used. Besides being a waste of money, smoking pot can cause disease from the bacterial organisms found crawling all over the plant.

DOCTORS SAY CONTAMINATED POT CAUSED FOOD POISONING EPIDEMIC

Boston (AP) -- Researchers have discovered that germ-laden marijuana can cause an illness like food poisoning, and they attribute a nationwide outbreak last year to bad pot.

The research provides the first evidence that marijuana can spread disease-causing bacteria.

Doctors from the Centers for Disease Control in Atlanta found that marijuana was the source of an outbreak of food poisoning in Ohio and Michigan in January 1981. The marijuana, probably imported from Colombia or Jamaica, was contaminated with salmonella bacteria from animal manure which had been added to the marijuana.

The doctors tracked down the source of the outbreak, which also affected marijuana users in Georgia, Alabama, California, Arizona and Massachusetts, by asking people whether they used drugs. In Michigan, they found that 76 percent of the victims were exposed to marijuana.

Symptoms of the infection included diarrhea, fever, abdominal pain, nausea and vomiting. The illness lasted an average of eight days, and 62 percent of the victims had to be hospitalized.

World Herald

What are the immediate effects of smoking pot?

In most people, the use of marijuana produces a sense of well-being, a state of relaxation, altered perception, particularly of distance and time, impaired short-term memory and impaired coordination. The "high" usually lasts from two to three hours after smoking one joint. High doses of THC can cause image distortion and hallucinations.

The most commonly observed adverse reaction to marijuana is the acute anxiety reaction. A single dose of THC can cause this reaction even in mentally healthy people. Persons suffering an acute anxiety reaction are anxious and may become paranoid. There can be a sense of general suspicion to a fear of losing control and going crazy. Some reactions require professional treatment, and approximately 10,000 Americans are treated in hospital emergency rooms each year suffering from the reaction.

Unfortunately, all pot smokers get their "high" from the poisonous effects of THC in the brain, where it first stimulates and then damages the cells in the brain's pleasure center, depriving users of a desire to obtain natural, non-chemical "highs."

POT SMOKER LEAPS TO HIS DEATH FROM HOTEL

Gedelle King told authorities that she and her husband Jay were smoking marijuana with friends in their Atlanta, Georgia, hotel room when Jay asked what time it was. Before she could answer he said, "It's time to end the world," ran outside and jumped 30 feet to his death below.

Atlanta Journal
Nov. 9, 1983

What is so dangerous about marijuana?

Marijuana is a special drug because it appears to be harmless. This appearance leads many people to believe that it really is harmless, and therefore not dangerous to use or to experiment with. In other words, the fact that there are no dramatic effects is one of its dangers. Marijuana is such a subtle drug that people don't realize how it is affecting them. Marijuana is dangerous precisely because it is not a killer weed. Its effects on the user at usual doses are often mellow, compared to alcohol intoxication. As long as marijuana users continue to use the drug, they do not permit themselves to consider the possibility that they are damaging themselves with the drug.

> "I believe (marijuana) to be our most dangerous drug because of widespread use, especially by our youth, and because the psychological as well as the physical effects are insidious and ultimately devastating."
>
> - Dr. Robert DuPont

> "Marijuana is our most dangerous drug because of its nation-wide prevalence and because people use it thinking nothing bad is happening to them. By the time it does psychological harm, the pot smoker's ability to judge that harm is impaired to such an extent that he rejects the evidence that is obvious to everyone else."
>
> - Dr. Harvey Powelson
> Director
> Psychiatric Department of the Student Health Service
> University of California, Berkeley

If pot is dangerous, then why do so many people think it's harmless?

Without question, in the past two decades, the cultural messages people picked up about drugs were, for the most part, pro-drug. One of the factors that encouraged use of marijuana was the one-sided publicity given to statements of scientists and others who advocated liberalizing marijuana laws. At the same time, there was a virtual blackout of scientific information describing the dangers of marijuana use. Dozens of pro-drug books were published and sold in the "popular" market, while no anti-drug books were published for that market, although such books were written. Not a single commercial film has been made in the past two decades which presents marijuana use in a cautionary light. At the same time, well-funded lobbying groups to promote drug interests were organized at the local, state and national levels. As a result, many intelligent people concluded that the bulk of the scientific evidence "proved" that marijuana was "harmless." The evidence, of course, "proves" exactly the opposite.

There is still more ignorance about marijuana than about any other widely used drug in society, and this is as true among some drug counselors as it is among users and the lay public.

Don't some scientists say marijuana is harmless?

Marijuana use is a major health problem in the United States, and the harmfulness of the drug is now widely perceived. No scientific authority argues today that marijuana is a harmless drug. That argument is over. Now, all medical authorities agree that marijuana use has hazards.

While knowledge of all the consequences of marijuana use is incomplete, studies finished so far demonstrate a variety of significant risks and dangers. No scientific study has found the drug to be completely safe. Over 8500 research papers have been done on the drug and none of them gives pot a clean bill of health.

Both the American Academy of Pediatrics and the American Medical Association strongly condemn use of marijuana by teenagers. The Surgeon General has concluded that marijuana is dangerous and harmful to health. Also, many people who once believed marijuana to be harmless have now concluded that it may be the most dangerous drug in America.

AMA CONCLUDES: 'POT DANGEROUS'

CHICAGO -- The American Medical Association says marijuana is not a "harmless amusement" and frequent use can lead to problems in the brain, circulatory system, heart, lungs, and nervous system.

"Marijuana can hurt you," the AMA said Thursday in promoting its new physicians' drug abuse handbook. "Marijuana is by no means the harmless amusement that many believe it to be. Structural changes occur in the brain with marijuana use, as well as changes in the patterns of brain waves.

"There is now no doubt at all that marijuana is a dangerous drug with great potential for serious harm to young American users," the AMA said.

Middlesex News
July 24, 1981

What about the books and authors who say pot is okay?

Marijuana research is a young scientific field. More research has been done in the past two decades than in all previous history. Most of the important physiological research on pot was done after 1972. Marijuana research is very difficult because marijuana is a very complex substance. Also, many of the early studies that supposedly "proved" that marijuana wasn't too harmful used amounts of THC that were much smaller than is found in pot on the street today. Thus, it is important to find recent research on marijuana.

It should also be remembered that it was only after many years of use by millions of people that the heart disease associated with smoking cigarettes was recognized. When the controversy about tobacco smoking was raging in the late 1950s, some scientists came to the defense of cigarettes, the way others do to marijuana today. For example, the chairman of the Cancer Commission of the California Medical Association, and one of the state's foremost cancer specialists, testified before a Congressional committee that "a pack of cigarettes a day will keep lung cancer away."

What organizations still say marijuana is harmless?

The Do It Now Foundation says that "marijuana has not been proven harmful, even in remote ways." It advises young people that "the mild psychological changes that occur in many people" are "generally beneficial in nature." In other words, marijuana may even be good for you. Not only that, but Do It Now also says that marijuana may be a cancer cure."

So, how can you be sure that Do It Now isn't right? Well, first, common sense says that becoming a burnout is not a "mild psychological change" and is not "generally beneficial". Secondly, it would be easier to believe Do It Now if it would tell readers who says smoking marijuana will cure cancer. It would be nice if they would cite a single study printed in a reputable scientific journal that says smoking dope helps cure cancer. It would be nice if they could find a single doctor in the whole world who treats his lung cancer patients by having them toke on a joint.

Who is Do It Now, anyway? Who writes their pamphlets?

The Do It Now staff relies for its "realistic" drug information on "over 150 collective years of former drug use and experimentation". Some of its writers regularly contribute articles to High Times magazine and Dean Latimer, the Executive Almighty Editor of High Times often writes articles for Do It Now. Vic Pawlak, once described as the "concept person" for Do It Now's Institute for Chemical Survival, became an expert on drug abuse while writing for underground newspapers. Dean Latimer admits in his articles that he has been a heavy pot and speed user. Do It Now's opinion about the harmfulness of drugs is at odds with the positions of the American Medical Association, the American Academy of Pediatrics, the National Institute on Drug Abuse, the Addiction Research Foundation, the World Health Organization, the Food and Drug Administration, the Institute of Medicine and the hundreds of physicians and scientists across the country who think pot is not only harmful, but dangerous.

Another pro-drug organization is N.O.R.M.L. -- the National Organization for the Reform of Marijuana Laws. They're the people who want to legalize dope. They get alot of their money from the businessmen who manufacture pipes and bongs. Their "official policy" is that they don't encourage people to use any drugs and they "strongly discourage" teenagers from using pot. Even N.O.R.M.L. admits marijuana can be dangerous, but they believe that it's no more dangerous than booze or cigarettes, so it should be made available in the same ways.

But, remember, N.O.R.M.L. is a lobbying organization. It doesn't want your money (although it will sell you a student membership). What it does want is votes. The more pot

smokers there are, the easier it will be to elect politicans who'll vote to ease up on dope. So, N.O.R.M.L. has a vested interest in having lots of adults use marijuana -- and lots of potential future voters turned on to pot.

N.O.R.M.L. says it provides "straight-forward", "assembled medical information", too. This is their idea of "straight-forward."

At one time, N.O.R.M.L. was working on a pamphlet called "NORML On Family Drug Awareness". In that pamphlet, the organization said that evidence of harm from pot was "tentative" and "inconclusive" (just like the American Tobacco Institute says proof of harmful effects from smoking cigarettes is exaggerated). To prove that claims that marijuana is harmful are "scare tactics", they claim to take some "selections" from the testimony of Dr. William Pollin to Congress in the fall of 1981. This is how N.O.R.M.L. quoted the director of the National Institute on Drug Abuse's report on evidence of lung damage:

> "On Lung Damage: 'There does not yet exist an animal model for the development of lung cancer by...marijuana. At this juncture, it is not possible, to predict what precisely the health effects in later life will be on those young people today who are regular marijuana smokers."

What follows is what Dr. Pollin really told the Senators:

> "The concentration of benzo(a)pyrene in marijuana tar is 70 percent higher than in the same weight of tobacco tar. There does not yet exist an animal model for the development of lung cancer by either tobacco or marijuana. However, in animal tests marijuana smoke residuals produce skin tumors. In fact, human lung tissue exposed in the test tube to marijuana smoke shows greater cellular changes than when exposed to similar amounts of standard tobacco smoke. Critical longitudinal studies are needed and are being supported by NIDA to evaluate the risk of long-term use."

Elsewhere in "NORML On Family Drug Awareness", the pro-pot lobby proposed to tell young people that Dr. Pollin said:

> "Thus, any attempt to compare the health impact of marijuana with that of alcohol and tobacco at current levels of use is certain to minimize the hazards of marijuana."

But, this is how that comment reads when taken in context:

> "Thus, any attempt to compare the health impact of marijuana with that of alcohol and tobacco at current levels of use is certain to minimize the hazards of marijuana. But any comparison at levels of anticipated use involves many assumptions that are at best dubious

> and at worst may be dangerously misleading. Such a comparison seems, therefore, useless and undesirable until such time as the parameters of risk are better specified than they can be at present.

Why do you suppose N.O.R.M.L. wanted to be "dangerously misleading" by making a "useless" and "undesirable comparison?"

Finally, there are some books that show up in a few book stores now and then that are classified as "non-Fiction", but when it comes to reporting on marijuana, their facts are fairy tales. Recreational Drugs is one such book. It is recommended reading by High Times magazine. The authors of the book, none of whom are physicians, never bother to cite a single footnote or study by name so that you can look it up on your own. There is no way you can find out how well they researched their material.

Recreational Drugs says "marijuana appears to be remarkably safe". Who says so? The authors don't say. They also tell you that the National Commission on Marijuana and Drug Abuse "verified the safety of marijuana" in a report that was rejected by President Nixon. But wait! You probably can't even remember when Nixon was president. How old is this study, anyway? Well, it's ten years old! It was prepared in 1972. That report never verified the "safety" of marijuana. It did admit that there was much more to learn about marijuana. Since 1972, we have learned much more.

Recreational Drugs also says that "much of today's reliable information about marijuana" comes from a 1972 study done in Jamaica. Since the dope promoters always refer to this study, and because they criticize every research study that says pot is harmful you need to take a good look at what evidence they think is reliable.

For example, the Jamaica study supposedly "proved" that "there was no difference in rate of employment, job stability, or academic achievement" between straights and potheads. What the authors of Recreational Drugs don't bother to tell you is that the small number of people studied were unskilled, uneducated, illiterate laborors who hoed sugar cane fields for a living. How do you test job stability or "academic achievement" among ditch diggers? You are also never told that this "reliable" study was never published by the government agency that sponsored it, that it does not have the support of Jamaican doctors, and that it was never printed in a single, reputable scientific journal. Besides, the Jamaica study is ten years old. What about all the studies that have been done in 1973, 1974, 1975, 1976, 1977, 1978, 1979, 1980, 1981, 1982, 1983 or 1984?

A partial list of popular books which favor or advocate social accaptance of drugs, while minimizing their damaging effects....

Ashley, R., Cocaine, Warner Books, New York, 1975.

Benitze, F., In the Magic Land of Peyote, Warner Books, New York, 1968, 1975.

Brecher, E.M. and Editors of Consumer Reports, Licit and Illicit Drugs, Little, Brown Co., Boston, 1972.

Drug Abuse Council, The Facts About Drug Abuse. The Free Press, a Division of MacMillan Publishing Co., New York, 1980.

Grinspon, M.D., L., Marihuana Reconsidered, Second Edition, Harvard University Press, Cambridge, 1977.

Horman, R., and Fox, A.M., Editors, Drug Awareness: Key Documents on LSD, marijuana and the drug culture, Avon Books, New York, 1972.

Lieberman, M., The Dope Book, Praeger Publishers -- a Division of Holt, Rhinehart & Winston, New York. Ninth Printing 1978.

Lloyd, P., The Book of Pot, The Ridge Press, New York, 1976.

Margolis, J.S. and Ciorlene, R., A Child's Garden of Grass (The Official Handbook for Marijuana Users), Ballantine Books, a Division of Random House, New York, 1978.

Novak, W., High Culture, Alfred A. Knopf, Inc., (New York) and Random House of Canada (Toronto), 1980.

Phillips, J.L. and Wynne, R.W., Cocaine The mystique and the Reality, Avon Books - A division of the Heart Corp., New York, 1980.

Rubin, V. and Comitas, L., Ganja in Jamaica, The Effects of Marijuana Use, Anchor Press/Doubleday, New York 1976.

Sabbag, R., Snow Blind, A Brief Career in the Cocaine Trade, Avon Books - A Division of the Hearst Corp., New York, 1979.

Weil, W., The Natural Mind A new Way of Looking at Drugs and the Higher Consciousness Houghton Mifflin Co., 1972.

Young, L.A., & L.G., Klein, M.M. & D.M. and Beyer, D., Recreational Drugs, Berkeley Publishing, by arrangement with Macmillan Publishing, New York, 1979.

Eng., R.C., Responsible Drug and Alcohol Use, Macmillan, New York, 1979.

Stafford, P., Pyschedelic Baby Reaches Puberty, Dell Publishing Co., 1971.

Kaplan, J., Marihuana, The New Prohibition, World Publishing Co., New York, 1971.

Grinspoon, L., Bakalar, J.B., Cocaine, Basic Books, Inc., New York, 1976.

Goode, Erich, The Marihuana Smokers, Basic Books, Inc., New York, 1970.

Woodley, R., The Dealer, Portrait of a Cocaine Merchant, Warner Paperback Library, 1972.

Ashley, R., Heroin, The Myths and the Facts, St. Martin's Press, 1972.

King, R., The Drug Hang-Up; America's Fifth Folly, W. W. Norton, 1972.

Lindesmith, A.R., The Addicts and the Law, Vintage Books, 1965.

Musto, D., The American Disease, Origins of Narcotic Control, Yale University Press, 1973.

Zinberg, N.E., Robertson, J.A., Drugs and the Public, Simon & Schuster, 1972.

Is it true that nobody has ever died from using marijuana?

Do people who smoke cigarettes and get lung cancer die from lung cancer or cigarette smoking? Do people who overdose on alcohol die of heart failure or alcohol overdose? Does a drug with 50 percent more cancer-causing tar than tobacco cigarettes cause death if the smoker eventually dies of lung cancer or emphysema?

It is true that nobody has ever proven that human beings have overdosed on pot and died, although such cases have been reported. At this point, few physicians would know how to diagnose a death caused, or contributed to, by marijuana. The fact that death from smoking marijuana does not happen immediately after using the drug, or cannot be proved, does not mean that it cannot happen.

> "And people who try to tell you there have been no deaths from marijuana should visit the cemeteries. Do you know that drug-related suicide is the number one cause of death among college students today? The number two cause of death is alcohol and drug-related traffic accidents. And in almost every case illegal drug use starts with marijuana."
>
> - Dr. Robert Heath

Who uses marijuana?

The United States has the highest level of marijuana and other drug use among young people of any developed country in the world. In America, the mainstream child is just as likely to use marijuana as the obviously deviant or rebellious kid. As a matter of fact, more high school seniors smoke marijuana than smoke tobacco cigarettes. Marijuana use begins as early as 12 years, although the most frequent ages of first use are around 14 and 15. Widespread use of marijuana by adolescents and females is unprecedented in human history.

Are there many parents who have smoked pot?

Unfortunately, many kids who grew up in the '60s smoking pot have grown up enough to have kids of their own, but haven't grown up enough to stop smoking weed. Their kids face an uphill battle if they want to be straight themselves. Many persons in the 35 to 49 age group are presently raising teenage children, and surveys show that one-fourth of those parents have at least tried marijuana. One in five parents of children aged 12 to 17 have tried marijuana at some point during their lives.

Why do kids smoke pot?

Teenagers know better why kids smoke pot than adults do. Many adults, especially those who work in drug treatment centers, are convinced that all kids who use drugs have "problems" which cause them to use drugs. They insist that solving the "underlying problems" is the way to battle drug abuse. However, increasing numbers of professionals and parents are beginning to understand that for many, if not most kids, drugs are the cause of their drug problems, and getting kids off drugs permits them to solve their drug problem and other problems with a healthy mind that is functioning normally.

The majority of adolescents who use marijuana and other drugs do so because of ignorance of the long-range harmful effects and because of the need to belong to a group. Many teenagers who use drugs have everything going for them. Their families are intact, their parents love them, they get good grades in school, they are involved in extracurricular activities, they have interesting hobbies, they have lots of friends and they are very popular. They aren't escaping reality, because their world isn't that unpleasant. To them, marijuana and other drugs are "mild, harmless intoxicants", which they can handle -- they think. What these kids lack is information about how drugs that make them feel good can hurt them, especially in ways that they cannot see or "feel".

Don't lots of people just "try" pot?

Just "trying" pot isn't a good idea because for many people, the first "try" produces no "high". Therefore, the experiment is repeated several times in order to achieve an effect. Surveys show that few persons who "try" marijuana stop after merely "trying it to see what it's like" on one or two occasions. Among kids 12 to 17, less than one in three of those who admit they have "ever used" marijuana say that they used pot just once or twice. About one-half of adults who tried marijuana before the age of 16 report that they eventually used marijuana on a daily basis.

Isn't it okay to use pot in "moderation"?

Even moderate use of marijuana is associated with school drop-out, psychoses, panic states and adolescent behavior disorders. Besides, how many current "burnouts" ever planned to become burnouts? Doesn't everybody think their pot use is "moderate" when they start? Doesn't every pothead still think his pot use is "moderate", even though to everyone else it is clear that he has become a burnout?

How long do the chemicals in marijuana stay in the body?

Marijuana is a unique drug because its chemicals accumulate in the user's body in much the same way as DDT. A week after a person smokes one joint, 30 to 50 percent of the THC remains in the body; it is estimated that four to six weeks are required for all the THC to leave the body. In other words, a kid who gets "high" on Saturday night and again on Wednesday night will build up the amount of THC in his body. His brain will never be free of the drug. At least a full month of not smoking would be necessary to rid the body of all the THC.

Since marijuana stays in the brain long after the user feels "high," it is very deceptive. Many professionals are worried that the slow, subtle accumulation of THC in the body and brain is responsible for the personality and behavior changes seen in users. And, the longer the drug remains in the system, the greater time it has to affect the other tissues of the body.

> "There is no other drug used or abused by man which stays in the body as long as cannabis does. And there is no other drug, legal or illegal, which affects every major organ of the body. And every system in the body. And every single cell in the body."
>
> - Dr. Carlton Turner, Deputy Assistant to the President for Drug Abuse

Where in the body does THC accumulate?

THC, and the other cannabinoids in marijuana, are stored in the fatty tissues of the brain and lungs. They are also accumulated in the ovaries and testicles for long periods of time.

How does marijuana affect the lungs?

Marijuana smoking constitutes the greatest single new threat to the health of lungs in the United States. Not only is the possible damage to the lungs very severe, but the changes associated with heavy pot smoking can appear within 18 to 24 months, which is a relatively short period of time.

Marijuana is much more harsh and irritating than tobacco. That is why users often cough and gag as they inhale the smoke. Marijuana smoke contains THC and other chemicals which irritate the lungs, as well as poisons like carbon monoxide and ammonia. The effect is so severe that some scientists have concluded that five joints irritate the lungs as much as 112 tobacco cigarettes.

Following exposure to marijuana, the lungs' defense systems against bacteria are impaired. Alveolar macrophages, which

are special cells designed to attack and destroy foreign material and bacteria in the lungs, have reduced effectiveness.

Chronic bronchitis and chest pain are common in teenagers who smoke pot. There have been studies of human users which have reported laryngitis, cough, hoarseness, asthma, sinusitis, pharyngitis, bronchitis and precancerous lesions in the lungs much like that found in heavy cigarette smokers. Emphysema, a deadly lung disease, also has been found. Studies done on U.S. Army soldiers in West Germany who had been smoking cannabis for a year or less found lung damage that was more severe than that found in older soldiers who had smoked at least 1½ packs of cigarettes a day for 10 years or more. The doctors were startled to find emphysema and bronchitis in the lungs of 18-year-old hash smokers. These lung diseases are rarely found in people under 45 years of age.

Unlike tobacco cigarettes, "joints" are unfiltered and smoked to a very small "roach". As a result, the lungs of the marijuana smoker are more blackened than those of tobacco smokers and there is extreme breakdown of the lung structure. Experiments have demonstrated that significant worsening of lung function occurs only six to eight weeks after smoking a few joints a day. These tests show that heavy pot smoking causes a narrowing of breathing passages. Vital capacity, the amount of oxygen the lungs can inhale and exhale in one breath, is decreased more by one or two joints than by a whole pack of regular cigarettes.

There is still a great deal to learn about the effects of pot on human lungs. It took many years of cigarette smoking before the ill effects of cigarettes were documented. It may take another 20 years before all the effects of pot smoke on lungs are learned.

Can marijuana cause cancer?

Since marijuana smoke is deeply inhaled and contains many chemicals known to be cancer-producing, it is virtually certain that heavy use can cause lung cancer. However, it takes 30 to 40 years for lung cancer to grow. Thus far, in the United States, people have been smoking pot heavily for only a decade or two, so there aren't many dead bodies yet. However, preliminary laboratory evidence is convincing -- and scary.

There is evidence that the products of marijuana smoke cause the growth of cancer cells in the test tube in a way similar that caused by the tar in tobacco cigarettes. There is evidence that heavy pot smokers have precancerous lesions in their lungs. These lesions have been found in samples of tissue removed from the lungs of smokers of cannabis in their early 20s. Similar lesions are found in heavy tobacco smokers only after they reach the age of 40.

None of these results is surprising considering the fact that cannabis produces 50 percent more tar than the same weight of regular cigarettes. Also, because a joint is smoked down to a tiny roach, more tar is inhaled than in a tobacco cigarette -- particularly if it is a filtered cigarette. Cannabis tar contains more than 150 hydrocarbons, including cancer-causing chemicals. These chemicals from marijuana tar produce skin tumors in laboratory tests.

Because marijuana has more cancer-causing chemicals than tobacco, it may take fewer joints than cigarettes to produce cancerous changes. Compounding the damage to the lungs is the fact that most pot smokers also smoke regular tobacco cigarettes.

Does marijuana affect the heart?

It is clear that marijuana changes heart function; it increases heart rates, and it changes the distribution of blood; it causes significant increase in chest pain in individuals who have heart diseases.

POTLUCK

A former Dade County Circuit Court Clerk will be spending time in jail for serving marijuana-laced brownies that sent 22 co-workers to the hospital.

One court clerk supervisor suffered a mild heart attack and was hospitalized for several days.

American Bar Association Journal
Jan., 1984

Marijuana stimulates the nervous system and causes quickened heart beat and irregular heart rhythm. Marijuana increases heart rate as much as 50 percent and can bring on chest pain in people experiencing a poor blood supply to the heart. During the early phases of cannabis intoxication, heart rate can increase up to 160 beats per minute or more, along with causing a decrease in standing blood pressure.

THC seems to have far more profound effects on the cardiovascular system than does nicotine. There is evidence that in patients with impaired heart function the use of marijuana may precipitate chest pain more rapidly and following less effort than tobacco. One study found that a single marijuana cigarette smoked for 15 minutes produced as much carbon monoxide in the blood as 10 to 20 tobacco cigarettes smoked in the course of a day.

How does marijuana affect personality?

Psychiatrists and physicians have begun to recognize severely harmful effects of marijuana on personality, especially in maturing adolescents. Marijuana affects judgment, motivation, perception and learning. It can lead to an overall deterioration of personality and an estrangement from the mainstream of life. Users tend, quite often, to

socialize only with other potheads who exhibit the same problems. At the same time, they withdraw from their families, causing disruption and sometimes devastation in the home.

AIR AGENCY PROBES MECHANIC'S POT CASE

Miami (AP) -- The Federal Aviation Administration said it is investigating a year-old marijuana case against one of two Eastern Airlines mechanics, whose mistakes almost forced a jumbo jet to ditch in the Atlantic.

World Herald
May 22, 1983

The most consistent and notable changes that are reported in marijuana smokers include apathy, lack of motivation, which is called the "amotivational syndrome", and reduced interest in socializing. There is less concern for the future. Some users lose contact with reality and suffer from hallucinations. It's clear that a larger percentage of children who are involved with marijuana drop out of school and do not achieve as well in school as children who don't smoke pot regularly. It is also important to note that kids who stop smoking pot often show dramatic changes in behavior. They become more interested in school and being on time, getting better grades and forming meaningful relationships with their friends, and they are less hostile. Sometimes they take more interest in their personal appearance and habits.

While not all, or even most, pot smokers become "burnouts", almost all marijuana smokers deny any damage to themselves from using the weed. The marijuana user does not realize that he has changed, and if his altered behavior is brought to his attention, he tries to justify it. What the pot smoker doesn't understand is that the very area of the brain that is affected by marijuana is the same area which is responsible for helping him regulate and evaluate his own behavior. As a result, even burned out "space cadets", who may be suffering from very severe drug-related mental impairment, do not consider themselves to be burned out. The marijuana smoker can become a liar and a con artist -- and he seems to be his own biggest victim.

Of particular importance to teenagers is the very real danger that marijuana use can interfere with growing up. To become an adult, an adolescent must learn to cope with emotional, social, mental and physical growing pains. Drugs like marijuana that protect kids from the stress of growing pains also prevent kids from growing up to be responsible, mature adults.

How does marijuana affect learning?

Marijuana can interfere with learning by impairing thinking, reading comprehension, verbal and arithmetic skills. Marijuana impairs the ability to concentrate, consider complexity, manage tension, postpone rewards, think abstractly, and consider hypothetical solutions to problems. Heavy marijuana users, not surprisingly, often find that their grades become worse because of pot smoking.

Marijuana particularly seems to impair short-term memory. It also seems to interfere with the transfer of information from immediate memory to long-term memory storage. There is now evidence of memory loss so great that some kids actually forget their own birth dates.

Unfortunately, marijuana seems to fool students into believing that pot improves their performance. They think they can drive better, study better, play music better, and play football better when they are "high" -- in spite of the fact that to everyone observing their performance, they have declining abilities.

Are teenagers more susceptible to the bad effects of marijuana?

Youngsters who are undergoing rapid and complex changes of body chemistry and emotional development may be more susceptible to the accumulation of THC and other chemicals in the body than are mature adults.

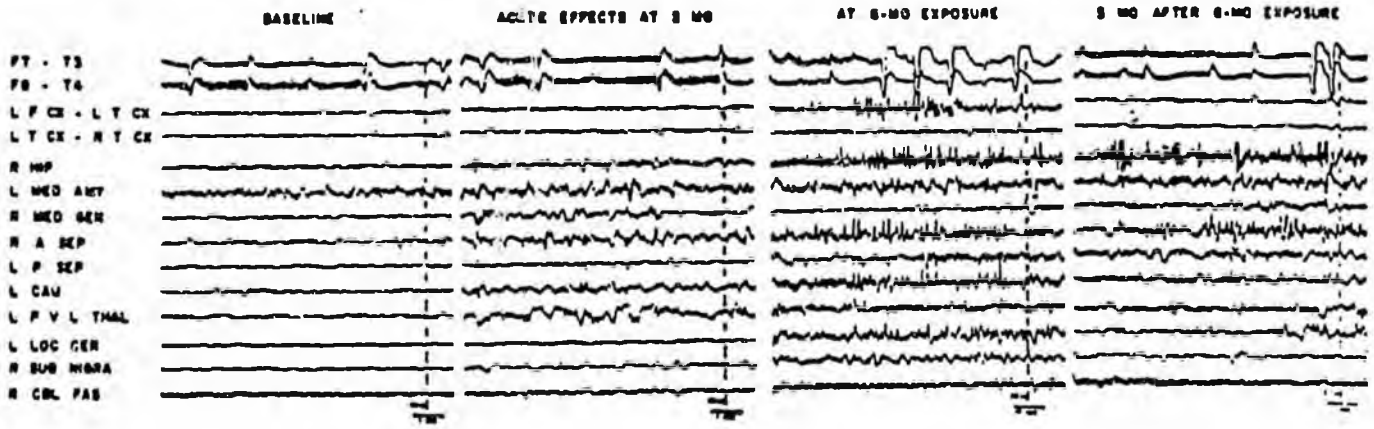
How does marijuana affect the brain?

THC accumulates in the brain. Because of the slow clearance of THC from the body, anyone who smokes more than once a month is never drug-free, and is constantly adding to the level of THC already stored in the body. Since the brain is the thinking organ of the human body, behavior changes could be expected.

There are personality changes in marijuana users. There is evidence that a person needs only to smoke two joints a week for three months before persistent changes in behavior begin to occur. The user may become more "laid back" and not care about things anymore. The user doesn't become upset -- even about things that should be upsetting. The pot smoker changes himself, not his problems. When his diminished mental capacity becomes a problem, he doesn't care enough to change to help himself.

The cause of the pot smoker's lack of concern for anything -- except getting "high" -- may be the result of pot's slowing of brain activity. Studies of brain waves of young people who smoke pot several times a week consistently show an inability of their forebrains to produce fast "beta" wave activity. Inhibiting fast wave activity means inhibiting powers of problem solving, discrimination and analysis. Studies in humans also reveal that continuous usage of marijuana may alter the roles of the right and left hemispheres of the brain with resulting impairment of verbal-analytic tasks.

Results in tests on rhesus monkeys have also yielded disturbing changes in brain wave patterns, as shown below.

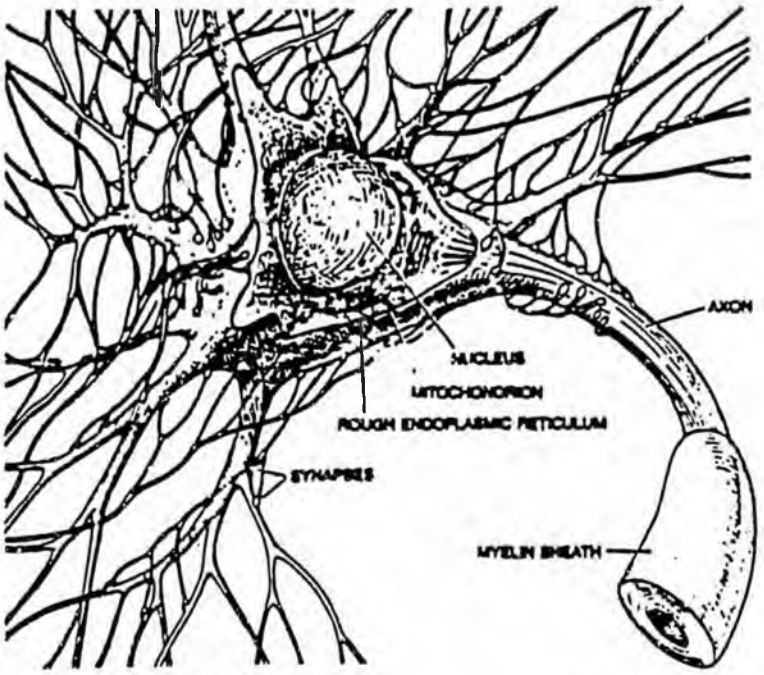


Electrical activity recorded in brain sites of rhesus monkeys. Moving left to right, the first series represents the electrical activity at 14 different brain sites before any exposure to marijuana smoke. The next series shows the acute effects after two months of exposure. The third shows brain waves after six months and the last series shows brain patterns five months after marijuana use was discontinued.

Changes have also been noted in the limbic region of the brain. The limbic, or "old" brain, is where the centers controlling instincts, memory storage, and emotions such as pleasure and reward have been identified. This part of the brain is also associated with the hypothalamus which regulates the sex hormones LH and FSH, both of which are decreased by pot smoking.

Persistent changes in brain wave patterns, which outlast exposure to the drug, have been reported in the limbic regions of the brains of monkeys and rats exposed to humanly-relevant amounts of marijuana smoke. Infant rats treated with THC show fewer structures that make protein, necessary for memory function, in the brain cells. Dr. Robert G. Heath of Tulane University Medical School, has studied the brains of rheaus monkeys treated with THC. His research demonstrates that smoking less than two joints a week for three months (possibly only 20 joints total) causes serious and possibly permanent alteration of brain

function. In addition to changes in brain waves, Dr. Heath found alterations in the structure of the brain cells. There was a widening of the synaptic cleft, the space between the cells, and other microscopic brain changes. Dr. Heath has concluded that users need to use pot only for a short time in moderate to heavy levels before there is evidence of brain damage. Such damage could be the cause of the memory loss, loss of general mental functioning, and paranoid thinking evident in some potheads.



Why isn't there more proof that marijuana causes brain damage?

Drug users demand proof that marijuana causes brain damage. What they fail to understand, however, is that studies to provide such proof are difficult to perform and that, even under to best laboratory conditions, brain cell damage is difficult to identify.

Even where laboratory animals are studied, there are limitations on the evidence of brain dysfunction that can be gathered, because the brains of animals are not as highly developed as humans'. And, even when animal brains can be studied, it is impossible, using present methods of microscopic examination, to inspect damage to cells affecting thought formation. Nevertheless, it is possible to have severe impairment of the brain function that is not visible by visual examination, microscopic examination, or physical testing. It is foolish, therefore, to assume that because damage cannot be seen or fully explained, that it does not exist.

Is marijuana a sexual stimulant?

There has been no research that indicates that marijuana acts as a sexual stimulant. There are reports, however, that among males who have smoked cannabis for five or more years, 20 percent may have impotence problems.

How does marijuana affect the male reproductive system?

Marijuana affects male reproductive function in all species studied.

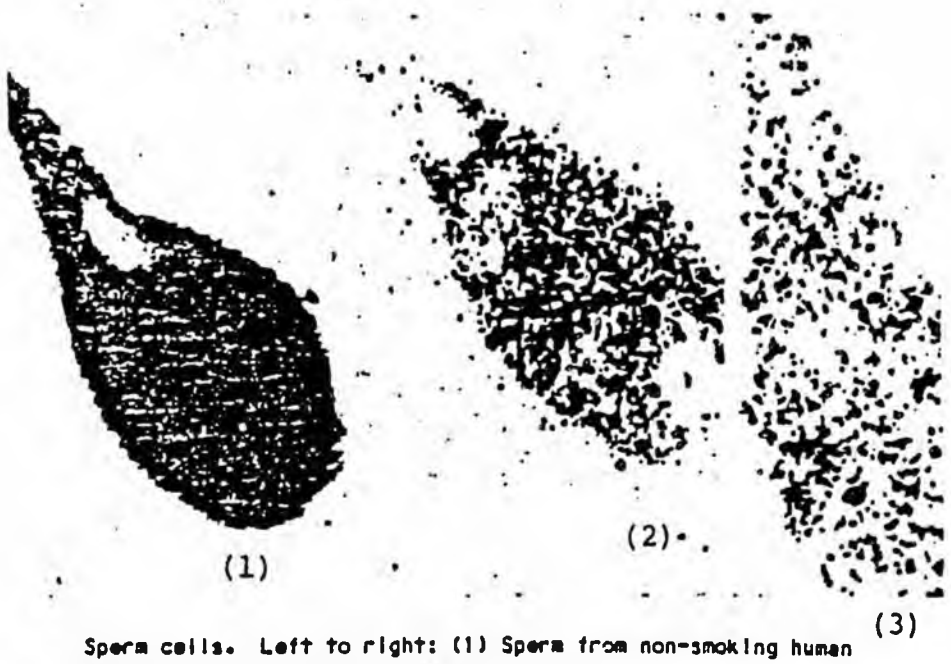
Studies show that THC reduces the amount of LH hormone in males. The LH hormone stimulates the testicles at puberty, causing them to produce the male hormone testosterone. THC produces a longer-lasting and greater depression of LH hormone than morphine, indicating that marijuana is more disruptive to reproductive function than narcotics.

Testosterone levels are reduced in males exposed to THC. The findings of one researcher revealed a five percent decline in testosterone level for each joint (of one percent THC) smoked per week. Scientists are particularly concerned that these results, obtained in mature males, will be even more pronounced and disturbing in adolescent males who are developing sexually.

Because their testicles are producing less testosterone, males exposed to marijuana may observe a decrease in the weight and function of their reproductive organs. And, because the male also produces female hormones, alterations in the balance of hormones has lead to reports of breast development in adolescent males who smoke pot.

The THC in marijuana is absorbed into the testicles and accumulates there. There is evidence that pot causes a significant decrease in sperm count and sperm motility. Thus, the fertility of pot smokers could be decreased. There is also an increase in the number of abnormal sperm. There is a possibility that abnormal sperm could lead to formation of a deformed fetus. Evidence is beginning to emerge that when the male parent alone is exposed to marijuana, there is a significant increase in the number of offspring born with deformities.

There have also been observations that in male animals exposed to marijuana, there is reduced sexual behavior. This is consistent with reports from other parts of the world that human males who use marijuana heavily develop impotence problems.



Sperm cells. Left to right: (1) Sperm from non-smoking human male. (2) & (3) Sperm from chronic hash smokers.

Does marijuana pose special problems for the teenage male reproductive system?

Marijuana's depressing effect on the production of male hormone is one of the greatest risks for adolescents, because a healthy balance of hormones is crucial for normal physical development of young men. The sexual maturation of adolescent boys depends largely on increased testosterone production. However, marijuana may restrict the normal growth of sperm-producing cells, causing under-developed testes. Such results have been produced in laboratory animals treated with THC during puberty. Physicians are concerned that depressed testosterone levels in teenage boys is responsible for the thin body, narrow shoulders, lack of chest, arm and buttocks muscle development, facial pallor and stunted beard growth that is frequently observed in pot-smoking teenage boys.

The study that follows was reported in the Journal of Pediatrics, June, 1980. It demonstrates that, for some boys, the bumper sticker is correct -- "If You Smoke Pot, Your Banana Will Rot".

MARIJUANA SMOKING AND PUBERTAL ARREST

CASE HISTORY

This boy was evaluated at 16 2/12 years of age for short stature and delayed puberty. He had always been in excellent health, growing at the fifth percentile until the age of 11 years when his height fell to below the third percentile. Family history revealed that his mother, who is 167 cm tall, had menarche at 12 years, and his father, who is 188 cm tall, had no delay of puberty. A 14-year-old sister who is pubertal but premenarchal, and an 8-year-old half-brother are in good health.

Pertinent laboratory and physical findings at the first and subsequent examination are summarized in the Table. On the first examination, the

patient was prepubertal in spite of unequivocal testicular enlargment. Six months later, he was found to have had progression of testicular growth without signs of androgen effect. His serum testosterone concentration remained low. At this visit, it was discovered that since the age of 11 years, the patient had smoked at least five marihuana "joints" per day, condoned as well as supplied by his mother. Despite a short period of abstinence followed by a reduction in marihuana exposure for five months, he continued to have testicular enlargment discordant with signs of androgen effect. Studies in addition to those listed in the Table included normal visual field and funduscopic examinations, a bone age of 13 years (at chronologic age of 16 8/12 years), and normal skull radiographs, electrolytes, BUN, creatinine and urinalysis. Prolactin and immunoreactive somatomedin-C values were normal (3.7 ng/ml and 0.86 U/ml, respectively).

			Testicular measurements			Public				
Age (yr)	Height (cm)	Penis (L x W) (cm)	Right (LxW) (cm)	Left (LxW) (cm)	Volume (ml)	Hair Stage (Tanner)	Testosterone (ng/dl)	Serum LH (mIU/ml)	Serum FSH (mIU/ml)	Marihuna Smoking (Joint/day)
16 2/12	152.7	6x2	3.2x1.8	3.0x1.8	6	I	16	-	-	5
16 8/12	154.6	7x2	3.3x2.0	3.2x2.1	8	I	32	2.9	1.9	5
16 9/12	-	-	3.6x2.2	3.4x2.2	9	I	47	4.3	2.2	0 (for 19 days)
17 1/12	156.7	7x2	4.1x2.1	3.8x2.0	12	I	82	4.1	3.0	1
17 3/12	159.3	9x2	4.6x2.4	4.1x2.2	-	-	392	5.7	2.5	0

* All measurements were made by the same observer.

How does marijuana affect the female reproductive system?

Marijuana affects the female reproductive system in a variety of ways:

* Studies show that marijuana users have three times as many defective monthly cycles as nonusers.

* Evidence from animal and human studies suggests that use of marijuana several times a week or more may reduce fertility.

* Animals treated with THC show marked decreases in uterine and ovarian weights as a result cf shrinkage of the organs.

* Marijuana accumulates in the ovaries. The ovary contains a girl's lifetime supply of only about 400,000 eggs at birth, so damage of an egg by marijuana is permanent, and raises the possibility of genetic damage.

* THC decreases the level of important reproductive hormones LH, FSH, and prolactin. Prolactin is a hormone important in producing mother's milk. Nursing could be impaired in marijuana-

using women following childbirth. Many other studies on female animals show that marijuana reduces the level of estrogen, the principal female sex hormone.

* Cannabinoids concentrate in the cells of the breast, and are transferred to the offspring in animals. Some infants have been bombarded with cannabinoids during pregnancy and after through their mother's milk.

Has the number of children born with birth defects increased in the past few years?

Physicians and statisticians who analyze the patterns of birth in the United States have concluded that the number of babies born with physical or mental defects has doubled over the last 25 years. Could marijuana have anything to do with this increase?

"Today's pot smoker may not only be damaging his own mind and body, but may be playing genetic roulette and casting a shadow across children and grandchildren yet unborn."

- Dr. Gabriel Nahas

"It certainly seems that cannabinoids are mutagenic -- they can transmit abnormalities across the generations."

- Dr. Susan Dalterio

Can marijuana harm a developing fetus?

Marijuana's chemicals pass from the mother to the developing fetus in her uterus. As a result, there is a distinct possibility that marijuana use could result in abnormal development.

;TUDY LINKS POT TO
;IRTH DISORDER

Washington -- A federally funded udy at Boston City Hospital has nked marijuana use by pregnant women a serious disorder in their babies own as "fetal alcohol syndrome". Fatal alcohol syndrome infants typally have a cluster of facial abnorlities and often are mentally rerded.

World Herald

In a study in Boston completed in 1982, it was found that babies whose mothers used marijuana during pregnancy were five times more likely than normal to be born with birth defects. The children had features that were similar to those found among women who drink during pregnancy (Fetal Alcohol Syndrome), although the defects occurred more often among pot smokers' babies than among drinkers' babies. While the defects such as specific facial deformities were apparent to

doctors upon the babies' births, there was no way to assess possible damage to the brain. However, researchers are concerned that mental retardation could also occur with greater frequency among the babies of pot smokers.

Even seemingly normal offspring could carry genetic defects which could affect their children as a result of their parents' drug use. When laboratory animals of one generation were exposed to cannabis during pregnancy, birth defects were found in the third generation, suggesting that a gene change had been transmitted through the second generation animals, which had not been exposed to pot except before their birth.

THC, even when given to pregnant animals at doses too small to produce visible defects, may produce changes in the behavior and development of the children. There is evidence that the offspring of mothers given marijuana during pregnancy show learning disabilities. Other studies have shown that when THC or other cannabinoids are given briefly to pregnant or nursing females, abnormal hormone changes occur in the male offspring when they go through puberty. Sons exposed to pot by their mothers are deficient in testosterone and have smaller testicles. At adulthood, the males are not interested in mating, are infertile or impotent. Much like a castrated animal, they are grossly overweight. In addition, there is evidence that there are chromosomal abnormalities which could be passed on to future offspring. There are similar reports of delayed sexual maturation in human males under similar circumstances. These adolescents show sparse beard growth and smaller testes.

Pot smokers' babies are more likely to experience difficulties at birth. They are more likely to suffer from stress and are more likely to need oxygen immediately after birth. Some are born stoned, with THC appearing in the umbilical cord blood. In animal experiments, up to 44 percent of all offspring conceived by THC-treated females are lost before or shortly after birth due to spontaneous abortion or stillbirth.

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CONGENITAL ABNORMALITIES OBSERVED IN BOSTON CITY HOSPITAL STUDY

ajor abnormalities

- Cleft palate
- Hypospadies
- Imperforate anus
- Vertebral anomalies
- Cardiac abnormalities
- Chromosomal abnormality
- Tuberous sclerosis
- Stenotic/atretic ear canals

inor

Head
- Large fontanel plus metopic sutures or third fontanel
- Small fontanel plus metopic sutures or third fontanel
- Large fontanel plus widely space sutures
- Micognathia

Ears
- Abnormal shape
- Low-set ears
- Posterior slant 10°
- Ear tags
- Ear pits

Mouth
- Prominent lateral bridge
- Highly arched palate
- Tounge enlargement
- Carp-shaped mouth

Eyes
- Epicanthic folds
- Slanted eyes
- Wide-spaced eyes

Nose
- Prominent bridge
- Anteverted nostrils
- Abnormal philtrum

Neck
- Short
- Excessive skin folds

Chest
- Accessory nipple
- Wide-spaced nipples

Abdomen
- Inguinal hernia

Genitourinary/anal
- Sacral dimple
- Sacral hair
- Lumbosacral sinus
- Hydrocele
- Large clitoris
- Small penis

Extremities
- Hypoplastic finger or toenails
- Clindactyly
- Syndactyly
- Increased space, toes 1 + 2
- Extra digits
- Metatarsus adductus
- Toe overlap
- Malpositioned toes
- Club feet
- Rocker bottom feet

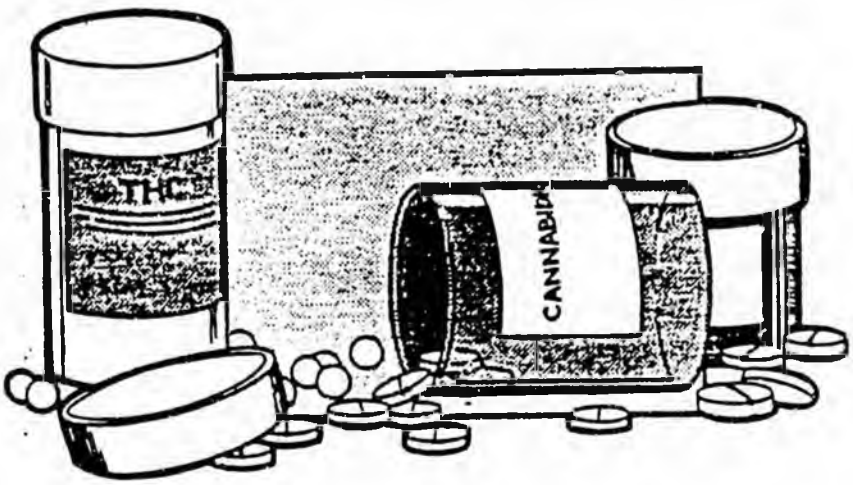
Skin
- Cafe-au-lait spots
- Hypopigmented spots
- Hemangioma
- Lipoma
- Hyperpigmented spots

How does marijuana affect cells in the body?

Changes have been found to occur in the membranes of brain cells, red and white blood cells, and sperm cells due to accumulation of THC in the body.

Many birth defects are related to abnormal number or structure of chromosomes in dividing cells. There are reports of breaks in chromosomes occurring in cells obtained from pot smokers. Other experiments show, however, that pot is more likely to cause abnormally low numbers of chromosomes than chromosome breaks. One study revealed that 30 percent of the white blood cells in marijuana users had reduced numbers of chromosomes compared to normal cells with 46 chromosomes.

THC also depresses cell division. Even small amounts impair manufacture of DNA. The observation that marijuana interferes with DNA in cells and chromosomes indicates that it disturbs the genetic balance of the cells. By altering hereditary DNA, THC could cause genetic mutations.



Does marijuana use effect the immune system?

Animal data consistently show a definite suppression of test animal's immune responses after they use marijuana.

Isn't marijuana being used as medicine?

There isn't such a thing as "marijuana" as medicine. Almost always, studies on the medical use of "marijuana" are studies using THC, or other single chemicals derived from the plant.

Marijuana is a mishmash of chemicals. Most of its chemicals do not have any benefit, and others produce undesirable effects such as bronchial irritation. Even if marijuana does prove to have some medical value, it is unlikely that it will ever be sold as a medicine.

On the other hand, THC appears to show some promise in the prevention of nausea and vomiting that accompany treatment of cancer using chemotherapy. THC weakens the brain's reflex to vomit when a person is poisoned. Some cancer patients say THC reduces the sick feeling their cancer treatment produces. However, marijuana does absolutely nothing to prevent or cure cancer. If anything, it weakens the body's natural defenses against cancer or other diseases. Knocking out the brain's vomiting reflex in a healthy person could cause the person to lose a natural defense against poisoning or drug or alcohol overdose.

Because THC may lower pressure inside the eyeball, it may be useful in treating an eye disease called glaucoma. However, its effects on the heart make the drug a poor choice for elderly patients, the group most likely to need glaucoma treatment. Most eye specialists believe other drugs treat glaucoma better than THC and with fewer side effects. And, many eye specialists also believe that smoking pot might do the glaucoma patient more harm than good by causing serious eye damage.

> "We must not allow a pro-pot publicity campaign to fool the American people into thinking that marijuana is being used as medicine and is, therefore, a safe drug."
>
> - Dr. Carlton Turner

How is marijuana different from alcohol?

Marijuana is different from alcohol in the following ways:

1. THC stays in the body for a long period of time. Alcohol is a water-soluble drug which is washed out of the body relatively quickly. Somebody who drinks too much will get sick and suffer from a hangover the next day as his stomach and liver work to quickly process the alcohol. Most of the alcohol will have left the body within 12 hours. THC, however, is not water-soluble, and its chemicals remain absorbed in the brain, lungs, and reproductive organs for weeks.

2. Marijuana has respiratory irritant effects and the probable effect of causing lung cancer.

3. Marijuana is very unpredictable, because of the huge variation in effects of 421 different chemicals in the body.

4. Marijuana is illegal.

Why shouldn't marijuana be legalized?

Marijuana today is an illegal substance in all 50 states and there are severe criminal penalties for dealing or intending to deal the drug. Cannabis and cannabis products are currently controlled in Schedule I of the 1960 Single Convention on Narcotic Drugs, an international treaty signed by 75 countries, in which it is agreed that marijuana, as well as other drugs, will not be legalized. Schedule I is the most restrictive schedule in the Single Convention. Other drugs included in Schedule I are heroin, morphine and cocaine.

Some people believe that marijuana should be legalized. If marijuana were legalized, a new intoxicant would be made available for use by the population, and there would be greater access to the drug. Once a new drug is accepted by the public, it is difficult to later prohibit its use. That is the lesson learned from Prohibition, when alcohol was considered an illegal drug. How many drugs can be available for general use and still maintain a vigorous and productive society? How will children in the future be able to grow up in a chemical culture?

If marijuana smoking is dangerous, then public policy should not support any policy which encourages increased use of the drug. Many people would incorrectly believe that if marijuana is legal, then it must not be too dangerous, just as people ignorantly assume that alcohol is not "too bad" or else it would be illegal.

It also needs to be made very clear that there is no n
for legislation to make marijuana available for medical
purposes. The legislation now on the books is more tha
adequate to make available any chemical ingredients in
marijuana that might be needed. The use of "marijuana
medicine is not relevant to legalization of the drug f
social use. For example, there are medical uses for m
and cocaine, but their non-medical use is prohibited.

Why not decriminalize marijuana?

Decriminalization is sort of a weird concept. Decriminalization means that the penalty for possession of marijuana is reduced from a jail sentence to a fine. Several state legislatures decriminalized marijuana in the '70s when many people thought pot was a mild drug. Since 1978, no additional states have decriminalized marijuana, although judges have not typically sent people to jail for possessing marijuana in the remaining states where possession of marijuana can still result in a jail sentence.

The problem with decriminalization is that it makes people believe that marijuana must not be "too bad", otherwise the legislature wouldn't have reduced penalties. By decriminalizing the possession of marijuana, the possessor is given more latitude in dealing with criminal suppliers. (Selling marijuana is a criminal offense in all states.) From the dealer's point of view, decriminalization is a boom for business, because his customers are not as reluctant to buy his product. Decriminalization doesn't do anybody any good except for the pothead adults who don't like to obey the law.

What about countries where marijuana has been used for years?

Decades of experience with marijuana in other countries is not necessarily relevant in the United States where a stronger form of pot is used, primarily by young people in their formative years, and where patterns of inhalation are likely to differ. (Eastern smokers don't inhale pot smoke as deeply as Americans). It may be 20 years or more before the necessary studies can be conducted on American heavy users to demonstrate the health effects of marijuana as it is used in the United States.

What about paraquat?

People read about paraquat everytime the government tries to spray illegal marijuana fields with the herbicide. They never hear about it when each year 10.7 million acres of American farmland is sprayed with the chemical. About four million pounds of paraquat is used each year on all kinds of legal fruits and vegetable plants, because it is the most widely used herbicide in the world. The United Nations Fund for Drug Abuse and Control recommends paraquat to all

nations as the safest, most effective agent for the control of marijuana and the government has not documented a single case of human paraquat poisoning from smoking marijuana. The big fuss about paraquat comes from marijuana growers and smokers who really aren't worried about health. (If they were, they wouldn't smoke the stuff anyway.) What they are worried about is the economics of supplying an illegal drug.

Is marijuana an addicting drug?

More and more cases are being reported of people who have trouble stopping a pot-smoking habit. This is not surprising, since marijuana contains powerful "self-reinforcing" chemicals that stimulate the pleasure center of the brain. Once brain cells are stimulated by a pleasure-producing drug, they are imprinted with a chemical "memory" that is associated with a pleasant feeling. This creates a desire to smoke more pot. Teenagers who are "hooked" on pot increase the amount of the drug they smoke because they build a tolerance to it in their bodies. They begin to smoke alone and in hiding. Their personality changes when they are "high". They are unable to control the amount they use, they are preoccupied with pot use, and they continue to use pot in spite of the adverse consequences occurring to them as a result of their drug use. This is evidence of psychological dependency.

Now there is also evidence of withdrawal symptoms when heavy users stop smoking, which indicates that marijuana is a physically addicting drug. Very high, frequent doses of THC produce withdrawal symptoms which include irritability, sleep problems, digestive upsets, and loss of appetite.

Today, marijuana accounts for the second largest number of admissions to drug treatment centers in the United States. The Drug Committee of the World Health Organization has concluded that marijuana fits its definition of an addictive drug.

Do users develop tolerance to marijuana?

It is well-known that pot smokers develop tolerance to the drug's effects. Tolerance to marijuana provides a physical basis for the necessity of the heavy smoker to smoke more pot or to use more potent drugs such as LSD, cocaine or heroin.

Are pot smokers more likely to use other drugs?

Often the first step in becoming involved with drugs is use of marijuana. Marijuana users tend to use other drugs to a significantly greater degree than nonusers. The earlier marijuana use begins, and the heavier it becomes, the stronger this tendency is.

High school seniors who smoke marijuana on a daily basis use other illegal drugs five to seven times more often than the rest of the senior class. People who hang out with people who are using marijuana find they have a whole variety of other drugs being offered to them all the time. And, people who are "high" on pot have impaired judgment, which makes them more likely to consider trying other illegal drugs.

MARIJUANA IS DESTROYING MY LIFE

...For the past three years, I've been smoking pot and thinking I was enjoying it. I'd always heard it was non-addictive. This is not so -- I find I'm psychologically dependent on the drug.

I used to smoke when I felt sad or angry to make myself forget what was bothering me. I soon found I was spending two-thirds of my weekly wages from the checkout counter on pot. I now have a hard time remembering things and I'm starting to stutter.

But that's not half my problem. My best friend has given up on me, and the girl I love is soon to follow. It's surprising that I have any friends at all since I've developed a mean, paranoid streak. At 18, I feel like a worthless bum. I've tried to stop smoking pot plenty of times but only made it for a month at the most. The drug counselors at school are no help.

Star
Oct. 5, 1982

How can you help someone who is using pot?

Like an alcoholic, a chronic pot user does not usually understand the role that marijuana plays in his problems. The user must recognize his problem and decide to stop. He must reorganize his life so that it no longer revolves around marijuana, and he must form new friendships and find new sources of satisfaction that are not drug-related. To help a chronic user who may be addicted to marijuana, you need to become part of a professionally guided intervention team which might include parents, teachers, doctors, counselors, friends, etc.

When experimenting, some people tend to stop smoking pot when they get the medical facts about what the drug is doing to them. Even if, when they stop, they get better. Quite often, that is enough to convince them to stay straight. Once the person is off pot, he can see very clearly that his pot-smoking friends, in spite of what they say, are going nowhere, except downhill.

Nevertheless, even if the marijuana user is convinced that the lifestyle of a pothead and the effects of pot are not what he wants out of life, he is likely to encounter difficulties with friends who are users and who try to pressure him into joining in the "fun" when the joint is being passed around.

See section B of this manual for a more detailed explanation of how you can help a user choose a more productive lifestyle.

All these things suggest important ways that friends can help the marijuana user out-grow marijuana.

27% of those high school seniors who report daily marijuana use, also report daily alcohol consumption, versus only 7% for this age group as a whole.

59% of high school seniors who report daily marijuana use report daily tobacco smoking, versus only 25% for the age group as a whole.

47% of high school seniors who report daily marijuana use report they are current users of amphetamines, generally 4-7 times the average for this age group as a whole.

31% of high school seniors who report daily marijuana use report that they currently use cocaine, generally 5-7 times the average for this age group as a whole.

How do people get high?

People who are "high" are "high" because the part of the brain that gives them memory and intelligence is weakened. The part that registers pleasure is on the loose. That may sound like fun. The problem is that since there is a chemical in the brain that isn't supposed to be there, the brain can't operate the way it is supposed to. When the part of the brain that supplies will power and thought and reason loses control, you've lost control. That's why people who smoke dope can't tell it's affecting them. The only part of the body that can help them see what it is doing to them is itself affected by the drug. At the same time, THC stimulates the limbic (or pleasure) area of the brain, reinforcing the desire to use more dope.

How do people become burnouts?

Burnouts don't become burnouts because they want to be that way. For them, the natural ability to regulate mental functions was lost to THC. They can only return to a normal state when they abstain from using marijuana. Unfortunately, they don't want to abstain because their brains have become so accustomed to THC that they are incapable of experiencing normal pleasure without that alien chemical stimulation.

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State of California

Department of Justice

George Deukmejian

(Pronounced Duke-May-Gin)

Attorney General

CANNABIS:

ADVERSE EFFECTS ON HEALTH

The government of Canada has indicated its intention of introducing new legislation concerning marijuana. All three major parties appear to be agreed that changes are needed. The Addiction Research Foundation understands that a public debate on the issue is likely to take place during the coming year, prior to the introduction of new legislation. One important consideration in the debate will be the consequences to health of cannabis use. The Foundation is anxious to ensure that reliable information on this subject is widely available and to this end has asked scientists on its staff to prepare the following summary.

John B. Macdonald
President
Addiction Research Foundation, Toronto

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Introduction

Since the mid-1960s, the increasing popularity of marijuana use has underscored the need for a valid and objective evaluation of the effects of this drug on health. Much contradictory opinion has been expressed on this matter. The reasons for this are rather simple. First, knowledge of these effects of marijuana is relatively scanty compared to the knowledge on other drugs such as alcohol and tobacco. Second, and probably more importantly, marijuana use, its effects, and the legal controls on its use have created ideological issues that have been quite unnecessarily confused with facts.

The Addiction Research Foundation (ARF), and individual members of its staff, have made periodic statements on marijuana since 1968. Furthermore, the Foundation has studied the problem continuously since 1965, and maintains one of the most complete archives on the marijuana literature anywhere in the world. At present, this amounts to about 5,000 articles, approximately 1,200 of which deal with the effects of the drug on health. This statement is based on a thorough study of this material, and on direct expertise of members of staff on specific experimental areas. We have assessed the evidence on marijuana according to the same medical and scientific standards that we apply to the evaluation of the effects on health of all other drugs, including alcohol. This is important, because much of the confusion about cannabis results from the use of different standards of assessment.

The statement is made at this time to assist in the public discussions that are likely to occur when the Government of Canada deals with a bill to alter the present marijuana laws.

The Drug

Marijuana and hashish are derivatives of the cannabis plant which has been cultivated for centuries for its fibre, oil, and psychoactive resin. There are more than 400 known chemical constituents in this plant. More than 60, known as cannabinoids, are found only in cannabis. One of these is delta-9-tetrahydrocannabinol, also referred to as delta-9-THC. It accounts for the major psychoactive effects of the plant. There are two varieties of the cannabis plant. One is resin-

producing and the other is fibre-producing. THC is found most abundantly in the upper leaves, bracts, and flowers of the resin-producing variety. Marijuana, the dried leaves, may contain up to 5% of this compound; hashish, the dried and pressed flowers and resin, up to 12%; and hashish oil, a crude extract of hashish, up to 60%. The fibre-producing variety has much lower concentrations of THC.

In the liver, THC is rapidly changed to a compound called 11-hydroxy-THC, which is also psychoactive, and to more than 20 other products that are inactive. Until recently, there were no reliable methods for estimating the concentration of THC and its breakdown products in body fluids, other than the measurement of radioactivity in blood and tissues after the administration of a dose of radioactive THC. Measurement of THC and "total cannabinoids" is now possible by either radioimmunoassay or gas-liquid-chromatography/mass-spectroscopy, but these methods are available only in a few research laboratories. This fact has seriously limited the study of the fate of THC and its breakdown products in humans, including the question of how long the THC remains in the body.

Accumulation of THC in the body fat has not been demonstrated unequivocally in humans, and has been observed only under very specific conditions in animals. Furthermore, long retention in the body does not necessarily imply toxicity. However, if a substance is inherently toxic, a long retention-time will increase the risk of cumulative toxicity in the regular user.

Some of the actions of cannabis are unquestionably toxic in that they either directly or indirectly can produce adverse effects on health, but others may be beneficial in certain situation. The use of marijuana, THC, and similar synthetic chemicals, either alone or in combination with other drugs, is currently being investigated as a possible treatment for epilepsy, wide-angle glaucoma, anorexia nervosa, asthma, and the relief of nausea and vomiting produced by anti-cancer drugs. The latter effect is the most promising of the possible therapeutic applications.

The therapeutic use of cannabis is not directly relevant to decriminalization of cannabis. This is clearly shown by the fact that

the medical use of morphine and cocaine is legal, while their non-medical use is prohibited. In contrast, the adverse effects of the non medical use of cannabis clearly constitutes one of the factors that the government will take into account in its debate on possible changes in the present laws. This document focuses on the known and potential health hazards of cannabis following both acute (single dose) and chronic (multiple dose) use. Heavy use is defined here as at least daily use of high potency cannabis. Where relevant, these effects will be compared to those of others psychoactive drugs.

Damage to health induced by any drug is often first suspected by observant physicians on the basis of individual cases. A casual relationship is usually indicated by a higher rate of occurence of the damage among users than among non users of the drug. Experimental prpof that the drug causes a particular health problem is relatively uncommon; for example, there is no experimental proof that alcohol causes liver cirrhosis or tobacco smoke causes lung cancer in humans, even though the connection is clinically and statistically clear. However, conclusions about the frequency of occurrence of a particular health problem among users of the drug can be reached only through large-scale epidemiological studies. Important but relatively infrequent problems, such as lung cancer in cigarette smokers, or liver cirrhosis in alcoholics, can not be detected in studies of a few dozen users, but may require observation of a whole population over many years. So far, our knowledge concerning cannabis is at the level of case reports, some experiments, and small group studies, but the crucial epidemiological observations are still lacking.

Behavioral and Mental Effects

In most individuals, the social use of low to moderate doses of cannabis produces euphoria, a pleasant state of relaxation, altered perception particularly of distance and time, impaired memory of recent events, and impaired physical coordination. The state of intoxication is usually mild and short-lived (two to three hours after one joint). An occasional "high" is probably not physically hazardous unless the user attempts to drive, fly, or operate heavy machinery during the state

of intoxication. It is now well recognized that even reaction time, in judgment probably account for these observations. Until a reliable, inexpensive, and simple method for the estimation of blood levels of THC and its breakdown products, comparable to the breathalyzer test for alcohol, is widely available, the detection of cannabis-intoxicated drivers will remain a major problem.

In some users, an acute dose of cannabis can produce adverse reactions ranging from mild anxiety, through panic and paranoia, to an acute toxic psychosis characterized by detachment from reality, delusions, hallucinations or illusions, and bizarre behavior. These reactions occur most frequently in individuals who are under stress, anxious, depressed, or borderline schizophrenic, and in normal users who inadvertently take much more than their usual dose. Limited evidence from survey studies suggests that the mild reactions have been experienced on one or more occasions by more than a half of regular users, although their exact frequency is unknown. They are mainly self-treated and usually go unreported. The severe reactions, which appear to occur in only a small percentage of users, usually respond well to non specific psychiatric treatment and last no longer than one or two days.

There has been a great deal of controversy about the effects of chronic heavy use of cannabis on brain function. There is evidence that chronic use can lead to lasting behavioral changes in some users. Apathy, lack of concern for the future, and loss of motivation have been described in some heavy users, and psychotic and paranoid symptoms in others. These symptoms usually disappear gradually when regular drug use is discontinued, and recur when use is resumed. These reactions are relatively rare, although case studies suggest that certain cannabis users may be particularly susceptible. Many psychiatrists are concerned about such reactions in youthful drug users (11 to 15 years of age), because of the possibility that regular use may produce adverse effects on psychological, as well as physical, maturation. This concern, of course, applies to the use of all psychoactive drugs by juveniles. For reasons that are still unclear, a few users experience spontaneous recurrences of the symptoms of acute intoxication ("flashbacks") days or weeks after consuming cannabis.

Are there any other changes in brain function that outlast the period of intoxication? Limited clinical evidence suggests that some users do not recover fully when drug use is discontinued. The psychological functioning (perception, coordination, intelligence, etc.) of presumably non intoxicated heavy users has been tested in countries such as Jamaica, Costa Rica, Greece, Egypt, and India. The conclusions from these studies have been conflicting, and confounded in some cases by methodological problems and biased investigators. Studies with the largest groups of subjects (in Egypt and India) have shown significant differences between users and matched non users, while the studies using much smaller samples (in Jamaica and Costa Rica) have not.

Experimental evidence from the ARF laboratory in rats, and elsewhere in monkeys, suggests that long-term exposure to doses of cannabis equivalent to those consumed by very heavy users can produce learning impairment and changes in brain waves that persist months after the end of chronic intoxication. These disturbances are accompanied by subtle changes in brain cell connections that can be seen under the electron microscope. This experimental evidence of brain damage is consistent with clinical observations in humans. On the other hand, the reports of gross brain atrophy, based on air encephalography, have not been confirmed by the more sophisticated tomographic technique ("CAT scan").

Respiratory System

Cannabis is usually smoked, either alone or in combination with tobacco. Smoke is an aerosol, consisting of tiny particles suspended in a vapor phase. The latter consists of gases such as carbon monoxide, while the particles form the solid residue called "tar". Cannabis produces 50% more tar than the same weight of a popular strong tobacco brand. A "joint" is usually smoked to leave as small a butt as possible, thus doubling the tar yield per "joint."

In addition, the tar contains more than 150 poly-nuclear aromatic hydrocarbons, including cancer-producing agents such as benzo(a)pyrene. The concentration of this component in marijuana tar is 70% higher than in the same weight of tobacco tar. Therefore, one cannabis cigarette, totally combusted, yields about five times as much benzo(a)pyrene as

one tobacco cigarette of equal weight, but smoked to a butt of 30 mm. The amount of benzo(a)pyrene retained in the lungs from one "joint" is probably even greater than from five normally smoked tobacco cigarettes, since cannabis smoke is inhaled deeply and held for as long as 30 seconds. Thus, two to three cannabis cigarettes a day may well carry the same risk of lung damage as a pack of tobacco cigarettes.

Cannabis tar, when painted on the skin of mice, causes pre-cancerous changes similar to those produced by tobacco. Cultures of isolated human and animal lung cells also undergo pre-cancerous changes when exposed to cannabis and/or tobacco smoke. In addition, some of these cells, the alveolar macrophages, appear to lose their ability to inactivate bacteria when exposed to certain components of cannabis smoke.

Long-term heavy smoking of cannabis is associated with chronic respiratory symptoms such as sore throat, rhinitis, and bronchitis. Although acute use increases the diameter of the airways, chronic heavy use conversely produces changes suggestive of early obstructive airway disease. In addition, pre-cancerous changes have been found in bronchial biopsies from 20-year-old heavy smokers of hashish and tobacco, that are not normally seen in heavy tobacco smokers under the age of 40. Many cannabis users also smoke tobacco, and the pulmonary toxicity observed is probably a reflection of the total tar inhaled from both sources.

Cardiovascular System

In humans, acute administration of cannabis produces reddening of the eyes, and a dose-related increase in heart rate. In normal individuals, these effects, as well as slight changes in heart rhythms, are transitory and appear to be of little significance. In patients with angina pectoris, however, the increased oxygen requirement associated with the increased heart rate results in an earlier onset of angina pain in response to exercise. The effect of cannabis on patients with irregularities of heart rhythm is not known.

Cannabis-induced changes in blood pressure tend to be inconsistent, although abnormally low pressure in the standing position has frequently been observed.

Chronic administration of large doses of THC to healthy volunteers results in tolerance to the increase in heart rate, decreased blood pressure, and an increased blood volume. The chronic effects of cannabis in patients with cardiovascular disease are not known.

Sex Hormones and Reproduction

Drugs can interfere with reproduction by altering sexual behavior, affecting fertility, damaging the chromosomes of the germ cells of the male or female, or acting directly on fetal growth and development.

Moderate doses of cannabis do not affect sexual behavior consistently, but a decrease in libido has been reported among heavy users in some but not all studies.

Drugs can affect fertility by changing the output of hormones that govern ovulation or spermatogenesis. In male animals, chronic cannabis treatment consistently produces decreased levels of serum testosterone, testicular degeneration, and arrested or abnormal sperm production. The drug appears to act both directly on the testes, and indirectly by suppressing hormone release from the hypothalamus.

In men, the situation is less clear. Decreased testosterone levels (that remain within the lower part of the normal range), decreased sperm counts, and abnormal sperm morphology and biochemistry have been reported in heavy users, although not all investigators have been able to replicate these findings. Differences in experimental methodology probably account for most of the inconsistencies and most investigators now believe that there is some interference with male hormonal function, but this is less marked than with heroin or alcohol. The clinical significance of small decreases in serum testosterone levels in healthy males is probably minimal. These changes may be more significant during intrauterine development of the male fetus, during adolescence, or in adult males with borderline testicular function.

In female animals, THC is known to suppress ovulation by interfering with the hypothalamic release of luteinizing hormone, but tolerance to this effect develops on chronic administration. Virtually no research

has been done in women, but there is preliminary evidence that cannabis smoking is associated with intermittent failure of ovulation. For ethical reasons, it has not been possible to study this effect in controlled experiments.

In some but not all studies, the chromosomes in white blood cells isolated from cannabis users have shown increased rates of breakage and other damage. This is a common finding among users of many street drugs, and more likely reflects the general lifestyle of the users, than the effect of any particular drug. Furthermore, it has never been established that chromosome damage in white blood cells indicates genetic damage in the egg or sperm cells or predicts an increase in the number of abnormal births.

THC does not produce genetic mutations in the test systems studied to date, although other components of the smoke are mutagenic. In animals, reported birth defects appearing in the third generation, after exposure of the first generation to cannabis smoke during pregnancy, suggest that the possibility of genetic damage cannot be discounted.

The ability of cannabis to produce birth defects has been studied in many animal species. Although THC crosses the placenta, very high doses must be given to produce visible abnormalities. However, cannabis smoke containing lower doses of THC has been shown to produce fetal toxicity including an increased number of fetal resorptions, decreased fetal weight, and an increased death rate around the time of birth. This suggests that components other than THC, such as carbon monoxide, are responsible for these effects.

In addition, THC, when given to pregnant animals at doses that are too low to produce visible abnormalities, can produce subtle changes in the behavior and development of the offspring.

Information in humans is scanty. In Eastern countries cannabis has been consumed almost exclusively by males, so that observations on pregnant women are lacking. There have been a few case reports in Western countries of deformed babies born to mothers who had smoked cannabis during pregnancy, but no cause-and-effect relationship can be determined on the basis of this evidence. Further research is

needed, particularly follow-up studies of behavior and development in the infants of marijuana smokers.

Immune System

THC and cannabis extracts and smoke, when given to animals at behaviorally relevant doses, suppress immune reactions. In humans, many but not all studies indicate that heavy use of cannabis may interfere with the function of one component of the immune system--the T-lymphocyte. This component is known to play a role in the resistance to viruses and to cancer. The combination of inhaled carcinogens and depressed T-lymphocyte function could entail a greater risk of cancer. An increased frequency of cancer has not been apparent in countries where cannabis use has been traditional; however, until recently the average life-span in these countries was relatively short, and the users may have died of other causes before cancer had time to develop. The question of decreased immunity in chronic users must be examined in North America and Europe by careful epidemiological studies.

Macromolecular Synthesis

THC and related compounds inhibit the intracellular synthesis of complex biological molecules, including proteins, DNA, and RNA, and inhibit cell division in test-tube experiments. Alcohol and opiates have similar effects. Some investigators have suggested that this inhibition may be responsible for the impaired immune response noted above, and for other effects observed in chronic users. The biological relevance of these test-tube effects is still unclear, because the dose required to produce them in the body is unknown and the consequences of such effects are often difficult to recognize.

Tolerance and Dependence

It has been known for many years that tolerance to some effects of cannabis occurs rapidly in animals, i.e., the drug effects become less intense on repeated administration. In experiments, frequent administration of high doses of cannabis or THC in humans produces tolerance similar to that observed in animals. For example, increasingly

high doses must be given to obtain the same intensity of subjective effects and increased heart rate that are observed initially with small doses.

Frequent high doses of THC can also produce mild physical dependence. Healthy subjects, given by mouth the equivalent of several "joints" a day, or volunteers who smoke comparable amounts, experience irritability, sleep disturbances, weight loss, inhibition of appetite, sweating, and gastrointestinal upsets when the drug is discontinued abruptly. Although this is a true abstinence syndrome, the intensity of the symptoms is not as marked as that produced by moderate chronic doses of other drugs such as alcohol, the barbiturates, or the opiates.

Heavy use of cannabis is also associated with psychological dependence which is responsible for sustained drug-seeking behavior. The existence of compulsive users has been well documented, although the percentage of cannabis users that reach this stage is unknown and probably rather small, as is the case with most other psychoactive drugs.

Miscellaneous

A number of minor effects of cannabis have been reported in humans and in experimental animals. These include gastrointestinal disturbances, reduction of gastric acid secretion, and weight loss in heavy users; true allergic reactions to cannabis and some of its individual constituents; and an increase in the difficulty of medical control of diabetes. Despite the fact that single doses of some constituents of cannabis can suppress seizures, some epileptics actually have more seizures when smoking marijuana. The mechanisms of these effects are not known, nor is their frequency of occurrence, though it is probably low.

Conclusions

Clinical observations from many parts of the world have long suggested that regular heavy use of cannabis may produce lung damage, impair reproductive and endocrine functions, cause long-lasting disturbances of behavior and brain function, and lower resistance to

infection. Well-controlled animal experiments have demonstrated that cannabis, in high dosage, can indeed produce such effects. It is probable that most of the remaining discrepancies among experimental findings will be resolved by standardization of experimental methods, and by the development of accurate sensitive methods for measuring the levels of THC and other cannabis constituents in blood and tissues, so that the exact degree of drug exposure is known.

What is not yet known, however, is the frequency with which these health problems occur among cannabis users, the degree of use needed to produce them in humans, and the percentage of users at risk. Sophisticated epidemiological studies of large populations of users, such as those already done in relation to alcohol and tobacco use, are needed to fill in these gaps in our knowledge. It may also be necessary to carry out studies on large groups of individuals, monitored before, during, and after many years of cannabis use. It is probable that any specific health problem due to cannabis will have a low incidence and prevalence among the total population of cannabis users, and that it will therefore take a generation or more of wide-ranging public health observations to provide a clear picture. This was true of alcohol and tobacco problems, and there is no reason why it should be different for cannabis.

It should also be emphasized that almost all of the available experimental data arise from studies of young healthy adult males. While some of the changes noted above may be relatively unimportant in a healthy young person, they may be very significant in an individual at risk because of age or pre-existing disease. For ethical reasons, however, these individuals cannot be studied experimentally. We feel that people especially at risk with even moderate doses include anxious, depressed, or unrecognized psychotic individuals; heavy users of other drugs; pregnant women; some epileptics; diabetics; individuals with marginal fertility; and patients with chronic diseases of the heart, lungs, or liver. In addition, as with any other psychoactive drug, adolescents who are undergoing rapid physiological and psychological development may be particularly susceptible to the development of a life-long pattern of use, and to the effects of long periods of cannabis

intoxication. They may also be more prone to cannabis-related traffic accidents because of their lack of driving experience, and may be affected more by possible disruptions of hormone balance.

(THE ABOVE ARTICLE WAS COPIED FROM THE JANUARY 1980 ISSUE OF "THE JOURNAL" AND WAS PREPARED BY SCIENTISTS OF THE ADDICTION RESEARCH FOUNDATION OF ONTARIO.)

NATIONAL ORGANIZATION FOR THE REFORM OF MARIJUANA LAWS

NORML

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March 17, 1988

Karla Hart
House Research Agency
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Juneau, AK 99811-3100

Dear Ms. Hart:

As per your request, I have researched the scientific basis for the various findings listed in Senate Bill No. 32 (Hess). NORML's comments, with appropriate citations, are listed below after each finding.

Many citations refer to the first chapter of the National Academy of Sciences report, Marijuana and Health, edited by Arnold Relman, M.D. I have enclosed a copy of the entire first chapter so you can evaluate our claims in context. I have also included an pre-publication article about marijuana's potency, a copy of the recent study by Dr. Tashkin on marijuana and smoking, and several copies of a recent "Harvard Medical School Mental Health Letter" on the subject of marijuana and health. I have quoted from these articles in my remarks below, but have omitted listing citations contained within those sources. Additional citations can be garnered from the full copies enclosed.

1) *Marijuana... may contain over 420 different compounds.*

There is no correlation, let alone a causal relationship, between the number of compounds a substance contains and its capacity to pose a serious health hazard. However, it must be pointed out that refined pharmaceuticals tend to be more toxic and hazardous to the body than natural substances - which tend to be more easily metabolized. Coca leaves and opium, for example, are less toxic than their refined by-products, cocaine and heroin. It could be argued that the lower the number of compounds present in a substance the more dangerous it is, but this would be equally as fallacious.

Finding number one suggests that the sheer number of compounds present in marijuana make it dangerous. First of all, it is only "a single cannabinoid, Delta 9 THC, (that) produces almost all the characteristic specific

pharmacological effects of the complex, crude cannabis mixtures."[1]

Secondly, marijuana is not a dangerous drug. A recent textbook for emergency room technicians states that "cannabinoids (marijuana) are very common but of little concern to ER clinicians because of their mild effects."[2]

2) *THC... takes as long as 30 days to be eliminated from the body.*

It is true that extremely small levels of unmetabolized THC remain in the body, however they have no effect on the body. Dr. Arthur McBay, North Carolina's chief medical examiner, holds that the psychoactive components in marijuana are metabolized fairly quickly, whereas the metabolites can be present for 30 days.[3] He also points out that arsenic and lead are present in the human body, but pose no health hazard because of the low amounts involved.[4]

Dr. John Morgan is the Director of Pharmacology at the City University of New York, and has testified before the Senate Judiciary Committee (and elsewhere) as an expert on this subject. He writes that:

> THC is detectable within the urine within 30 minutes of smoking marijuana. It may persist in the urine and in the blood for an appreciable period of time...
>
> (Though) unchanged THC scarcely appears in the urine and falls to extremely low concentrations in the blood within 4 hours of smoking. Although a large portion of smoked or eaten THC will appear in the urine as THC-COOH (the primary metabolite - 11-Nor-delta-9-tetrahydrocannabinol carboxylic acid), the absolute amount is very small. Testing usually detects between 50 and 100 nanograms per milliliter of THC-COOH. A nanogram is one billionth of a gram...

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[1]A.S. Relman (Chairman); Marijuana and Health (Washington D.C.: National Academy Press, 1982), 13.

[2]M. Bishop; J. Duben-Bon Laufen; E. Fody; Clinical Chemistry Principles, Procedures, Correlations (Philadelphia: J.B. Lippincott Company, 1985).

[3]Arthur McBay; "Technical Problems with Urine Testing" (Remarks made at a conference entitled Marijuana Related Problems sponsored by the Council on Marijuana and Health, February, 1987).

[4]Arthur McBay; Personal communication.

> Depending upon the amount of THC in the marijuana and the smoker's efficiency, the serum THC will peak in 15 to 30 minutes somewhere between 100 and 500 ng/ml. A fairly precipitous decline in concentration follows as the THC is distributed from the central compartment (the blood) to the deeper compartment, the rest of the body. The brain is included in the rest of the body. After the THC falls to nearly undetectable concentrations within 3-4 hours (usually less than 2 ng/ml) another process intervenes. Some equilibrium between the THC in the blood and other tissues reenters the blood stream. The concentration of THC in the body now declines very slowly in a second phase... During this lengthy stay in the body, THC is continually metabolized to the THC-COOH which is filtered at the glomerulus and excreted into the urine...
>
> Despite its persistence and its tendency to accumulate in body tissues with repeated dosage, there is no reliable evidence that this burden of THC, much discussed, has any effect on repeated users. The small concentration of THC carried in the blood and storage tissue is below the threshold to provoke an effect.[5]

The National Academy of Science's review of studies reports a variance in the half-lives of Delta-9-THC from 19 hours in experienced users to 57 hours in naive users.[6] Whether the difference is due to the experience of the user was not established, but the range suggests that any buildup of THC or metabolites would also be offset by an increase in the time taken to metabolize the chemicals.

It is incorrect to conclude from finding number two that the active component of marijuana, THC, has the potential to exert its psychoactive effects for a thirty day period. THC has a psychoactive effect only for several hours.

3) *"The buildup... means that... even small doses may lead to an accumulation of the drug higher than levels reached at any time after a single dose."*

In a general sense this is true of any drug, however as explained above the "high" associated with marijuana lasts for approximately four hours. Repeated doses in that time

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[5]J.P. Morgan; "Marijuana Metabolism in the Context of Urine Testing for Cannabinoid Metabolites" (Paper to be published by the Council on Marijuana and Health in the Fall of 1988)

[6]A.S. Relman; (1982), 23.

frame will extend the "high", but not for thirty days. The only way a person can be under the influence of marijuana for thirty days is to smoke marijuana about every four hours for thirty days.

This finding is a virtual quote from the National Academy report.[7] It concludes a paragraph which begins with a report of data from an experiment involving an injection of Delta-9-THC. To infer from the finding that THC builds up in the system and affects an individual far after their use of marijuana is incorrect.

Furthermore, the NAS report warns of difficulty in making any conclusions about marijuana's safety based on individual clinical indications. "The intensity and duration of a drug effect depends on at least three major factors... With cannabis, many or even most of these factors are not always measurable or under control of an investigator."[8]

4) *"The buildup... causes the user to smoke more marijuana to achieve the desired high and may result in loss of sleep, appetite, and initiative, as well as moodiness and depression."*

This finding confuses and merges the symptoms of tolerance and withdrawal, and misattributes them to a buildup of THC which is inadequate to explain these effects. The NAS report on the matter of tolerance:

> Tolerance to most cannabinoid effects has been demonstrated both in animals and human beings. Tolerance can develop rapidly after a few small doses. It disappears at an equally rapid rate for many effects, although after large doses in experimental animals some tolerance may persist for long periods...
>
> The development of such tolerance to cannabis does not necessarily have health implications. However, if tolerance should lead to higher or more frequent doses, adverse consequences, e.g., respiratory effects, associated with higher usage could result.
>
> Physical dependence, manifested by withdrawal signs and symptoms, can develop rapidly in animals and in human beings. The withdrawal syndrome is not life threatening... Withdrawal symptoms can include restlessness, irritability, mild agitation, insomnia, and sleep EEG disturbance.

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[7]A.S. Relman; (1982), 20.

[8]A.S. Relman; (1982), 19.

> Cannabis dependence does not mean the same thing as cannabis addiction. Dependence means only that a withdrawal syndrome can occur when drug taking is stopped. Addiction implies compulsive behavior to acquire the drug. The relationship between dependence and increased drug seeking or drug using is more theoretical than well-documented, particularly in experiments with human beings.[9]

5) *"It is possible for a human being to overdose from the use of marijuana, especially if it is used in conjunction with alcohol, because it increases the effects of alcohol."*

It may be possible, but it is highly unlikely that a human being will die from a marijuana overdose. According to the Harvard Mental Health Letter, "No human being is known to have died of an overdose. By extrapolation from animal experiments, the ratio of lethal to effective (intoxicating) dose is estimated to be on the order of thousands to one." Generally, an oversufficient dose of marijuana will put a subject to sleep. According to the NAS, "delta-9-THC and related cannabinoids have a very low lethal toxicity... The lack of well-authenticated cases of human deaths from acute delta-9-THC or cannabis overdose is consistent with the experimental animal data."[10]

Alcohol abuse can cause accidental death or injury regardless of whether or not marijuana is involved. There has been speculation that because marijuana is effective as an anti-emetic for chemotherapy patients that it could inhibit vomiting on the part of individuals who have consumed unsafe quantities of alcohol. However, marijuana appears to be an insufficient deterrent to vomiting when excessive quantities of alcohol are involved.

6) *"...the THC content... has increased from less than one percent... to as high as 10 percent today."*

According to the Harvard Medical School Mental Health Letter:

> New breeding and cultivation techniques have raised the THC content of marijuana smoked in the United States as much as ten times over the last 20

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[9]A.S. Relman; (1982), 26-27.

[10]A.S. Relman; (1982), 24.

years, from an average of 0.4 percent to 4 percent. Some varieties now contain as much as 10 percent.[11]

There is nothing new, or dangerous, about high potency marijuana, despite the emergence of domestically grown high potency marijuana in the United States.

The high THC potency cannabis preparation 'hashish', has existed and been used, like marijuana, for thousands of years. In an upcoming article in the Journal of Psychoactive Drugs, Drs. Tod Mikuriya and Michael Aldrich cite references to the use of high-potency cannabis preparations in papers written in 1839, 1857, 1860, 1869, 1884, and 1890.[12] Then, as now, the response to stronger preparations is to titrate the dose. More importantly, "From the time of its introduction to Western medicine in 1839, right up to the present day, quite potent cannabis products have been available and have been used in research."[13]

Furthermore, the NAS reports that "about half of the delta-9-THC originally in a cannabis cigarette is lost by combustion, by butt entrapment, in smoke not inhaled, and in smoke exhaled."[14] This factor indicates that potency itself is not an indicator of the amount of THC actually consumed in social use.

8) *"marijuana may cause schizophrenia, illusions,..."*

According to the Harvard Mental Health Letter:

> The idea has persisted that in the long run smoking marijuana causes some sort of mental or emotional deterioration. In three major studies conducted in Jamaica, Costa Rica, and Greece, researchers have compared heavy long-term cannabis users with non-users and found no evidence of intellectual or neurological damage, no changes in personality, and no loss of the will to work or participate in society. The Costa Rican study showed no difference between heavy users (seven or more marijuana cigarettes a day) and lighter users (six or fewer cigarettes a day). Experiments in the United States show no effects of fairly heavy

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[11]Lester Grinspoon, ed.; The Harvard Medical School Mental Health Letter, Vol. 4, No. 5 (Boston: Department of Continuing Education of Harvard Medical School, 1987), 1.

[12]T. Mikuriya and M. Aldrich; "Cannabis 1988: Old Drug, "New Dangers" -- The Potency Question" (San Francisco: Journal of Psychoactive Drugs, April, 1988).

[13]ibid

[14]A.S. Relman; (1982), 21-22

marijuana use on learning, perception, or motivation over periods as long as a year.[15]

9) *"...one marijuana cigarette a day may cause lung cancer in three years."*

If this finding is true, America would have between 15 and 30 million cases of lung cancer directly attributable to marijuana use recorded in this decade alone. The burden of proof for this claim lays with its author.

NORML concedes that marijuana smoke can cause lung damage, and can contribute to respiratory and heart problems. The NAS claims that:

> It is not easy to compare the toxicity of a given number of marijuana cigarettes to a given number of tobacco cigarettes. There are general similarities in the composition of the smoke, but the variations in composition of both tobacco and marijuana cigarettes and differences in smoking techniques make simple extrapolations of risks of tobacco versus marijuana smoking not valid.[16]

A new study published early this year by Dr. Tashkin and his associates concludes that one marijuana cigarette produces the tar and carbon monoxide of approximately four tobacco cigarettes.[17]

However, Dr. Tashkin concedes:

> Long-term adverse pulmonary consequences of tobacco smoking have been shown to be related to dose. For example, the incidence of chronic obstructive pulmonary disease or bronchogenic carcinoma in smokers of fewer than 5 to 10 tobacco cigarettes a day is substantially less than in habitual smokers of more than 20 tobacco cigarettes a day. Although regular tobacco smokers consume more than 15 tobacco cigarettes a day, most current smokers of marijuana smoke less than 1 marijuana cigarette a day. Even among the estimated six million daily smokers of marijuana in the United

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[15]L. Grinspoon, ed. (1988), 3.

[16]A.S. Relman (1982), 15.

[17]D. Tashkin; T. Wu; B. Djahed; J. Rose; "Pulmonary Hazards of Smoking Marijuana as Compared With Tobacco" (Boston: New England Journal of Medicine, Vol. 318, No. 6., 1988), 347 - 351.

States, smoking more than five marijuana cigarettes a day is unusual[18]

Accordingly, despite the presence of four times the tar and carbon monoxide of a tobacco cigarette, a single marijuana cigarette consumed daily presents less of a health risk than a quarter pack of tobacco cigarettes.

Furthermore, the tar and carbon monoxide levels were unaffected by THC potency. The lung damage associated with marijuana use is produced by the physical burning of the plant material, not THC, the active ingredient. Oral ingestion of marijuana does not produce lung damage. Incidently, as far as respiratory effects, high potency marijuana is safer to use because less material is actually burned, thereby exposing the lungs to less tar.

10) *"THC affects eggs, sperm, sexual hormones, and the development of a fetus and marijuana use may result in deformed or undersized offspring."*

The Harvard Letter:

The effects of marijuana on the reproductive system are a more complicated issue. In men, a single dose of THC lowers sperm count and the level of testosterone and other hormones. Tolerance to this effect apparantly develops; in the Costa Rican study, marijuana smokers and controls had the same testosterone levels. Although the smokers in the study began using mariuana at an average age of 15, it had not affected their masculine development. There is no evidence that the changes in sperm count and testosterone produced by marijuana affect sexual performance or fertility.

In animal experiments THC has also been reported to lower levels of female hormones and disturb the menstrual cycle. When monkeys, rats, and mice are exposed during pregnancy to amounts of THC equivalent to a heavy human smoker's dose, stillbirths and decreased birth weight are sometimes reported in their offspring. There are also reports of low birth weight, prematurity, and even a condition resembling the fetal alcohol syndrome in some children of women who smoke marijuana heavily during pregnancy. The significance of these reports is unclear because controls are lacking and other circumstances make it hard to attribute causes. To be safe, pregnant and nursing women should follow the standard

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[18]ibid, 349.

conservative recommendation to avoid all drugs, including cannabis, that are not absolutely neccessary.[19]

Many of the women involved in studies suggesting lower birth weight also smoked tobacco. There are also questions as to what extent diet affected the birth weight in the cases studied. Women who have smoked marijuana during pregnancy, had appropriate diets and did not smoke tobacco, have produced childen of normal birth weights.

There is no evidence that marijuana has ever caused congenital anomalies[20]; there is persuasive evidence that "...neither marijuana nor delta-9-THC causes chromosome breaks."[21]

Findings 11 and 12 are refuted by both the National Academy report and the Harvard Mental Health Letter. The additional findings relate to evaluating data about trends of marijuana use in Alaska. Being unfamiliar with the data, I am reluctant to offer criticism. However, anomalies in data on the supply and consumption of marijuana in the United States suggest that far more people use marijuana than surveys have indicated in the past. It may be that in a non-criminal atmosphere such as Alaska's, people are more open with surveyors concerning personal marijuana use. If so, the supposed increase in mairjuana use is actually a reflection of more accurate polling.

An example of this anomoly can be found in the June report of the National Narcotics Intelligence Consumers Committee report. On page 6 they list marijuana consumption in the United States as being close to 10 million pounds per year. On pages 12 and 13 they list supply as being approximately 30 million pounds a year. The low consumption figure is based on the NIDA household survey of how many people use marijuana and how frequently. Since consumption figures do not account for all the marijuana available on the market, it obviously underreports the extent of marijuana use. Furthermore, government reports about marijuana seizures typically include "tip of the iceberg" comments which suggest that their estimate of supply, if anything, is low.[22]

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[19]L. Grinspoon, ed. (1988), 4.

[20]A.S. Relman (1982), 99.

[21]A.S. Relman (1982), 101.

[22]National Narcotics Intelligence Consumers Committee (NNICC) "The Supply of Illicit Drugs to the United States from Foreign and Domestic Sources in 1985 and 1986" (1987).

In my opinion, concerns about adolescent marijuana use can best be addressed by educational programs - such as discussions by groups of parents and children about the differences between adulthood and adolescence. I suggest that raising the age requirement for the purchase and use of tobacco to 21 would send a far stronger message of disapproval of teenage smoking than the recriminalization of adult possession of marijuana.

Thank you for requesting this information. On behalf of NORML's members in Alaska, we appreciate the opportunity to comment on these proceedings. Please let me know if I can be of any further assistance in this matter.

Sincerely,

Jon B. Gettman
National Director

JBG:jje
enclosures

ALASKA STATE LEGISLATURE
HOUSE OF REPRESENTATIVES
RESEARCH AGENCY

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March 10, 1987

MEMORANDUM

TO: Representative Pat Pourchot

ATTN: Jeannie Larson

FROM: Penelope Weyhrauch
Legislative Analyst

RE: The Physiological Effects of Marijuana, Alcohol, Tobacco, Aspirin, and Salt
Research Request 87.155 (Supplemental Information)

I have attached some information I recently received on the effects of salt, sugar, caffeine and tobacco on the body. I hope this information is of use to you.

Attachment

Defective salt excretion proposed as cause of essential hypertension

ST. PETERSBURG, FLA.—Essential hypertension evolves from a defect in the body's salt excretion mechanism, two investigators told the American Heart Association's science writers' forum here.

Both researchers focus on natriuretic chemicals in their hypotheses, and they predict eventual development of assays to detect the chemicals and identify people whose salt intake should be restricted. But they differ in their opinions on the ultimate cause of salt sensitivity and on the type of assays needed.

One line of research, presented by biochemist Tadashi Inagami, implies that salt sensitivity predisposing to hypertension results from a genetic deficiency of certain cardiac peptides. He says an abundance of these peptides can protect people from the ravages of high-salt diets.

On the other hand, Dr. Mordecai P. Blaustein points to an inherent kidney defect as the underlying cause of essential hypertension. "It may be that the disease we call essential hypertension is really several different diseases," says Dr. Blaustein, chairman of physiology at the University of Maryland School of Medicine.

Peptides probed. Dr. Inagami and his colleagues at Vanderbilt University School of Medicine in Nashville, Tenn. have purified—and are attempting to synthesize—atrial peptides that produce diuresis and increase sodium excretion by the kidneys.

"The atrium senses blood volume expansion due to excess salt and releases atrial natriuretic factor [ANF] directly to the kidneys," says Dr. Inagami, director of Vanderbilt's hypertension center. "We do not yet know the normal concentrations of ANF, but we are driving at this hypothesis: Clinical significance and dietary recommendations can be drawn from ANF levels, and the peptide can also be given to patients in acute renal failure."

The Tennessee researchers expect to complete peptide and antibody synthesis within a year, and Dr. Inagami says that ANF radioimmunoassay should be feasible within five years.

Dr. Blaustein

Dr. Inagami

An as-yet-unidentified natriuretic agent is crucial to Dr. Blaustein's approach to the relationship between sodium and hypertension. Natriuretic hormone (NH), thought to originate in the hypothalamus, has eluded discovery for 20 years, but its existence is accepted on the basis of its biologic activity.

NH is released in response to increased extracellular fluid, which signals the kidneys' inability to excrete sufficient amounts of sodium. The hormone inhibits renal sodium-potassium exchange, thereby reducing sodium resorption and promoting its excretion.

Inhibition of the kidneys' sodium pumps isn't a problem in itself. But NH also inhibits sodium pumps in surface membranes of cells all over the body, explains Dr. Blaustein, including blood cells, arterial-wall muscle cells, and nerve cells. The resulting increase in intracellular sodium causes increased intracellular calcium, which in turn increases arterial contraction and elevates blood pressure.

"We think a functionally defective kidney is the culprit to begin with," says Dr. Blaustein. "If too much salt is ingested, the defective kidney can't handle it, the brain hormone is released, and the sodium-calcium mechanisms come into play. The final common pathway of all types of hypertension may be increased vascular reactivity due to increased calcium in the vascular smooth muscle."

Screening potential. Once NH is purified, persons with family histories of hypertension could be screened for high levels of the hormone, which would indicate a need to restrict their dietary salt. Hypertensive patients also could be tested, first to confirm the hypothesis linking natriuretic hormone, sodium-calcium exchange, and hypertension, says Dr. Blaustein, and then to monitor efficacy of antihypertensive regimens.

Dr. Inagami notes that atrial natriuretic factor—unlike natriuretic hormone—doesn't appear to affect the salt-retention mechanism of cells outside the kidney. And Dr. Blaustein concedes ANF could play a pivotal role in the development of one class or subgroup of hypertension.

But he maintains an intrinsically defective kidney is the problem for many hypertensives. In support of his position, he cites a report of six kidney transplant patients who remained normotensive without medication for six months to six years posttransplant, despite having had essential hypertension, which culminated in the earlier nephrosclerosis. ■

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Surveillance and Control of Infectious Diseases: Progress Toward the 1990 Objectives

WALTER R. DOWDLE, PhD

Dr. Dowdle is Director, Center for Infectious Diseases, Centers for Disease Control, Atlanta, Ga. 30333. Contributors to this report were Dr. John Bennett, Dr. Claire Broome, Dr. Donald Francis, and Ms. Ladene Newton, Center for Infectious Diseases; Dr. Kenneth Powell, Center for Prevention Services; Dr. Philip Brachman, Global Epidemiology Program; Dr. Carl Tyler, Epidemiology Program Office; Dr. Joyce Essien, Laboratory Program Office, all of the Centers for Disease Control; Dr. Dennis McIntyre, Indian Health Service; and Dr. George Galasso, National Institute of Allergy and Infectious Diseases, National Institutes of Health.

Tearsheet requests to Dr. Dowdle.

SYNOPSIS

Great progress has been made in the United States in reducing infectious disease mortality. However, infectious diseases remain the greatest cause of morbidity in this country. Newer infectious diseases or agents have been recognized, but newer tools for surveillance and control have also been made available. Specific objectives for the reduction of infectious diseases by 1990 have been set by the Public Health Service. The opportunities appear to be good for achieving by 1990 objectives for nosocomial infections, Legionnaires' disease, tuberculosis, and surveillance and control of infectious diseases. Achievement of the 1990 objectives for hepatitis B, pneumococcal pneumonia, and bacterial meningitis, however, will require both scientific advances and additional resources.

GREAT PROGRESS HAS BEEN MADE in the United States in this century in reducing mortality attributable to infectious diseases. Infectious diseases were the fourth leading cause of death in the United States in 1976 (fig. 1) after heart disease, malignant neoplasms, and cerebrovascular diseases, according to data extracted from information published by the National Center for Health Statistics (*1*). Data are not available for all infectious diseases, but in 1980, influenza and pneumonia ranked seventh in years of potential life lost by the total U.S. population ages 1 to 64 years (*2*), as the following tabulation shows.

Cause	*Total years lost*
1. Accidents and adverse effects	2,684,850
2. Malignant neoplasms	1,804,120
3. Diseases of the heart	1,636,510
4. Suicides, homicides	1,401,880
5. Chronic liver disease	301,070
6. Cerebrovascular diseases	280,430
7. Pneumonia and influenza	124,830
8. Diabetes mellitus	117,340
9. Chronic obstructive pulmonary diseases and allied conditions	110,530
All causes	10,006,060

By comparison, in 1900 tuberculosis, influenza and pneumonia, and diphtheria were the three leading

• to monitor changes in sodium consumption and sodium content of foods, trends in sodium labeling of retail foods, and shifts in consumer perceptions and marketplace practices—all in order to assess progress toward achieving objectives; and
• to consider the need for legislation in the event this voluntary program does not succeed.

This program was discussed with food industry representatives on June 30, 1981, and was presented in detail in the Federal Register proposal of June 18, 1982 (47 FR 26580). Both the Department of Health and Human Services and the FDA have stressed that the goals of the sodium program are to provide more information to the public about the sodium content of foods they buy and to encourage industry to reduce the amount of sodium in processed foods, where this is safe and feasible.

Results have been encouraging. For example, several major food manufacturers have stated that they will supply sodium labeling for all of their products containing more than 35 mg of sodium per serving. In addition, many manufacturers have indicated that they have programs in progress to study the feasibility of reducing sodium in their products. FDA representatives have met with some 30 major groups from the food industry, including both large individual firms and trade associations representing them. Each of these groups has made a commitment either to moderate the sodium content of the foods they process or to provide much more sodium labeling. Collectively, these efforts already affect processed foods amounting to many billions of dollars in retail sales value. We estimate that the amount of sodium labeling in the marketplace will double or triple over the next year, applying to 40 percent or more of the processed food supply in terms of retail sales value. By mid-1982, 19 percent (by dollar volume) of the foods regulated by FDA carried quantitative sodium labeling, up from 14 percent in the preceding year.

We believe that another positive aspect of the program has been the perspective and balance that have been built into it. We are not advocating measures that have the potential for risk to the population. We simply seek to lower sodium consumption to a moderate level—one that still will provide more than two times the physiological need for sodium for virtually all environmental conditions. We recognize that hypertension is likely to have a multifactorial etiology and that other hypotheses, not associated with sodium intake, have been put forth that may be proven to be valid for some individuals. No aspect of our program is designed to conflict in any way with the investigation of such hypotheses, and we encourage continued research where such hypotheses are judged to have merit.

'We are not advocating measures that have the potential for risk to the population. We simply seek to lower sodium consumption to a moderate level—one that still will provide more than two times the physiological need for sodium for virtually all environmental conditions.'

But the most significant part of this program, from a scientific perspective, is its capacity to measure any positive or negative benefits that accrue as the program is implemented. The FDA is currently involved in several monitoring programs designed to do just that. These programs include measurement of sodium consumption and the prevalence of hypertension in the population, estimation of the prevalence of quantitative sodium declarations on the labels of processed foods, and annual assessment of the effectiveness of public education campaigns and the impact of the sodium-labeling initiative on buying habits. A thorough discussion of this aspect of the overall program was presented in the September-October 1982 issue of Hypertension (*10a*).

These efforts, together with fundamental and applied research by the National Institutes of Health, will contribute measurably to our understanding of the basic mechanisms underlying development of hypertension and to our knowledge about the benefits of moderation of sodium intake as a preventive measure.

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1/3 RK From BH

passion. We are seeing the breakdown of values through Hollywood jive; the brutal funniness of this play draws blood. Working on their scripts, their shows, these guys are professional junk artists and they know it (with different degrees of rationalization). Junk looms over this play like a Moloch of the technopop age; Rabe sees the human spirit itself in danger of turning into spiritual junk. The one who feels this the most is Eddie. He stays up most of the night watching TV and talking back to it. He sees all their lives with the eye of the minor casting director that he is: "We're all just background in one another's lives, cardboard cutouts bumping around in this vague hurlyburly, this spinoff that was once prime-time life."

One of the strongest things in the play is Rabe's vision of wasted intelligence. Eddie and Mickey are smart guys, but their intelligence floats uselessly in a moral void. Rabe has a marvelous ear for their speech; masters of b.s., they take pride in snakelike sentences that are arabesques of evasiveness, showbiz sophistry turned into a dialectic of nihilism. The women, too, are affected by this hollowness: Darlene says, "Everything is always distracting me from everything else." Intentionally or not, this is an echo of T. S. Eliot's "Four Quartets": "Distracted from distraction by distraction." Rabe shares Eliot's vision of a world of intelligent nervous wrecks who've lost their moral center and, not knowing where to turn, turn everywhere. The climax, with its casual, nutty, almost comedic violence, has a frightening inevitability.

Vitality: Rabe's vision of the wasteland may not be impeccably structured, but it has a savage sincerity and a crackling theatrical vitality. Mike Nichols's staging has never had more electricity, and the interplay of the extraordinary cast has the energy and emotional fearlessness of American acting at its best. This is the kind of play and the kind of cast that will produce some fascinatingly different performances on any given night. The actors are all superb: Keitel's complex, scary primitivism; Walken's slick, flip, self-protective cynicism; Weaver's razor-edged beauty and haute-couture vulnerability, and Jerry Stiller's pathos and malarkey. Cynthia Nixon brings a Felliniesque redemptive innocence to what may be the best bimbo part ever written. Tony winner Judith Ivey is sensational as the smart stripper. In the two performances I saw, William Hurt was tremendously implosive once and tremendously explosive once. He is a clear, powerful center for one of the best ensemble performances on any American stage.

This deeply felt play deserves as wide an audience as possible. David Rabe's wishes for it are reasonable enough. "I'd like to think a play like this could go to Broadway and have a year's worth of vital life. Having come from off-Broadway, that would be good for both." Off or on Broadway, "Hurlyburly" is going to be seen all over America for a long time.

JACK KROLL

MEDICINE

Salt: Should I or Shouldn't I?

Americans by the millions have been hiding their salt shakers in the hope of protecting themselves against high blood pressure. But some experts r question whether a high level of sodi chloride in the diet is really all that bad d last week, in a controversial report r ntradicts the diet advice Americans have been getting for many years, researchers sprinkled more doubt on the issue by suggesting that too little calcium and other nutrients rather than too much sodium may be major culprits in hypertension.

In the study, described in the journal Science, a team headed by Dr. David McCarron of the Oregon Health Sciences University analyzed the diets of more than

BILLY GRIMES—BLACK STAR

Hypertension: New questions about diet

10,000 U.S. adults. They found, somewhat to their surprise, that the prevalence of high blood pressure was lowest among those consuming the most salt and highest among people with low salt intake. At the same time, the analysis showed that people whose diets were low in calcium and potassium had an increased risk of hypertension, as were those with reduced intakes of vitamins A and C.

Milk, cheese and other dairy products are prime sources of calcium and potassium, and it was in a deficiency in this food group that McCarron and his colleagues found the strongest link to high blood pressure. Some dairy foods are also a rich source of sodium and would be among the foods to avoid by anyone going on a low-salt diet. The report notes that sodium chemically interacts with both calcium and potassium in the physiology of the body, which may be why a deficiency in all three might be related to elevated blood pressure. The findings are important, says McCarron, because they suggest that the part played by nutrition in high blood pressure is more complex than had been thought. "We have dietary patterns that are deficits, not excesses," he says. "One of the real risks of a low-sodium diet is that you inadvertently restrict other nutrients."

The new report drew quick fire from both consumer groups and hypertension experts. A spokesman for the Center for Science in the Public Interest, which takes a strong anti-salt stand, suggested that McCarron's emphasis on dairy products stems from the fact that "much" of his research support comes from the dairy industry. McCarron replies that, of the $500,000 his Oregon Hypertension Program received last year, only $28,000 came from the industry. Moreover, this particular study was supported by two private foundations unrelated to dairy interests.

Recall: Others criticized the way the study was carried out. They noted, for example, that the diet data were based on what the study subjects recalled eating in the previous 24 hours and should have covered at least one week. Also, it did not include the amount of salt added from the shaker, but only the natural content of sodium in the foods consumed. And they warned that people should not base any changes in diet on this single study. "If it gets misread and misinterpreted, people could act inappropriately," said Dr. William Friedewald of the National Heart, Lung and Blood Institute. Friedewald argued that the findings about sodium fly in the face of most previous studies and that none ever suggested that hypertension was linked to too little sodium in the diet.

McCarron himself emphasizes that the study doesn't prove a cause-and-effect relationship between low sodium or a deficiency of other nutrients and hypertension. And in his view the results shouldn't be taken as a license to eat salt. There is no doubt, he says, that salt intake is involved in some cases of hypertension and these patients can benefit from low-sodium diets. The important issue, he feels, is whether a blanket recommendation for everyone to reduce salt intake is really justified. The findings, McCarron says, "should be a note of caution, particularly to public-health people and government agencies, that perhaps we should rethink what we've been telling our society."

MATT CLARK with MARY HAGER in Washington and DEBORAH WITHERSPOON in New York

13 LUNG CANCER

Paul Van Houtte, M.D., Radiation Oncology
Omar M. Salazar, M.D., Radiation Oncology
Clay E. Phillips, M.D., Surgical Oncology
Robert F. Asbury, M.D., Medical Oncology

Why do people smoke?
The heart has its reasons which reason knows not.
Blaise Pascal (78).

Perspective

Lung cancer accounts for 22% of all cancer in men, compared with 9% in women. It is responsible for 35% of cancer-related deaths in men and 17% in women. Furthermore, the overall 5-year survival rate is still below 10% (75). Only one third of the patients are eligible for surgical resection with curative intent, and among them, less than one third will be alive 5 years later. Little progress has been made in the past decade to improve long-term survival significantly. Nevertheless, all disciplines involved in lung cancer management have advanced notably. Today, lung cancer is not considered to be a single disease entity, but 1 composed of several diseases conditioned by histopathologic types that determine patterns of spread, treatment, and prognosis. Furthermore, the modern management of lung cancer requires, more than ever, cooperation between all specialties involved in diagnosis and therapy.

EPIDEMIOLOGY AND ETIOLOGY

Epidemiology

1. In 1983, there will be about 94,000 new cases of lung cancer in men and about 41,000 in women (75).

2. Most striking is the rising incidence among women during the last decade. The percentage of change in the rate of lung cancer incidence over the period from 1947 to 1969 was 133% for men and 108% for women (20,75).

3. The average age at onset is about 60 years (less than 1% of cases occurred under the age of 30).

Etiology

A variety of agents have been proven to be carcinogens in humans:

1. *Tobacco smoke* is the dominant agent and represents a complex mixture of physical and chemical carcinogens. There is a direct relationship between the amount of tobacco exposure and risk for developing lung cancer (Fig. 13.1). In addition to the increased lung cancer risk, smoking is also associated with an increased risk of upper respiratory and digestive tract cancer. The type of cigarettes seems to also influence the risk, i.e., a filter apparently decreases the risk. Stopping smoking is associated with a gradual decrease in the risk, but a long period of time (more than 6 years) is necessary before an appreciable diminution of the risk occurs (Fig. 13.2) (86).

2. *Asbestos* exposure is associated with the development of mesothelioma and also bronchogenic carcinoma. The risk from asbestos is particularly more pronounced when combined with cigarette smoking (73).

3. *Atmospheric pollution* has been implicated as a causative agent in view of the higher incidence of lung cancer in urban as opposed to rural areas.

4. A more direct relationship has been also shown in cases of *pitchblende miners* who are involved with radioactive ores.

5. *Metals*, mostly nickel and silver, but also chromium, cadmium, beryllium, cobalt, selenium, and steel have proven to be carcinogenic in animals and are occupational hazards, particularly when combined with other factors.

6. *Chemical products* such as chloromethyl ethers have been associated with the development of lung cancer, especially small cell cancers (10).

DETECTION AND DIAGNOSIS (23)

Clinical Detection

1. *Clinical manifestations* are varied and mimic other pulmonary conditions.

a. A change in pulmonary habits is the most significant sign of lung cancer.

b. Cough, chest pain, rust-streaked or purulent sputum production, hemoptysis, and dyspnea are common symptoms of this disease.

2. *Local complications* depend upon the location of the tumor and include:

a. Superior vena caval obstruction.

Caffeine Scoreboard

Caffeine seems to pop up in all sorts of places.

This central nervous system stimulant is found in many foods, beverages, and drugs in addition to coffee. In fact, caffeine removed from coffee through decaffeination is sold to beverage and drug makers who then add it to their products.

The main health problem connected with caffeine is caffeineism whose well-known symptoms include insomnia, nervousness, and anxiety. But there also appears to be an association between caffeine intake and birth defects, benign breast lumps, irregular heartbeats, and other serious medical problems. In 1980, the Food and Drug Administration advised pregnant women to avoid or minimize consumption of products containing caffeine.

While sensitivity varies greatly from person to person, CSPI considers it prudent to minimize consumption of products containing caffeine.

Unfortunately, there may still be slight risks for those who have switched to decaffeinated coffee. The high temperatures of the roasting process may create cancer-causing substances in the beans themselves. Test results are mixed, but there are some indications that both regular and decaffeinated coffee may contribute to bladder and pancreatic cancers.

Concerns have also been raised in recent years about methylene chloride, the main chemical solvent used in the decaffeination process.

Research released in 1981 sponsored by the National Toxicology Program, showed that methylene chloride caused liver cancer in laboratory mice. The tests have since been questioned because of improper laboratory practices, and more reliable experiments are needed. But methylene chloride—a popular industrial solvent—is a chlorinated hydrocarbon that is chemically related to other, demonstrated cancer-promoting agents.

At the extremely low concentrations present in decaffeinated coffee, methylene chloride is only a very small health hazard. Nevertheless, for those who would prefer to avoid the chemical, we list below by brand name a sampling of coffees decaffeinated with methylene chloride and coffees that use other processes.

Caffeine Content of Beverages And Foods

Item	Milligrams of Caffeine Ave.	Range
Coffee *(5-oz. cup)*		
Brewed, drip method	115	60-180
Brewed, percolator	80	40-170
Instant	65	30-120
Decaffeinated, brewed	3	2-5
Decaffeinated, instant	2	1-5
Tea *(5-oz. cup)*		
Brewed, major U.S. brands	40	20-90
Brewed, imported brands	60	25-110
Instant	30	25-50
Iced (12-oz. glass)	70	67-76
Cocoa beverage (5-oz. cup)	4	2-20
Chocolate milk beverage (8 oz.)	5	2-7
Milk chocolate (1 oz.)	6	1-15
Dark chocolate, semi-sweet (1 oz.)	20	5-35
Baker's chocolate (1 oz.)	26	26
Chocolate-flavored syrup (1 oz.)	4	4

Source: FDA, Food Additive Chemistry Evaluation Branch, based on evaluations of existing literature on caffeine levels.

Which Decaffeinated Coffee Brands Use Methylene Chloride?

*Brands using methylene chloride, includes both ground roast and instant by manufacturer**

Chase & Sanborn
Chase & Sanborn

Chock Full O'Nuts
Chock Full O'Nuts

Coca-Cola
Butter-Nut
Maryland Club

General Foods
Sanka
Brim
Maxwell House
Yuban

Schonbrunn
Savarin

Tetley
Martinson

Brands using decaffeination processes without methylene chloride, includes instant only by manufacturer

Nestle
Taster's Choice
Nescafe

Nestle says it uses a "component occuring naturally in the coffee bean itself" and does not add any "foreign substance solvent" to decaffeinate its products. The company says categorically that the component is not methylene chloride, but otherwise refuses to identify it.

Procter & Gamble
High Point

Procter & Gamble uses ethyl acetate to decaffeinate High Point. Ethyl acetate occurs naturally in many foods, and is safe.

Other
Specialty coffee stores, groceries, co-ops, and health food shops offer a variety of instant, ground roast, and whole bean brands. Ask to learn what decaffeinating agents they use.

Hills Brothers uses either methylene chloride or ethyl acetate "depending on the decaffeination facility," according to a company spokesperson. The representative was unable to say how often Hills Brothers uses one solvent compared to the other.

Caffeine in Soft Drinks

(12-oz. serving)	Caffeine (mg)
Sugar-Free Mr. PIBB	58.8
Mountain Dew	54.0
Mello Yello	52.8
TAB	46.8
Coca-Cola	45.6
Diet Coke	45.6
Shasta Cola	44.4
Shasta Cherry Cola	44.4
Shasta Diet Cola	44.4
Mr. PIBB	40.8
Dr. Pepper	39.6
Sugar-Free Dr. Pepper	39.6
Big Red	38.4
Pepsi-Cola	38.4
Aspen	36.0
Diet Pepsi	36.0
Pepsi Light	36.0
RC Cola	36.0
Diet Rite	36.0
Kick	31.2

Source: Institute of Food Technologists (IFT), April 1983, based on data from National Soft Drink Association.

CAFFEINE

Caffeine is a powerful central nervous system (CNS) stimulant. Caffeine can cause an increase in blood pressure (2-3 cups of coffee can increase the blood pressure by about 14%), muscle tension, and stomach acid, metabolic rate and wakefulness. It is also implicated in fibrocystic breast disease and birth defects. Large doses can be fatal - 10 grams, or 80 to 100 cups of coffee.

Caffeinism may affect about 4-15% of Americans. This is a condition similar to anxiety neurosis. Ever experience any of these?

Extreme nervousness
Irritability
Shakiness
Chronic muscle tension
Sleeping problems
Rapid and extra heartbeats
Frequent urination and loose stools
Gastrointestinal upsets

Caffeine is addictive. When deprived of caffeine, addicts can experience depression, throbbing headache, disorientation, constipation, nausea, and/or irritability. Yet, two billion pounds of coffee are drunk each year in the U.S.A. Caffeine is also found in teas, chocolate, many over-the-counter drugs, and colas. Its effects depend on dose and body weight. A child who drinks a cola may experience an effect similar to an adult drinking four cups of coffee.

People tend to underestimate their caffeine intake. What is your caffeine intake?

Table One
Caffeine content of coffee, tea, and cocoa (*milligrams per serving—average values*)

Coffee, instant	66
Coffee, percolated	110
Coffee, drip-olated	146
Teabag—3 minute brew	46
Teabag—1 minute brew	26
Loose tea—3 minute brew	40
Cocoa	13

Table Two
Caffeine content of cola beverages (*milligrams per 12-ounce can*)

Coca Cola	65
Dr. Pepper	61
Mountain Dew	55
Diet Dr. Pepper	54
TAB	49
Pepsi-Cola	43
Diet RC	33
Diet Rite	32

Table 3
Caffeine Content of Over-the-Counter Drugs (*per tablet*)

Anacin	32mg
Aqua-ban	100mg
Bivarin	200mg
Caffedrine	200mg
Dristan	16mg
Empirin	32mg
Excedrin	64mg
Midol	32mg
No Doz	100mg
Pre-mens Forte	100mg
Vanquish	33mg

Source: M.L. Bunker and M. McWilliams, "Caffeine Content of Common Beverages," Journal of the American Dietetic Association, Vol. 74, pp. 28-32, January 1979

Carefully consider the health risk factors involved in consuming caffeine.

Food And Drug Interactions

If you're taking a drug, the food you eat could make it work faster or slower or even prevent it from working at all. Eating certain foods while taking certain drugs can be dangerous. And some drugs can affect the way your body uses food.

by Phyllis Lehmann

Would it occur to you not to swallow a tetracycline capsule with a glass of milk? Or to avoid aged cheese and Chianti wine if you are taking a certain medicine to combat hypertension? Or to eat more green leafy vegetables if you are on The Pill? Probably not. Yet the effects foods and drugs have on each other can determine whether medications do their job and whether your body gets the nutrients it needs.

The extent of interaction between foods and drugs depends on the drug dosage and on the individual's age, size, and specific medical condition. In general, though, the presence of food in the stomach and intestines can influence a drug's effectiveness by slowing down or speeding up the time it takes the medicine to go through the gastrointestinal tract to the site in the body where it is needed.

Food also contains natural and added chemicals that can react with certain drugs in ways that make the drugs virtually useless. Some reactions can be downright dangerous, triggering a medical crisis or, in rare instances, even death.

It is because of these interactions that your doctor tells you to take certain medications on an empty stomach, some just before meals, and some with meals.

A major way food affects drugs is by enhancing or impeding absorption of the drug into the bloodstream. There are a few cases in which foods speed up absorption. For example, blood levels of griseofulvin, a substance that combats fungus infections such as ringworm, rise markedly if the patient eats fatty foods before taking the drug.

More commonly, though, food and beverages interfere with absorption. A classic interaction is the one between tetracycline compounds and dairy products. The calcium in milk, cheese, and yogurt impairs absorption of tetracycline. On the other hand, taking some iron supplements with citrus fruits or juices which contain ascorbic acid enhances absorption of the iron.

In general, it is unwise to take drugs with soda pop or acid fruit or vegetable juices unless you check with your doctor first. These beverages can result in excess acidity that may cause some drugs to dissolve quickly in the stomach instead of in the intestines where they can be more readily absorbed into the bloodstream.

Some foods contain active substances which can enhance a drug effect or which can interact with a drug to produce an unexpected or counter effect. For example, licorice extracted from natural sources contains a substance which, when consumed regularly in excess amounts, may cause an elevation in blood pressure. Licorice is a favorite ingredient in candy and a flavoring for some pharmaceuticals. Most American manufacturers now use a synthetic flavoring but many imported products still contain licorice from natural sources. Continued regular use of products containing natural licorice extract could aggravate high blood pressure or counteract the effect of medication for high blood pressure.

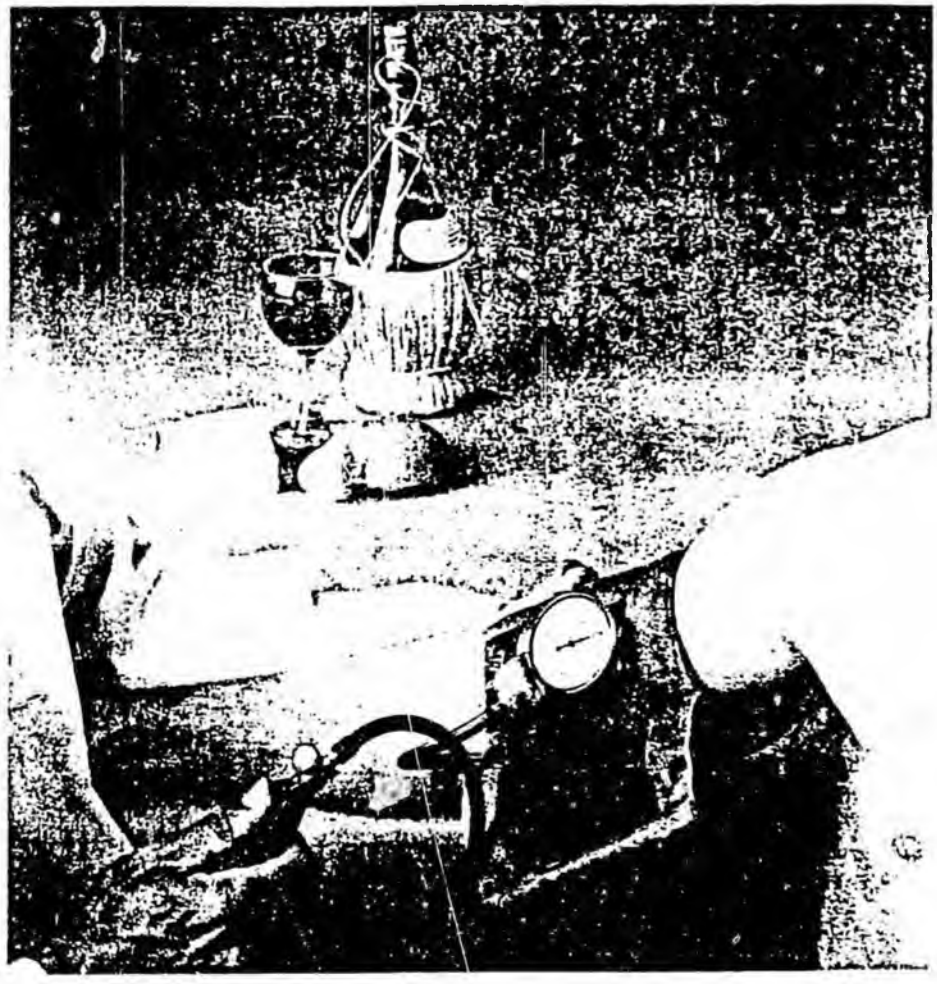
Excessive consumption of foods high in vitamin K, such as liver and leafy green vegetables, may hinder the effectiveness of anticoagulants. Vitamin K, which promotes clotting of the blood, works in direct opposition to these drugs, which are intended to prevent clotting.

Perhaps the most hazardous food-drug interaction is the one between monoamine oxidase (MAO) inhibitors, drugs at times prescribed for depression and high blood pressure, and such foods as aged cheese, Chianti wine, and chicken livers. MAO inhibitors can react with a substance called tyramine in these foods and force the blood pressure to dangerous levels, sometimes causing severe headaches, brain hemorrhage, and, in extreme cases, death.

To prevent a possible reaction, anyone taking MAO inhibitor drugs should avoid aged and fermented foods, including pickled herring; fermented sausages, such as salami and pepperoni; sharp or aged cheeses; yogurt and sour cream; beef and chicken livers; broad beans, such as fava beans; canned figs; bananas; avocados; soy sauce; active yeast preparations; beer; Chianti wine, sherry, and other wines in large quantities. MAO inhibitors also are suspected of reacting adversely with cola beverages, coffee, chocolate, and raisins.

Alcohol, which is actually a drug itself, although not regulated as a drug under the Food, Drug, and Cosmetic Act, does not mix well with a wide variety of medications, such as antibiotics; anticoagulants; antidiabetic drugs, including insulin; antihistamines; high blood pressure drugs; MAO inhibitors; and sedatives. Alcohol combined with antihistamines, tranquilizers, or antidepressants causes excessive drowsiness that can be especially hazardous to someone driving a car, operating machinery, or performing some other task that requires mental

Perhaps the most hazardous food-drug interaction is the one between monoamine oxidase (MAO) inhibitors, drugs often prescribed for depression and high blood pressure, and such foods as aged cheese, Chianti wine, and chicken livers.



alertness. A good rule of thumb is to avoid alcoholic beverages when taking any type of prescription or over-the-counter medication.

Just as some foods can affect the way drugs behave in the body, so some drugs can affect the way the body uses food. Drugs may act in various ways to impair proper nutrition: by hastening excretion of certain nutrients, by hindering absorption of nutrients, or by interfering with the body's ability to convert nutrients into usable forms. Nutrient depletion of the body occurs gradually, but for those taking drugs over long periods of time these interactions can lead to deficiencies of certain vitamins and minerals, especially in children, the elderly, those with poor diets, and the chronically ill.

Some drugs inhibit nutrient absorption by their effect on the bowel wall. Among these are colchicine, a drug prescribed for gout, and mineral oil, an ingredient used in some over-the-counter laxatives.

A number of drugs affect specific vitamins and minerals. The antihypertension drug hydralazine and the antituberculosis drug INH can deplete the body's supply of vitamin B_6 by inhibiting production of the enzyme necessary to convert the vitamin into a form the body can use or by combining with the vitamin to form a compound that is excreted.

Similarly, anticonvulsant drugs that are used to control epilepsy can lead to deficiencies of vitamin D and folic acid because they increase the turnover rate of these vitamins in the body.

Quite a few drugs—for example, colchicine, oral antidiabetic agents, and the antibiotic neomycin—can

impair absorption of vitamin B_{12}. But because most Americans have good stores of B_{12} in their livers, it takes prolonged ingestion of these drugs to cause a deficiency.

Long term use of diuretics, or "water pills," to treat such conditions as congestive heart failure, can lead to serious potassium depletion. If the potassium loss is not corrected in heart patients taking digitalis, the heart may become more sensitive to the effects of the drug. People taking diuretics regularly should eat foods which are good sources of potassium. These include tomatoes and tomato juice, oranges and orange juice, dried apricots, cantaloupes, figs, raisins, bananas, prunes, potatoes, sweet potatoes, and winter squash.

Modifying the diet to include more foods rich in the vitamins and minerals that may be depleted by certain drugs generally is preferable to taking vitamin or mineral supplements. In fact, supplements of some vitamins can counter the effectiveness of certain drugs.

Fortunately, the diets of most Americans are sufficiently well-balanced so that the threat of drug-related nutritional deficiencies can be easily overcome.

Because oral contraceptives are used so widely, their effect on nutrition has been getting increasing attention. The Pill is known to deplete the blood's content of certain vitamins, notably folic acid and vitamin B_6, but usually the vitamin depletion is not serious enough to cause overt symptoms. In most healthy women with good diets, these vitamin levels do not go down to a point that is alarming, says Dr. Daphne Roe, a Cornell University nutritionist. "But in a poverty group of young women who are trying to make do with very little and who have limited nutritional knowledge, you may find a different situation," Dr. Roe says. "It is this group we are most concerned about."

Because her requirements for several vitamins may be increased, it is especially important for any woman on The Pill to eat a nutritionally balanced diet. In particular, if a woman on The Pill is living on snack foods, she is more likely to develop folate deficiency than her neighbor who every day eats green leafy vegetables, which are a good source of folic acid, according to Dr. Roe.

Drugs readily available without prescription also can lead to nutritional problems. The worst offenders are antacids, Dr. Roe says, because they are so widely abused by the public. Chronic use of these remedies without a doctor's supervision can cause phosphate depletion, a condition that in its milder form produces muscle weakness and in more severe form leads to a vitamin D deficiency. "Unfortunately," says Dr. Roe, "some people get into the habit of taking enormous amounts of these drugs to treat gastric upset that in itself is due to their abuse of some other substance, such as alcohol, coffee, or food."

Mineral oil, an old-fashioned laxative still widely used by elderly people and in nursing homes, can hinder absorption of vitamin D. One study reported that as little as 20 milliliters (4 teaspoons) of mineral oil twice daily can interfere with absorption of vitamin D, vitamin K, and carotene, a substance the body converts to vitamin A.

What can consumers do to prevent undesirable food-drug interactions? Here are a few suggestions:

- Read the labels on over-the-counter remedies and the package inserts that come with prescription drugs.
- Follow your doctor's orders about when to take drugs and what foods or beverages to avoid while taking medications.
- Don't be afraid to ask how drugs might interact with your favorite edibles, especially if you consume large amounts of certain foods and beverages. While taking drugs, be sure to tell your doctor about any unusual symptoms that follow eating particular foods.
- Eat a nutritionally well-balanced diet from a wide variety of foods. Use of a needed drug, even on a long term basis, is less likely to cause depletion of vitamins and minerals if your overall nutritional status is good.

Drug labeling and informed health professionals can be helpful to you, but your doctor and pharmacist cannot follow you to the dinner table or the snack bar. Remember that warnings about food-drug interactions are only as good as the patient's willingness to heed them.

Phyllis Lehmann is a freelance writer.

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FDA CONSUMER

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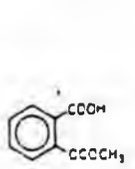
DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
5600 Fishers Lane
Rockville, Md. 20857

Aspirin

Acetylsalicylic Acid
ASA



Chemistry and Stability

CHEMISTRY

Aspirin, the prototype of the salicylates, is a nonsteroidal anti-inflammatory agent (NSAIA). Aspirin is the salicylate ester of acetic acid. In vivo, the drug rapidly hydrolyzes to salicylate and acetate. Aspirin occurs as white crystals, which are usually tabular or needle-like, or as a white, crystalline powder. The drug may have a faint odor, is slightly soluble in water and freely soluble in alcohol, and has a pK_a of 3.5. Each gram of aspirin contains approximately 760 mg of salicylate.

STABILITY

Aspirin is stable in dry air. However, in moist air or in aqueous or hydroalcoholic solutions, the drug gradually hydrolyzes to salicylate and acetate and emits a strong vinegar-like odor; the rate of hydrolysis is increased by heat and is pH-dependent.

In aqueous solutions, aspirin is most stable at a pH of 2–3, less stable at a pH of 4–8, and least stable at a pH less than 2 or greater than 8. In a saturated aqueous solution at a pH of 5–7, aspirin is almost completely hydrolyzed within 1 week at 25°C. If a liquid dosage form of aspirin is desired for short-term treatment of pain, an oral solution may be prepared from commercially available buffered effervescent tablets (Alka-Seltzer®). Following dissolution of one Alka-Seltzer® tablet in approximately 90 mL of water, the solution has a pH of 6–7. In the resultant solution, aspirin is about 99% ionized and is at least 90% unhydrolyzed for approximately 10 hours at room temperature and about 90 hours at 5°C.

Chewable aspirin tablets containing 81 mg of the drug should be stored in child-resistant containers holding not more than 36 tablets each in order to limit the potential toxicity associated with accidental ingestion in children. Aspirin suppositories should be stored at 2–15°C.

Pharmacology

Aspirin exhibits analgesic, anti-inflammatory, and antipyretic activity. Although aspirin hydrolyzes to salicylate and acetate, the drug does not require hydrolysis to produce its effects and appears to have some pharmacologic effects that are distinct from those of salicylate. The ability of aspirin to acetylate proteins (e.g., platelet proteins, hormones, DNA, hemoglobin) results in some effects, such as inhibition of platelet aggregation, which other currently available salicylates do not exhibit.

ANALGESIC, ANTI-INFLAMMATORY, AND ANTIPYRETIC EFFECTS

While unhydrolyzed aspirin has been shown to be more potent than sodium salicylate in relieving pain in animals, it remains to be clearly established that aspirin has greater analgesic effect than salicylate in humans. A direct correlation between onset, intensity, or duration of analgesia and the time course of serum aspirin (or salicylate) concentrations or peak serum aspirin (or salicylate) concentrations also remains to be established. There are relatively few controlled comparative studies of aspirin and other salicylates (e.g., salicylate salts), but the analgesic, anti-inflammatory, and antipyretic effects of aspirin and other salicylates are generally considered to be comparable. However, in terms of antipyretic activity, aspirin is approximately 1.6 times as potent as sodium salicylate on an equimolar basis.

For further information on analgesic, anti-inflammatory, antipyretic, and other effects of aspirin, see Pharmacology in the general statement on Salicylates 28:08.04.

HEMATOLOGIC EFFECTS

At usual dosages (e.g., 1.3–6 g daily), aspirin may rarely prolong the prothrombin time (usually only by 2–3 seconds) by inhibiting hepatic synthesis of blood coagulation factors VII, IX, and X.

Aspirin (but not other salicylates) inhibits platelet aggregation induced by epinephrine or low concentrations of collagen but not that induced by thrombin or high concentrations of collagen. Aspirin inhibits the second phase of platelet aggregation by preventing release of adenosine diphosphate (ADP) from platelets. The drug also prevents release of platelet factor 4 from platelets. Mean bleeding time may be prolonged by several minutes (approximately doubled) in healthy individuals and longer in children or in patients with bleeding disorders (e.g., hemophilia). In healthy individuals receiving a single 325-mg oral dose of aspirin, bleeding time may increase to a maximum within 12 hours and generally return to normal within 24 hours; any increase is usually of little clinical significance. Some clinicians have reported that mean bleeding time is progressively prolonged with increasing single doses of up to 1 g, but may be only slightly prolonged or unaffected by higher single doses; however, this has not been consistently found. The effect on bleeding time depends on the measurement method (e.g., Duke, Ivy, Mielke) used and technical variables (e.g., venostasis), and this may partially account for conflicting reports.

Like the analgesic and anti-inflammatory effects, the effects of aspirin on platelets appear to be mainly associated with inhibition of prostaglandin synthesis. Aspirin irreversibly acetylates and inactivates cyclooxygenase in circulating platelets and possibly in megakaryocytes. A single 325-mg oral dose of the drug results in about 90% inhibition of the enzyme in circulating platelets. This inactivation prevents platelet synthesis of prostaglandin endoperoxides and thromboxane A_2, compounds which induce platelet aggregation and constrict arterial smooth muscle. Since cyclooxygenase in platelets is not resynthesized, this effect of aspirin on platelet function persists for the life span of platelets (4–7 days). When approximately 20% of circulating platelets have not been exposed to aspirin (about 36 hours after the last dose), the hemostatic function of the platelet pool generally returns to normal; however, altered hemostasis has been reported to persist longer in some patients receiving long-term therapy.

ANTITHROMBOTIC EFFECT

Because of its ability to inhibit platelet aggregation via platelet cyclooxygenase inhibition, aspirin has been extensively investigated for potential therapeutic effects in the prevention of thrombosis (particularly arterial thrombosis). Uses: Thrombosis.] Aspirin has also been found to inactivate cyclooxygenase in venous endothelium and thereby inhibit venous synthesis of prostacyclin (epoprostenol, PGI_2). Since prostacyclin inhibits platelet aggregation and causes vasodilation, it appears to oppose the effects of thromboxane A_2 and prostaglandin endoperoxides on hemostasis. Therefore, it has been suggested that the relative extent to which the formation of these compounds is inhibited by aspirin might result in an increased or decreased likelihood of thrombosis. Although prostacyclin is synthesized by arterial endothelium and in vitro studies suggest that arterial cyclooxygenase is less sensitive to inhibition by aspirin than venous cyclooxygenase, the actual effects of aspirin on arterial synthesis of prostacyclin in healthy or diseased human arteries remain to be established.

In most clinical studies to date which evaluated the effect of aspirin in preventing thrombosis, the dosages of aspirin (900 mg to 1.5 g daily in divided doses) probably inhibited the synthesis of prostacyclin as well as that of thromboxane A_2. Although concomitant inhibition of prostacyclin synthesis by aspirin may potentially decrease the antithrombotic efficacy of the drug, it is unlikely that this effect increases the risk of thrombosis since an increased risk has not been observed in these studies or in patients with rheumatoid arthritis receiving higher dosages of the drug. Cyclooxygenase in both platelets and venous endothelium has been found to be inhibited by single oral aspirin dosages of 80–300 mg. However, at these doses, the duration of inhibition of thromboxane A_2 synthesis in platelets (about 48–96 hours) is longer than inhibition of prostacyclin synthesis in venous endothelium (about 24–48 hours), apparently because cyclooxygenase is resynthesized in venous endothelium but not in platelets. Since cyclooxygenase in platelets appears to be more sensitive to inactivation than cyclooxygenase in venous endothelium, it has been suggested that low dosages of aspirin might prevent thrombosis by selectively inhibiting prostaglandin endoperoxide and thromboxane A_2 synthesis; however, an optimum dose and schedule of administration of aspirin have not been clearly determined, and the actual clinical importance of such a selective inhibitory effect remains to be clearly established. In addition, salicylate appears to competitively inhibit the effect of aspirin on platelets; the relevance of this effect to the prevention of thrombosis is not known.

Since results of numerous clinical studies indicate that the antithrombotic effect may be limited to males, it has been suggested that this effect of aspirin is sex related and may be related to differences in hormonal factors, sensitivity of cyclooxygenase inhibition in platelets and blood vessel walls, and/or other platelet factors in the pathogenesis of thrombosis. However, this has not been clearly established and further evaluation is needed.

Aspirin and dipyridamole appear to have at least additive inhibitory effects on platelet function (e.g., aggregation) in vivo. Aspirin has been shown to potentiate the effect of dipyridamole in normalizing reduced platelet sur-

in patients with prosthetic heart valves. Aspirin and dipyridamole also appear to have a synergistic antithrombotic effect, at least in small blood vessels. The exact mechanisms have not been fully elucidated, but the platelet-inhibiting effects of the combination appear to depend on aspirin dosage. Since prostacyclin appears to be necessary for the action of dipyridamole on platelet function, it has been suggested that the inhibition of platelet aggregation and antithrombotic effect of dipyridamole may be potentiated by selective inhibition of platelet cyclooxygenase and thromboxane A_2 synthesis with low dosages of aspirin. In one study, the combination of 120 mg of aspirin once daily and 75 mg of dipyridamole 3 times daily was shown to maximally inhibit platelet functions (e.g., aggregation) in vivo without prolonging bleeding time; it was suggested that prostacyclin synthesis was not substantially inhibited by this regimen. Further studies evaluating the effects of varying dosages of the drugs in combination are needed.

Pharmacokinetics

Since both unhydrolyzed aspirin and its metabolite, salicylate, are pharmacologically active, the pharmacokinetics of both compounds must be considered.

For additional information on the distribution and elimination of *salicylate*, see Pharmacokinetics in the general statement on Salicylates 28:08.04.

ABSORPTION

Approximately 80–100% of an oral dose of aspirin is absorbed from the GI tract. However, the actual bioavailability of the drug as unhydrolyzed aspirin is lower since aspirin is partially hydrolyzed to salicylate in the GI mucosa during absorption and on first pass through the liver. There are relatively few studies of the bioavailability of unhydrolyzed aspirin. In one study in which aspirin was administered IV and as an oral aqueous solution, it was shown that the solution was completely absorbed but only about 70% reached the systemic circulation as unhydrolyzed aspirin. There is some evidence that the bioavailability of unhydrolyzed aspirin from slowly absorbed dosage forms (e.g., enteric-coated tablets) may be substantially decreased. Food does not appear to decrease the bioavailability of unhydrolyzed aspirin or salicylate; however, absorption is delayed and peak serum aspirin or salicylate concentration may be decreased.

Most studies reported to date determined the bioavailability of aspirin preparations in terms of salicylate. Effervescent or noneffervescent oral aqueous solutions of aspirin appear to be completely absorbed. Oral buffered aspirin tablets, uncoated plain aspirin tablets, and methylcellulose film-coated (nonenteric) plain aspirin tablets are approximately 80–100% absorbed. Erratic and incomplete absorption of some enteric-coated aspirin tablets (particularly those with shellac coatings) has been reported, but recent studies indicate that the extent of absorption of currently available enteric-coated aspirin tablets is similar to that of buffered, uncoated plain, and film-coated plain aspirin tablets. Although well-designed studies are lacking, the extent of absorption of extended-release aspirin tablets appears to be similar to that of uncoated plain aspirin tablets. There are apparently no published studies on the bioavailability of aspirin capsules. Following rectal administration as a suppository, aspirin is slowly and variably absorbed; the extent of absorption increases with increasing rectal retention time. In general, 20–60% of the dose is absorbed if the suppository is retained for 2–4 hours and 70–100% is absorbed if the suppository is retained for at least 10 hours.

The rate of absorption of aspirin depends on the same factors that determine the rate of absorption of other salicylates and the relative rates of absorption from various oral aspirin dosage forms are generally the same as for oral dosage forms of other salicylates (e.g., aqueous solutions are the most rapidly absorbed). As with other salicylates, dissolution is usually the rate-limiting process in the absorption of tablets containing aspirin; however, the in vitro dissolution rate of a specific preparation does not necessarily reflect the in vivo absorption rate. According to the manufacturer, the in vitro dissolution of film-coated aspirin tablets does not differ from that of uncoated plain tablets; however, the film-coated tablet does not undergo dissolution in the mouth during administration.

Effects of Buffers

There has been controversy over the relative rates of absorption of buffered aspirin tablets and uncoated plain aspirin tablets and their relative potential for producing gastric irritation and analgesia.

The buffers contained in buffered aspirin tablets may increase the pH in the microenvironment of aspirin particles and thereby increase solubility of the drug in surrounding GI fluids; as a result, the dissolution rate of the tablets may be increased. However, it cannot be stated that *all* buffered aspirin tablets are dissolved and absorbed more rapidly than *all* uncoated plain aspirin tablets. The types and amounts of buffers affect dissolution rate, and claims for a specific preparation should be substantiated by appropriate data. Conflicting reports of the relative rates of absorption of buffered or uncoated plain aspirin tablets are most likely due to differences in the specific preparations studied. Some studies have shown that, like aqueous aspirin solutions, some buffered aspirin tablet preparations may be absorbed slightly more rapidly than some uncoated plain aspirin tablet preparations and may produce slightly higher peak serum salicylate concentrations; however, clinically important differences in the onset or intensity of analgesia produced by these dosage forms or specific preparations have not been established. Crossover studies directly comparing peak serum concentrations of unhydrolyzed aspirin attained with these dosage forms are lacking.

It has been suggested that buffered aspirin tablets cause less gastric irritation than uncoated plain aspirin tablets since the potentially more rapid dissolution of the former may reduce contact time between aspirin particles and gastric mucosa. However, several recent, well-designed studies indicate that buffered aspirin tablets do not cause less gastric irritation than uncoated plain aspirin tablets.

Rapidly Absorbed Dosage Forms

Following oral administration of single doses of rapidly absorbed aspirin dosage forms, salicylate is detected in serum within 5–30 minutes, and peak serum salicylate concentrations are attained within 0.25–2 hours, depending on dosage form and specific formulation. Clinically important differences in the onset or intensity of analgesia produced by rapidly absorbed dosage forms or specific preparations have not been established.

Following oral administration of a single 650-mg dose of aspirin as an effervescent or noneffervescent aqueous solution in healthy adults, average peak plasma aspirin concentrations of about 13 µg/mL are attained within 15–40 minutes and average peak plasma salicylate concentrations of about 40–55 µg/mL are attained within 30–60 minutes. After a single 650-mg oral dose of aspirin (as two 325-mg uncoated plain tablets) in fasting healthy adults, average peak plasma aspirin concentrations of about 7–9 µg/mL occur within 25–40 minutes and average peak plasma salicylate concentrations of about 35–50 µg/mL occur within 1.5–2 hours. Following oral administration of a single 650-mg dose of buffered aspirin (as 2 tablets, each containing 325 mg of aspirin), average peak plasma salicylate concentrations of about 40–60 µg/mL are attained within 45–60 minutes.

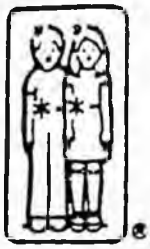
In one study in healthy fasting adults given a single 975-mg oral dose of aspirin (as three 325-mg uncoated plain tablets), peak serum salicylate concentrations averaged 60–75 µg/mL and occurred within 2 hours. In another study in fasting rheumatoid arthritis patients given a single 1.95-g oral dose of aspirin (as six 325-mg uncoated plain tablets), peak plasma aspirin concentrations of about 12–16 µg/mL occurred within 1 hour and peak plasma salicylate concentrations of about 110–160 µg/mL occurred within 4 hours. When these patients were given the same dose of buffered aspirin (as 6 tablets, each containing 325 mg of aspirin), peak plasma aspirin concentrations of about 14–18 µg/mL occurred within 1–2 hours and peak plasma salicylate concentrations of about 140–160 µg/mL occurred within 1–2 hours.

Enteric-Coated Tablets

There are few published studies reporting plasma aspirin or salicylate concentrations after single oral doses of enteric-coated aspirin tablets. In one crossover study, following single 975-mg oral doses (three 325-mg tablets) of 2 commercially available enteric-coated aspirin preparations in healthy adults, average peak serum salicylate concentrations of 48 µg/mL occurred at 8 hours with one preparation, and average peak serum salicylate concentrations of 25 µg/mL occurred at 14 hours with the other preparation. In one study in fasting rheumatoid arthritis patients given a single 1.92-g oral dose (as six 320-mg enteric-coated tablets), peak plasma aspirin concentrations of about 4–7 µg/mL occurred within about 4 hours and average peak plasma salicylate concentrations of about 70 µg/mL occurred within about 8 hours.

Extended-Release Tablets

There are few published studies reporting plasma aspirin or salicylate concentrations after single oral doses of extended-release aspirin tablets. Combining data from several small studies, some clinicians report that following a single 1.3-g oral dose of aspirin as two 650-mg extended-release tablets, an average peak serum aspirin concentration of about 3 µg/mL was attained within 1 hour and peak serum salicylate concentrations of about 70–80 µg/mL were attained within 4 hours; the serum aspirin concentration declined to less than 1 µg/mL by 3 hours and the serum salicylate concentration was about 60 µg/mL



BE WISE ABOUT REYE'S

• AWARENESS BULLETIN •

The flu or various symptoms identified as influenza occur more frequently during the winter months. Influenza is a viral infection, and as such, warrants our special attention because a fatal children's disease is associated with it. The disease, *Reye's Syndrome*, affects children from infancy through adolescence and can develop 3 to 5 days after the onset of the chicken pox, an upper respiratory illness, or other viral infections. It affects the liver and brain, is non-contagious and is often misdiagnosed as encephalitis, meningitis, diabetes, poisoning, drug overdose, or sudden infant death.

After a viral infection has seemingly run its course and the child is feeling better the following symptoms should be treated as serious and as possibly the first indication of *Reye's Syndrome*. Anti-nausea medication may mask the symptoms of the disease and because of the possible association of aspirin with *Reye's Syndrome*, parents should consult their physician before using these drugs. Watch for these symptoms, usually occurring in this order:

- PERSISTENT OR CONTINUOUS VOMITING
- LISTLESSNESS (LOSS OF PEP AND ENERGY, DROWSINESS)
- PERSONALITY CHANGE (SUCH AS IRRITABILITY, COMBATIVENESS OR SLURRED SPEECH)
- DISORIENTATION (UNABLE TO IDENTIFY WHEREABOUTS, OR FAMILY MEMBERS)
- DELIRIUM, CONVULSIONS

A child's life can depend on <u>early</u> diagnosis. *Reye's Syndrome* should be suspected in any child with chicken pox who vomits repeatedly. Phone your physician immediately if these symptoms develop and tell him you suspect *Reye's Syndrome*. If your doctor is not available take your child to an emergency room promptly. Two liver function tests (SGOT/SGPT) can be done to determine the possibility of *Reye's Syndrome*. There is a 90% chance of recovery when the syndrome is treated in its earliest stages by physicians and nurses experienced in the treatment of Reye's.

Epidemiologic research has shown an association between the development of *Reye's Syndrome* and the use of aspirin for treating the symptoms of influenza-like illnesses, chicken pox, and colds. The U.S. Surgeon General, the Food and Drug Administration, and the Centers for Disease Control recommend that aspirin and combination products containing aspirin not be given to children 18 years of age and under during episodes of these illnesses.

The NRSF is a non-profit, tax-exempt organization with chapters in forty states. The NRSF has pioneered the movement to disseminate knowledge about the disease in an effort to aid in early diagnosis, and also provides funds for research into the cause, cure, care, treatment, and prevention of *Reye's Syndrome*.

For more information contact the NATIONAL REYE'S SYNDROME FOUNDATION, P.O. BOX 829AB, BRYAN, OHIO 43506, OR CALL 419/636-2679, 800/233-7393, OHIO RESIDENTS CALL 800/231-7393.

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The human body has no physiological need for refined sugar, yet the average American consumes 128 pounds of it every year.[1] That's a per capita consumption of one teaspoon every hour, 24 hours a day,[2] more than any other nation on earth. It's difficult *not* to eat sugar. To sweeten or not to sweeten is no longer a matter of individual discretion. In 1910, 75 percent of the sugar Americans consumed was added to foods in the kitchen; the other 25 percent came from processed foods.[3] Today, the situation is almost reversed. The sugar added by food and beverage manufacturers to what we eat and drink accounts for 65 percent of American sugar consumption[4]; these days only 35 percent is added in the kitchen. Sugar has become a staple ingredient in a staggering number of processed foods (see sidebar)—even cigarettes are laced with sugar.

Average Americans obtain about one-quarter of their calories from sugar.[5] Only a small proportion of that amount comes from the natural sugars in carbohydrates, fruits, vegetables and dairy products. Most of it is refined white sugar, sucrose. Children consume even more sugar than adults. Some children obtain as much as 48 percent of their calories from sugar—almost *half* their caloric intake.[6] Growing evidence strongly suggests that this level of sugar consumption is a major factor in increased rates of degenerative diseases, including dental caries (cavities), obesity, diabetes, coronary heart disease, vitamin deficiencies and psychological disturbances.

Eating sugar can be worse than eating nothing. Refined sugar provides only empty calories. It contributes none of the protein, fat, vitamins or minerals needed for its own metabolism in the body, so these nutrients must be obtained elsewhere. Sugar tends to replace nourishing food in the diet. It is a thief that robs us of nutrients. A dietary emphasis on sugar can deplete the body of nutrients. If adequate nutrients are not supplied by the diet—and they tend not to be in a sugar-rich diet—they must be leached from other body tissues before sugar can be metabolized. For this reason, a U.S. Senate committee labeled sugar as an "antinutrient."[7]

Sucrose and the Blood Sugar Roller Coaster

Of the more than 100 chemicals called "sugar," one of them, glucose, is essential to human metabolism. Refined white sugar, however, can interfere with the body's delicate metabolism. The human body manufactures life-sustaining glucose from carbohydrates. Carbohydrates come in two forms: simple sugars in fruits, vegetables and dairy products and starches, complex chains of simple sugars in grains, beans and vegetables. Unrefined foods contain enough sugars and/or starches to provide all the glucose necessary for a healthy metabolism *without adding any sucrose to the diet.* Carbohydrates also provide a variety of other nutrients lacking in refined sucrose, for example, vitamins, minerals, protein, fiber and fats.

The body processes simple sugars and carbohydrates in the same way, but at different speeds. Sucrose is digested quickly into two simple sugars, glucose and fructose (fruit sugar). These sugars enter the blood stream through the small intestine, and are carried to the liver where they are either used immediately or converted into glycogen for storage until needed. When glycogen storage space in the liver is filled to capacity, excess glycogen is returned to the blood in the form of fatty acids, which are stockpiled first in the inactive parts of the body—buttocks, breasts, abdomen and thighs—then in active organs, for example, the heart and kidneys. The minerals sodium, potassium, magnesium, calcium and chromium, and the B-complex vitamins, are all used to create glucose.

The sugar units bound together into starch chains are metabolized the same way as simple sugars, but their complex structures take longer to break down. During carbohydrate digestion, these complex glucose chains are converted first into dextrine, then into maltose, and finally into individual glucose molecules.

The amount of glucose circulating in the blood determines our appetite. When blood sugar levels fall below a certain trigger point, we experience hunger. The feelings of weakness, irritability and anxiety that often accompany hunger result from a low level of glucose in the blood, a condition called "hypoglycemia." The feeling of hunger is a signal that our cells are not

Jacquetta Nisbet

THE SWEET THIEF

By Janice Fillip

getting enough glucose to function properly. Eating a meal readjusts the amount of sugar in the blood. The simple sugars in unprocessed foods provide an immediate burst of glucose-energy to our bodies. Then, the more complex sugar chains in the starches in the meal provide a slower but sustained supply of glucose-energy.

Glucose circulating in the blood cannot enter cells to nourish them without the help of insulin, a hormone produced by the Islets of Langerhans, a group of cells in the pancreas. Fructose enters the blood stream somewhat more slowly than glucose, and is metabolized by the enzyme fructokinase rather than insulin. This difference between glucose and fructose metabolism allows some diabetics, whose bodies do not produce enough insulin to metabolize glucose, to have fructose-sweetened foods in their diets.

Since simple sugars work faster than the sugars in starches to counteract the effects of hypoglycemia, many people prefer to satisfy their hunger pangs with a sugary snack instead of a balanced meal. But substituting a brief burst of energy for a gradual, sustained supply of glucose has significant adverse consequences for the body.

Although blood sugar levels are suddenly boosted by a sucrose "rush," they drop just as quickly after that sugar has been metabolized, often leaving a person feeling droopy, tired and irascible. To recapture the same sugar-induced feeling of energy and alertness, a person may eat more sugar. As sucrose-induced glucose rushes replace the sustained glucose release from carbohydrates, the peaks and valleys of blood sugar concentration tend to become more pronounced. This cycle of sugar highs and lows is similar to the kind of physiological dependence produced by some drugs. Although sucrose is not addictive in the same way that, for example, narcotics are, it may be considered to have some addictive properties, and many people refer to themselves as "sugar addicts."

The minor feelings of weakness, irritability and anxiety that accompany normal hunger are magnified by the large variations in blood sugar levels that result from replacing carbohydrates in the diet with so much sucrose. These fluctuations have been shown to trigger changes in behavior, including reduced ability to concentrate, fatigue, depression, confusion, forgetfulness and headaches. As a result, a growing number of physicians and nutritionists now consider hypoglycemia not only a state of low blood sugar, but also a factor in health and behavioral problems as well. They reason that meals high in refined sucrose quickly boost blood sugar levels and stimulate the pancreas to secrete large quantities of insulin. This insulin spurt allows too much sugar to pass from the blood into the cells, thus lowering the blood sugar level *below normal*. This low blood glucose level may interfere with the proper functioning of nerve cells by depriving them of glucose fuel and resulting in the symptoms of hypoglycemia. A survey of 134,000 people conducted by the Department of Health, Education and Welfare showed that 49.2 percent said they suffered symptoms typically associated with hypoglycemia.[8] And one psychiatric study of people with emotional problems showed that 70 percent of those diagnosed as schizophrenic showed some form of hypoglycemia.[9]

Hypoglycemia's role in emotional problems remains a point of controversy. Much of the medical establishment maintains that the emotional problems experienced by alleged sufferers of hypoglycemia reflect not dietary imbalances but rather psychological problems best treated with drugs. (Editor's note: For more on the traditional medical view of the role of nutrition in health, see "Doctors and Nutrition: A Conversation with Marion Nestle," in this issue.)

The precipitous drop in blood sugar level that follows a sugar binge decreases the functional capacity of brain cells. The brain then signals the adrenal glands to secrete the hormone adrenalin (epinephrine), which stimulates the liver to release stored glycogen into the blood, and the pituitary gland to secrete hormones to aid the conversion of glycogen into glucose. Adrenalin also activates many metabolic processes necessary to respond to emergencies. It accelerates heart rate, makes breathing more rapid and stimulates feelings of anxiety and apprehension, reactions that tend to influence emotions and behavior.

continued

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Average Americans obtain about one-quarter of their calories from sugar

continued

The adrenal glands supervise the glucose-oxygen balance in the blood. Excessive sucrose intake alters this balance and stimulates the adrenals to release hormones which stimulate the production of gastric juices in the stomach. This heightened gastric activity tends to duplicate conditions found in people with gastric or duodenal ulcers,[10] and may explain why some people develop upset stomachs after eating sugary snacks or sugar-rich processed foods.

The Sweet Thief Steals Teeth—and Health

Although sugar was judged "safe" in 1976 by the Senate Select Committee on Substances Generally Regarded as Safe (GRAS), mounting evidence strongly suggests that sucrose consumed in quantities typical in the American diet is associated with diabetes, obesity, tooth decay, heart disease, vitamin deficiencies and possibly premature aging. The chief of the U.S. Department of Agriculture's Human Nutrition Institute estimated that as many as 20 million Americans may be "sugar sensitive," meaning that they experience adverse health effects from sugar.[11] Other scientists are more outspoken. John Yudkin, M.D., Ph.D., professor emeritus of nutrition at London University, has written: "... if only a small fraction of what is known about the effects of sugar were revealed in relation to any other food additive, that material would promptly be banned."[12]

Even the sugar industry is hard-pressed to deny that sugar is a leading cause of dental caries. Sugar makes foods sticky, so they adhere to teeth more tenaciously. Bacteria in the mouth feed on food residues glued in place by sugar and produce acid that eats away at teeth. The National Institute for Dental Research has determined that sucrose is the favorite growth medium for the acid-producing bacteria that cause tooth decay.

Sugar that has not been denatured in the refining process appears less instrumental in promoting tooth decay. One study[13] exposed cavity-free teeth from the same source to either saliva mixed with sugar cane juice or saliva mixed with sucrose. After a few weeks, the teeth in the sugar cane juice had not decalcified as much as about one-half of those in the refined sugar had.

Dental caries are the most prevalent degenerative disease in the world. Virtually all Americans have some tooth decay and one-half the U.S. population has *no teeth left* by age 55.[14] We pay dearly for our national sweet tooth—every year Americans spend $10 billion for dental care.[15]

In a nation where about one-third of the population is overweight,[16] obesity is a major health problem. Animal studies show that a high-sugar diet increases the body's fat content while reducing the amount of protein.[17] Eating sugar makes people fat in several ways. First, when sugar is a staple in the diet, the overall nutritional value of the foods consumed is reduced, and a person must eat more to obtain adequate nutrition. Second, the sugar hidden in processed foods adds to the number of calories we unwittingly consume. But sugar has a more sinister link to obesity. It appears that children who consume large amounts of sugar during childhood may become physiologically predisposed to obesity later in life. Scientists have observed that babies bottle-fed with formulas that contain sucrose show a higher rate of obesity than breast-fed babies.[18] Feeding babies sugar-empty calories not only packs more fat into existing fat cells, it may also cause the body to produce *more* fat cells, cells that tend to stay with the child throughout life. Later dieting may reduce the size of fat cells, but not their total number.[19]

Diabetes is another sugar-related illness. Insulin regulates the metabolism of sugar and the passage of glucose into the cells. When the body cannot produce enough insulin to metabolize all the sucrose present, excess sugar remains in the blood. Cells cannot function without glucose, and if a body lacks sufficient in-

Sweet Deals: The International Sugar Trade

The hunger for sweet treats has profoundly influenced world history. The African slave trade originated to provide labor for sugar plantations in Spain and the Caribbean. British historian Noel Deerr writes, "The 'death' toll of the slave trade was 20 million Africans of which two-thirds should be charged against sugar."[1]

After slavery was abolished, the United States obtained most of its sugar from Cuba. Cuba's most fertile land was diverted from food crops for Cubans to sugar cane plantations to produce sugar for export. Until the Castro government came to power in 1960, Cuba remained an economic colony of the United States, governed to a considerable extent by the boards of directors of a few sugar companies.

This system is not unique to Cuba. In most sugar-producing countries, the richest lands are appropriated for sugar cane, an export crop, precluding self-sufficiency in food production and forcing these nations to import food. In 1980, more than half the raw sugar imported into the U.S. came from the Dominican Republic, Brazil, the Philippines, Guatemala, and South Africa.[2] Every one of these countries is ruled by an authoritarian regime accused of major human rights violations by Amnesty International. The political strife in these nations today can, to some extent, be traced to the inequities that result when a small group of landowners controls most of the arable land and plants it with sugar cane or other export crops, for example, bananas and coffee, while the majority of the population lacks land to grow food.

Sugar production and pricing are determined by the International Sugar Organization (ISO), a cartel similar to OPEC, composed of representatives of the major sugar exporting and importing nations. The United States, which buys 20 percent of the sugar traded on world markets, wields great influence in the ISO. The importing nations have always refused to buy finished refined sugar from the exporting nations. This trade restriction was developed to protect the profits of sugar refining industries in the importing nations, many of which could not compete with sugar refined in producer nations and sold on a free-trade basis. In effect, the ISO has prevented producer nations from industrializing their sugar industries.

U.S. sugar policy, outlined in the Sugar Act of 1934, was designed to protect U.S. sugar refiners from foreign competition and at the same time to protect American consumers from speculative price increases. This program cost U.S. taxpayers more than $300 million in 1972 alone.[3] But despite abundant world sugar supplies, sugar prices have steadily increased over the past few years. The Federal Trade Commission has pronounced U.S. sugar policy "spectacularly unsuccessful in protecting consumers from rising world sugar prices."[4] The world price for sugar, at eight cents a pound in 1979, jumped to 24 cents a pound by February 1980. Consumers grumbled at paying 300 percent more for sugar, but that's only part of the story. According to the U.S. Department of Agriculture, every one-cent-per-pound increase in the price of sugar adds $215 million to America's annual food costs[5]—a bitter pill, even if it has a sugar coating.

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sulin, cells may die. Diabetics lack sufficient insulin, and 4.5 million Americans suffer from this serious illness. Diabetes is usually controlled by dietary restrictions or by injection of commercially-produced animal insulin. These treatments allow diabetics to live reasonably normal lives, but they do not cure the illness.

Dr. Frederic Banting, whose discovery of insulin won him the Nobel Prize, recommended that the best way to deal with diabetes was to prevent it, and that the best prevention was to reduce sugar consumption.[30] Persuasive evidence supports his opinion. During the two World Wars, incidence of diabetes dropped sharply among civilians whose sugar supply was severely rationed, but rose steadily among soldiers who continued to receive ample sugar allotments.[31] Although the cause of diabetes is not entirely clear, some physicians and nutritionists maintain that a diet high in sugar overtaxes the body's ability to produce insulin and promotes diabetes, particularly adult-onset diabetes. Animal studies have shown that high-sugar diets cause abnormalities in the pancreatic cells that produce insulin, and studies of humans have shown that as sugar consumption increases, so does the blood insulin level.[32] Harvard Nutrition Professor Jean Mayer has noted that adult-onset diabetics "usually produce near-normal amounts of insulin, but apparently not enough to cope with the demand."[33]

Diabetics usually develop mild myopia or far-sightedness, and sometimes severe retinal disease if their blood sugar level is not properly controlled. Both animal and human studies show that a high-sugar diet can change the refraction of the eye and cause these problems.[34]

Although the evidence linking sugar consumption to coronary heart disease is controversial and far from conclusive, it suggests that sucrose consumption may play a significant role in the development of the nation's leading killer. Sucrose deprivation in Europe during World War II was associated with a significant drop in coronary heart disease,[35] an association strengthened by recent European research. Finnish researchers monitoring the incidence of heart attacks among patients at two mental hospitals there, found the hospital with the lower number of heart attacks also had 40 percent less sugar in its institutional diet. In England and Israel, separate studies show that a high-sugar diet raises cholesterol levels, particularly in young men and post-menopausal women. High cholesterol level is a significant risk factor for heart disease. Another study[36] showed that sugar and salt, the second most popular food additive, tend to work synergistically to increase susceptibility to high blood pressure, another risk factor for heart disease. Other studies[37] have suggested that the relationship between sugar and heart disease is stronger

continued

As many as 20 million Americans may . . . experience adverse health effects from sugar

continued

than the one between fat consumption and heart disease.

The connection between sugar and vitamin deficiency is clearer. In fact, researchers use sucrose-based diets to induce riboflavin (B_2) deficiency in test animals.[28] Because refined sucrose does not supply the B vitamins or minerals necessary for its own digestion, these nutrients must be supplied by other foods or leached from stored deposits in the body, but these vitamins are needed elsewhere. B vitamins, for example, are essential to the formation of glutamic acid, required for the proper functioning of the brain. Not only does sucrose "steal" vitamins for its metabolism, it also harms the intestinal bacteria that produce the B vitamins.[29] The trace mineral chromium is particularly important in sucrose metabolism. Chromium deficiency may contribute to diabetes and to the eye problems associated with it.

Few Americans believe that the serious illnesses that result from nutritional deficiencies could occur in the richest nation on earth. But American teenagers who consumed large quantities of high-sugar junk foods were recently shown to have hazardously low levels of thiamin (B_1), and some early symptoms of beriberi, the thiamin-deficiency disease.[30] While the sometimes severe behavior problems symptomatic of this disease improved through treatment with thiamin supplements, the researchers who monitored the cases concluded: "Our experience suggests that such (vitamin deficiency) states may well be seen in an affluent modern society, and possibly be dangerous since (the resulting) personality changes were frequently aggressive in nature."

Another behavior problem apparently linked to sugar consumption is "hyperactivity." Although it is poorly defined and highly controversial, hyperactivity is a label applied to a broad range of behavior problems that make children moody, indigent, unable to concentrate and subject to temper tantrums. Up to 20 percent of school-aged children in the United States may be hyperactive.[31] Children diagnosed as hyperactive at the New York Institute of Child Development registered abnormal results on glucose tolerance tests, suggesting that they have a problem metabolizing sugar.[32] Dr. Keith Conners, who has investigated the sugar-hyperactivity link at Children's Hospital in Washington, D.C., speculated, "Sugar may act like a stimulant drug insofar as it alters body metabolism."

Related research at the Massachusetts Institute of Technology is focusing on the possibility that sugar may alter the brain chemicals serotonin, acetylcholine and norepinephrine, neurotransmitters known to affect aggressive, sexual and eating behavior, sleep and sensitivity to pain. Neurobiologist Richard Wurtman explained: "We know that all carbohydrates affect brain serotonin because they cause insulin to be released. Since sugar causes insulin to be released more rapidly, it may have a greater effect on serotonin levels."[33]

Finally, sugar may even accelerate human physical maturation and the aging process. Studies show that sugar promotes the release of hormones involved in sexual maturation, and extrapolations from longevity studies with rats suggest that high-sugar diets may reduce human life expectancy as much as several years.[34]

Kicking the Habit

Faced with the growing evidence linking sugar consumption to various health problems, many people are trying to kick their sugar habits. Many health authorities caution people to eat less sugar: the American Heart Association, the Department of Health and Human Services, the Surgeon General, the U.S. Department of Agriculture and the American Medical Association. But a sweet tooth can be hard to control. Some people who try to renounce sugar are surprised to find that it feels like an addiction, not quite a clinical addiction, but certainly a habit that's hard to break.

Eliminating sugar from the diet is easier said than done. Most of the sugar in our food is put there by processed food and beverage manufacturers. The amount of sugar in these foods and drinks is often surprising (see sidebar), but it is very difficult to know exactly how much sugar is in any food because food labels do not list the amount of each ingredient. Many consumer organizations have pennoned the

continued

Other Sugars

Honey is a combination of fructose, glucose, maltose and sucrose formed through enzyme action on nectar gathered by bees. It also contains some vitamins and minerals—but not much. Honey is sometimes promoted as a "healthier" substitute for sugar. It isn't. It has basically the same effects on the body as white sugar. In fact, some commercial honey has sugar added to it.

Brown Sugar (turbinado) is simply white sugar mixed with either molasses, or artificial colors and flavors that mimic molasses. The physiological effects of white sugar and brown sugar are identical.

Corn syrup and *dextrose* are processed sugars made from corn starch. They are popular with the food industry. They are no better for you than white sugar.

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EATING

High sugar diets may reduce human life expectancy as much as several years

continued

Food and Drug Administration to require percentage labeling, so consumers can make more informed decisions about the amount of sugar—and other additives—in their diets, but to date the agency has taken no action.

Although food labels do not specify the proportions of ingredients, the more sugar in a product, the closer to the beginning of the ingredient list it is placed. Read food labels carefully, and select products without sugar, or those that place it toward the end of the ingredient list.

One way to assess your sugar consumption is to write down how much sugar you eat in one week. You may be surprised at how much you consume.

Then, try to cut back on the sugar added to foods and beverages. It's not that much of a hardship. Sugar tends to blunt the sensitivity of the palate. When sugar is restricted, the natural flavors of foods tend to become more noticeable. Try to treat sugar as a condiment, not as a staple to be eaten in bulk.

When you do eat sugar, try to eat it at the end of a meal, not between meals. Sugary snacks on an empty stomach can put you on the road to the sugar rush/sugar crash cycle. Sugar's effects on the body are reduced when eaten at the end of a meal because the foods eaten before it slow its entry into the blood stream.

Reducing your sugar consumption may produce some symptoms of withdrawal, for example, irritability, depression or nervousness. These generally pass in about a week. It's a good idea to continue to keep a sugar diary as you reduce your sugar consumption. It allows you to see where you're making progress and where more effort needs to be applied.

In Chicago, a group called Sugar Beaters Anonymous has formed to help people kick their sugar habits. Sugar Beaters began as a wager between two brothers, Lawrence and James McManus. They both decided to give up sugar, and to "sweeten" the deal, they laid $100 on the line. Whoever ate sugar first would lose his money. Two years later, the bet remains to be collected. The brothers said they felt so much healthier after giving up sugar, they decided to help others do the same.

Sugar Beaters is organized along the lines of Alcoholics Anonymous (see "Alcoholics Anonymous: 45 Years of Self-Help One Day at a Time," in MSC #11). At meetings three times a week, members discuss their feelings of powerlessness over sugar, and the ways they deal with the problems sugar causes them. Lawrence McManus, a nutritionist, said there are many similarities between the obsessions for sugar and alcohol. "To us, sugar is an addiction. Whether it's sugar or alcohol, people are hooked on a chemical high (they're) unable to control, and suffer malnutrition because neither alcohol nor sugar has nutritional value."

Sugar Beaters appears to work for some people. One alumnus said, "For the first time in about three years, I'm not spaced out, my vision isn't blurred, I'm not tired and best of all, I feel satisfied with a normal amount of food. I feel like my old self again." ☐

Janice Fillip has written extensively on nutrition, food politics and ecology for Whole Foods, Women's Sports, Not Man Apart *and other publications.*

Resources

Sugar Beaters Anonymous,
Sugar Detox Center
4800 N. Milwaukee
Chicago, IL 60630
(312) 736-8888

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Sugar Content of Selected Foods:

Sugar Smacks	61%
Cap'n Crunch	43%
Count Chocula	44%
100% Bran	19%
Lucky Charms	51%
Heartland	23%
Carnation Instant Breakfast (chocolate)	23%
Pepperidge Farm Pirouettes	
Cookies	40%

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Figure 10-3. Satisfaction from Consuming Sugar.

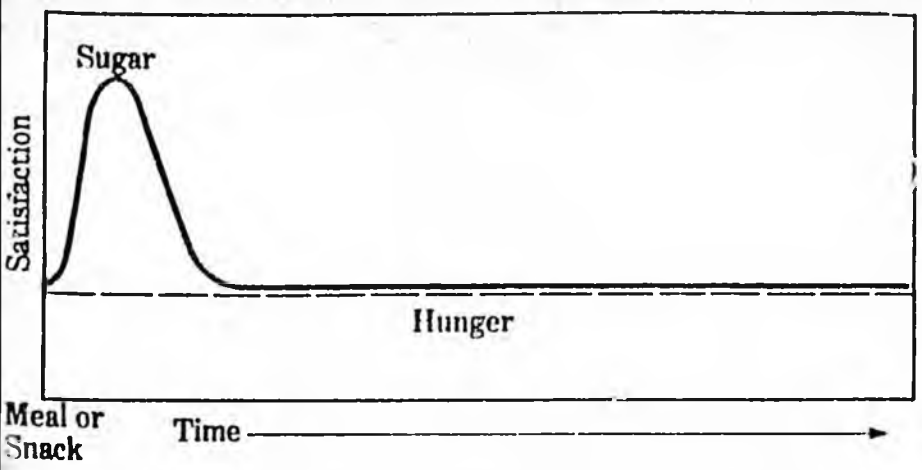


Figure 10-4. Satisfaction from Consuming Sugar and Starch.

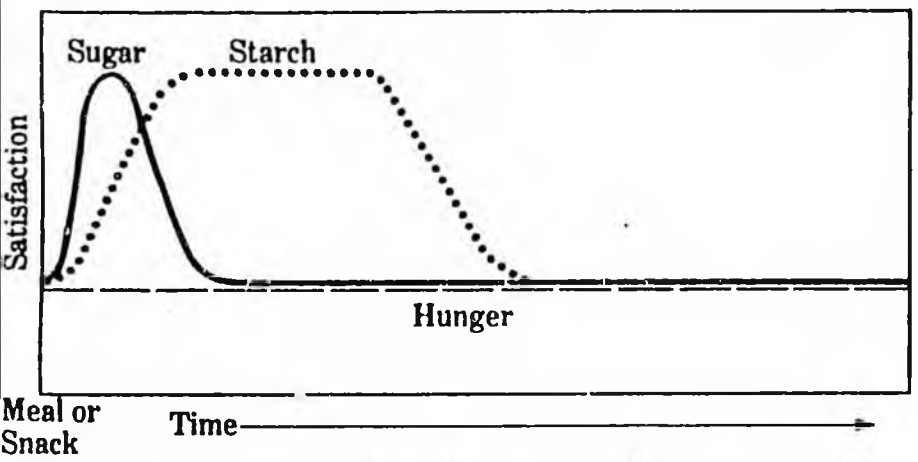


Figure 10-5. Satisfaction from Consuming Sugar, Starch and Protein.

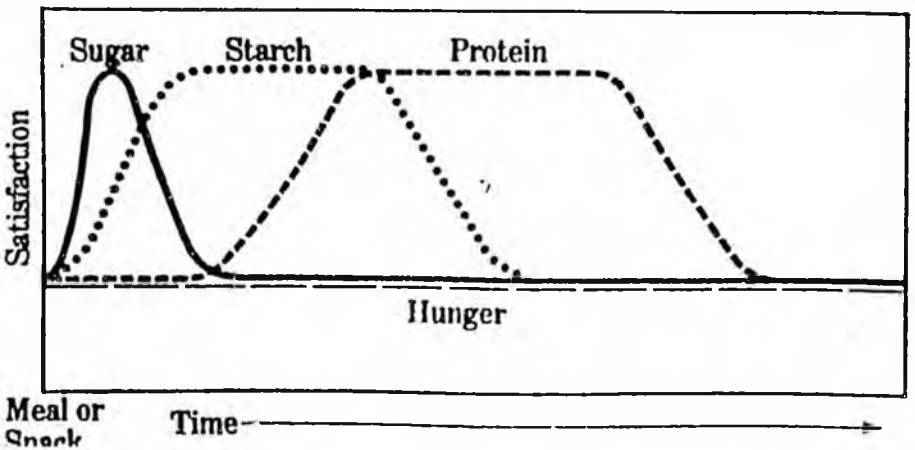


Figure 10-6. Satisfaction from Consuming Sugar, Starch, Protein and Fat.

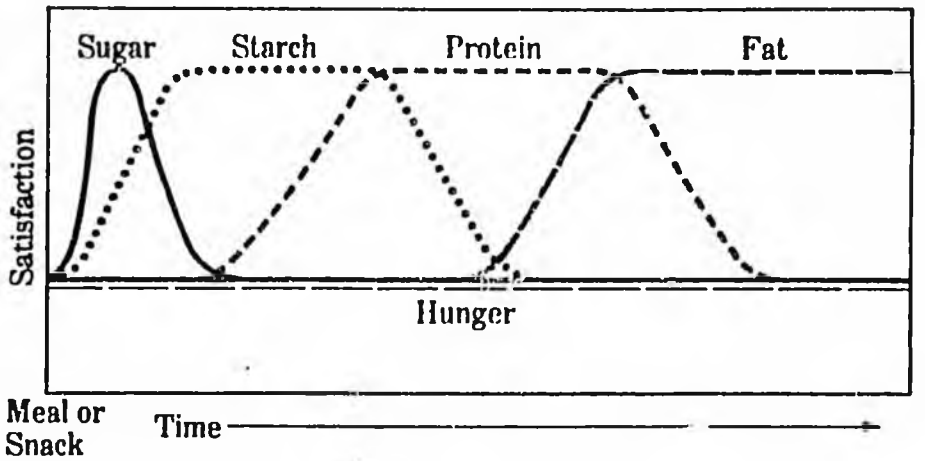
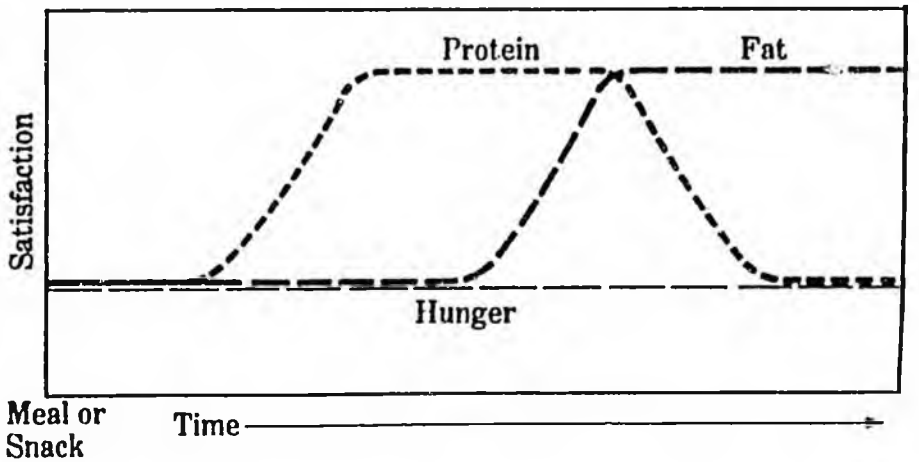


Figure 10-7. Satisfaction from Consuming Protein and Fat.



SUGAR IN BREAKFAST CEREALS

Percent Total Sugar (Dry Weight)

0.1%	Puffed Rice
0.5	Puffed Wheat
0.6	Shredded Wheat-spoon size
3.0	Cheerios
3.6	Corn Chex
3.7	Wheat Chex
4.4	Rice Chex
4.6	Kix
5.1	Special K
5.4	Post Toasties
5.4	Corn Flakes
7.1	Rice Krispies
7.1	Grape Nuts
8.1	Total
8.2	Wheaties
9.6	Concentrate
9.8	Product 19
12.0	Buckwheats
12.8	Grape Nut Flakes
13.0	Bran Flakes, 40%
13.6	Team
16.5	Life
18.3	Fortified Oat Flakes
19.4	All Bran
20.5	100% Bran
21.2	Life Cinnamon
21.7	Country Crisp
25.6	Frosted Mini Wheats
27.8	C. W. Post (Plain)
29.1	Raisin Bran
29.3	C. W. Post (Raisin)
29.6	Golden Grahams
30.0	Raisin Bran
30.1	Cracklin' Bran
31.7	Cap'n Crunch Peanut Butter
34.5	Cocoa Puffs
35.7	Trix
36.5	Frosted Rice
37.4	Honey Combs
37.7	Alpha Bits
39.4	Count Chocula
39.9	Cap'n Crunch
40.2	Quisp
40.2	Cookie Crisp, Oatmeal
40.2	Crazy Cow, Strawberry
40.6	Sugar Frosted Flakes
40.8	Corny Snaps
41.3	Lucky Charms
41.5	Cookie Crisp, Chocolate Chip
41.6	Fruity Pebbles
42.1	Cocoa Pebbles
42.7	Cookie Crisp, Vanilla
42.8	Frosted Rice Krinkles
43.3	Cocoa Crispies
43.7	Cap'n Crunch, Crunchberries
44.5	Frankenberry
45.3	Crazy Cow, Chocolate
45.4	Super Sugar Crisp
46.0	Sugar Corn Pops
48.4	Fruit Loops
54.0	Apple Jacks
55.5	Sugar Smacks

Source: Li, B.W., and Schuhmann, P.J., "Gas-Liquid Chromatographic Analysis of Sugars in Ready-to-Eat Breakfast Cereals". J. Food Sci. (in press).

Hidden Sugar

The approximate sugar content of popular foods expressed in teaspoons

100 grams sugar = 20 teaspoons = 1/2 cup = 3 1/2 oz. = 400 calories

			tsp. sugar
Candy*	Chocolate bar	1 average size	7
	Chocolate cream	1 average size	2
	Chocolate fudge	1 1/2" sq. (15 to 1 lb.)	4
	Chocolate mints	1 medium (20 to 1 lb.)	3
	Marshmallow	1 average (60 to 1 lb.)	1 1/2
	Chewing gum	1 stick	1/2
Cakes and cookies	Chocolate cake	1/12 cake (2 layer icing)	15
	Angel food cake	1/12 of large cake	6
	Sponge cake	1/10 of average cake	6
	Cream puff (iced)	1 average custard filled	5
	Doughnut, plain	3" diameter	4
	Macaroons	1 large or 2 small	3
	Gingersnaps	1 medium	1
	Molasses cookies	3 1/2" diameter	2
	Brownies	2" x 2" x 3/4"	3
Ice cream	Ice cream	1/8 quart (1/2 cup)	5-6
	Sherbet	1/8 quart (1/2 cup)	6-8
Pie	Apple	1/6 med. pie	12
	Cherry	1/6 med. pie	14
	Raisin	1/6 med. pie	13
	Pumpkin	1/6 med. pie	10
Soft drinks	Sweet carbonated beverage	1 bottle, 6 oz.	4 1/3
	Ginger ale	6 oz. glass	3 1/3
Milk drinks	Chocolate	1 cup, 5 oz. milk	6
	Cocoa	1 cup, 5 oz. milk	4
	Eggnog	1 glass, 8 oz. milk	4 1/2
Spreads and sauces	Jam	1 tbs. level	3
	Jelly	1 tbs. level	2 1/2
	Marmalade	1 tbs. level	3
	Syrup, maple	1 tbs. level	2 1/2
	Honey	1 tbs. level	3
	Chocolate sauce	1 tbs. thick	4 1/2
Cooked fruits	Peaches, canned in syrup	2 halves, 1 tbs. syrup	3 1/2
	Rhubarb, stewed, sweetened	1/2 cup	8
	Apple sauce (unsweetened)	1/2 cup scant	2
	Prunes, stewed, sweetened	4 to 5 med., 2 tbs. juice	8

* Candy is from 75 to 85% sugar. Popular candy bars are likely to weigh from 1 to 5 oz. and may contain 5 to 20 teaspoons of sugar. Adapted from current publications on food values. Courtesy of Dr. Herman Becks, University of California.

Dried fruits	Apricots, dried	4 to 6 halves	4
	Prunes, dried	3 to 4 medium	4
	Dates, dried	3 to 4 stoned	4 1/2
	Figs, dried	1 1/2 to 2 small	4
	Raisins	1/4 cup	4
Fruits and fruit juices	Fruit cocktail	1/2 cup, scant	5
	Orange juice	1/2 cup, scant	2
	Pineapple juice, unsweetened	1/2 cup, scant	2 3/5
	Grapefruit juice, unsweetened	1/2 cup, scant	2 1/5
	Grapefruit, commercial	1/2 cup, scant	3 2/3

Information from the American Dental Association, 211 E. Chicago Avenue, Chicago Illinois 60611

A Basic Sugarless SHOPPING GUIDE

On the following pages is a shopping list free of refined sugar, starch, and flour. But it's only a beginning list, because processors are realizing the need for natural products and are introducing more of them regularly. More sugarfree foods are coming to the grocery shelves.

Read labels very carefully. A brand in one area of the country may be sugarless while the same brand in another part of the country may have sugar added.

I believe shopping can be fun. Here are a few suggestions to help make it so:

1. Set aside a time of day or night when you can do your shopping in a leisurely manner.

2. Avoid the peak hours of shopping.

3. Make sure you have just eaten so as not to run the risk of becoming tired and irritable (and of overspending your budget).

4. Choose a pleasant store, one that gives you wide aisles, soothing music, appealing produce, fresh poultry, seafood, and meat, with much variety.

5. Snack while you shop. Take along some nuts, seeds, or cheese.

Grocery Items without Refined Sugar, Starch, or Refined Flour
Sample Brands Shown
Other brands are usually available—please read the label.

Crackers, etc. (if allowed)
Natural RyKrisp
Hol-Grain Brown Rice Wafer-ets
Hol-Grain Whole Wheat Wafer-ets

Fruit, canned (fresh preferred)
Pineapple in own juice—Dole, Townhouse
Grapefruit in own juice—Dole, Townhouse
Peaches—S & W Nutradiet Blue Label
Pears—S & W Nutradiet Blue Label
Fruit Cocktail—S & W Nutradiet Blue Label
Apple sauce—S & W Nutradiet Blue Label

Fruit, frozen
Strawberries—Bel Air Whole Unsweetened
Boysenberries, Bel Air
Blueberries, Bel Air
Most loose-bag packs

Fruit Juice, canned or bottled
Most items labeled simply "juice" are without sugar. For example:
Apple—Tree Top, Townhouse
Pear-apple—Townhouse
Grapefruit—Texsun Pink, Libby's, S & W
Pineapple—Dole, S & W
Prune—Townhouse
Grape—Welches, Empress
Cranberry—Ocean Spray
Orange and grapefruit—Townhouse
Orange—Libby's, Texsun
Avoid fruit drink, nectar, cocktail, and punch.

Fruit Juice, frozen concentrate
Orange—Minute Maid, Bel Air
Grapefruit—Bel Air
Apple—Tree Top
Pineapple—Minute Maid
Avoid frozen grape—sugar added.

Dairy Items
Cream, butter, milk
Cottage cheese
Cream cheese
Natural cheddar cheese (not processed)
Plain yogurt

Gelatin
Knox unflavored

Grains and Cereals (if allowed)
Brown rice, wild rice
Oatmeal, unflavored
Wheat germ
Whole grain mixes, 4-grain or 7-grain cereals

Meat, Poultry, Seafood, canned
Normally without sugar:
Tuna, salmon, sardines (except with tomato sauce), shrimp, clams, crab, and oysters.
Chicken—Swanson boned
Turkey—Swanson boned
Following brands are sugarless but unfortunately contain nitrite:
Luncheon meat—Majesty
Corned beef—Hereford
Ham—Armour Golden Star

Meat, etc., frozen
Unbreaded fish or meat patties

Nuts (preferably raw)
Most bag packages

Oils
To avoid hydrogenation and preservatives, pure cold-pressed vegetable oils are preferred—available at health food stores.

Olives
All

Pasta (if allowed)
Whole grain spaghetti, macaroni, and noodles are available in health food stores.

Peanut Butter
The "old fashioned" type is not hydrogenated and is therefore preferred.

Pickles
Dill

Salad Dressings
French--Girard's Original
Trader Vic's Javanese
Others at health food stores.

Salt
Morton's 5-lb. bag pack
Shilling Garlic Salt
Vegetable salt—health food stores
Sugars are often added to salt—please read label.

Sauces and Condiments
Prepared mustard--French's, Kraft
Tomato sauce—Del Monte, Progresso, Contadina
Maggi Seasoning
Tobasco Pepper Sauce
Ketchup—health food store
Soy sauce—Kikoman's, Tamari

Sausage, etc.
Although Ball Park wieners and Jones sausage are sugarless, they contain nitrite. Check locally made brands and health food stores for products without sugar or nitrates/nitrites. Some physicians feel pork should be avoided.

Vegetables, canned (fresh vegetables are much preferred)
Normally sugarless:
Green beans
Carrots
Asparagus
Spinach
Beets (except pickled)
Tomatoes—Townhouse, Hunts, Gardenside
Mixed veg—Freshlike, Veg-All
Sweet potatoes—Taylor's
Hearts of artichoke—S & W
Garbanzo beans—Janet Lee
Lima beans—Del Monte
Avoid canned peas, corn, and kidney beans, which are typically canned with sugar. Packaged dry beans are without sugar.

Vegetables, frozen
Normally any plain frozen vegetable (that is, without sauce) is sugarless. Read the label.

Basic Dietary Guidelines for Hypoglycemics

If you are hypoglycemic, your doctor will give you special instructions on nutrition. As a reminder, some basic instructions are listed below. If your doctor's instructions differ, please disregard these and follow his advice.

1. **Avoid refined sugar, starch, and flour** and everything containing them. Get in the habit of *reading labels*. Look not only for sugar, starch, and flour, but also for:

Dextrin	Sucrose	Honey
Dextrose	Sorbitol	Raisin syrup
Lactose	Hexitol	Malt syrup
Fructose	Arrow root	Corn starch
Maltose	Brown sugar	Corn syrup
Glucose	Molasses	Corn sweeteners
		Natural sweeteners

Foods containing refined sugars, starches, and flours (not allowed):

Candy	Cocoa	Most steak sauces
Cookies	Chocolate milk	Cheese spreads
Cakes	Chocolate drinks	Processed cheeses
Pies	Soft drinks	Certain canned meats
Pasteries	Alcohol	Most luncheon meats
Ice cream	Fruit drinks (not juices)	Sausage
Doughnuts	Dessert toppings	Most hot dogs
Most breads	Chewing gum	Most commercial soups
Various jellos	Sweet pickles	Most canned fruits
Pretzels	Ketchup	Some frozen fruits
Potato chips	Mayonnaise	Some canned vegetables
White rice	Relishes	Some frozen vegetables
Chocolate	Most condiments	Pancakes
		Pastas (spag., macaroni)

2. **Avoid natural sweeteners** such as honey, molasses, and date sugar until your doctor allows them. Thereafter, use only in small amounts (for example, one-fourth teaspoonful).

3. **Follow your doctor's advice on quantity of fruit.** Physicians vary in amount of fruit allowed. Some feel that fruit intake should be restricted; others allow unlimited amounts.

> Dates, prunes, raisins, and other dried fruits are very high in fruit sugar. Grape juice and prune juice are also high.

4. **Limit other high carbohydrate foods.** Restrict, for example, wheat, rice, corn, beans (other than green), and potatoes. If you are permitted to have whole grains, take only *half* a slice of bread. Take only *half* a potato.

5. **Eat at least 4 vegetables a day.** Expand your taste to include at least 15 to 20 different vegetables in your regular diet. Such variety will give you important vitamins and minerals.

6. **Use mostly fresh foods** and cook them as little as possible. Raw vegetables are very desireable. Fresh is better than frozen, and frozen is better than canned, bottled, or otherwise processed.

7. **Include a moderate amount of protein** in whatever number of portions per day your doctor directs. Protein is essential, but we frequently eat more than we can digest. Use moderate portions of eggs, seafood, poultry, cheese, and meat. Examples of portions: 2 eggs, 4-5 ounces of seafood, 2 pieces of chicken, a slice or two of cheese, a medium sized hamburger patty. Milk is considered by many to be difficult to digest and is often not permitted in a hypoglycemic diet. Cream, however, is a wonderful substitute. It can be used as is or diluted with water to the consistency of milk.

8. **Eliminate caffeine.** This means no coffee, tea, cola drinks, or Tab. Substitutes include weak herb teas and Sanacaf.

9. **Avoid chemical additives as much as possible.** The dangers of some widely used additives (e.g., sodium nitrite and BHT) are known. Others are probably equally as harmful.

10. **Limit alcohol.** Ideally it should be eliminated altogether because it breaks down into sugar very quickly.

11. **Include vegetable oils in your diet.** Most contain polyunsaturated fatty acids (if not hydrogenated in processing), which are needed for weight control.

12. **Snack at night if necessary.** If you tend to waken during the night, have snacks available at your bedside.

13. **Eat many small meals a day.** This rule is important. Eating often is essential to maintaining an even blood sugar level. For many people this means preparing adequate mini-meal snacks for mid-morning and afternoon breaks, eating smaller meals, and snacking before bedtime. Some individuals may need to snack as often as every hour in the beginning.

SUGAR

How Sweet It Is — And Isn't

Sugar is getting a lot of attention because it's in so many processed foods. Many people want to know how much they're getting in their food, and many nutrition and health experts are dubious of its contribution to the American diet and health. We find that more than one kind of sugar is getting into food, and so we're eating more of the stuff all the time.

by Chris W. Lecos

Sugar, "that honey from reeds," as one author described it more than 2,000 years ago, has been a part of mankind's diet for as long as anyone cares to remember.

Cave drawings tell us of prehistoric man's taste for honey, figs, and dates. The beekeeping practices of Egyptians are depicted in the artwork in tombs dating around 2600 B.C.

The Bible tells us that the "promised land" flowed with milk and honey. It turned into a flood once sugarcane was discovered.

In the writings of an obscure officer in Alexander's army during its invasion of India, one finds the first written mention of sugarcane. That was around 325 B.C.

Yet, despite this long history, the use of sugar in the diet has become a controversial issue in recent years that has involved doctors, scientists, nutritionists, private citizens, the Government, and the industry itself.

Why all the fuss?

- Because there is a growing body of expert opinion that believes Americans would be healthier if they ate less sugar, not because it's bad for you, but because its only real contribution is taste and Calories.
- Because sugar has become the leading ingredient added to foods in the United States today. That is, most of the sugar consumed is added before it gets to the consumer.
- Because most people don't know how much sugar they eat, and many want to know. This is a principal reason the Food and Drug Administration wants the total amount of all sugars identified on more foods. The total would include both naturally occurring and added sugar.
- Because sugar, though blamed wrongly for many ills, is one of a number of contributors to dental caries. Americans are spending $10 billion a year for dental care.

To most people, sugar is what you find on the kitchen table, put into coffee, or mix in a cake. This, of course, is the sugar refined from cane and beets.

Actually, there are more than a hundred substances that are sweet and which chemists can correctly describe as sugars. Sucrose, or table sugar, is just the most common and abundant of them all.

Industry literature describes sugar as a cheap source of food energy, a major contributor to food processing and general nutrition, and a substance that makes many foods with other nutrients taste better.

"Good nutrition," says a brochure from the Sugar Association, "begins with eating."

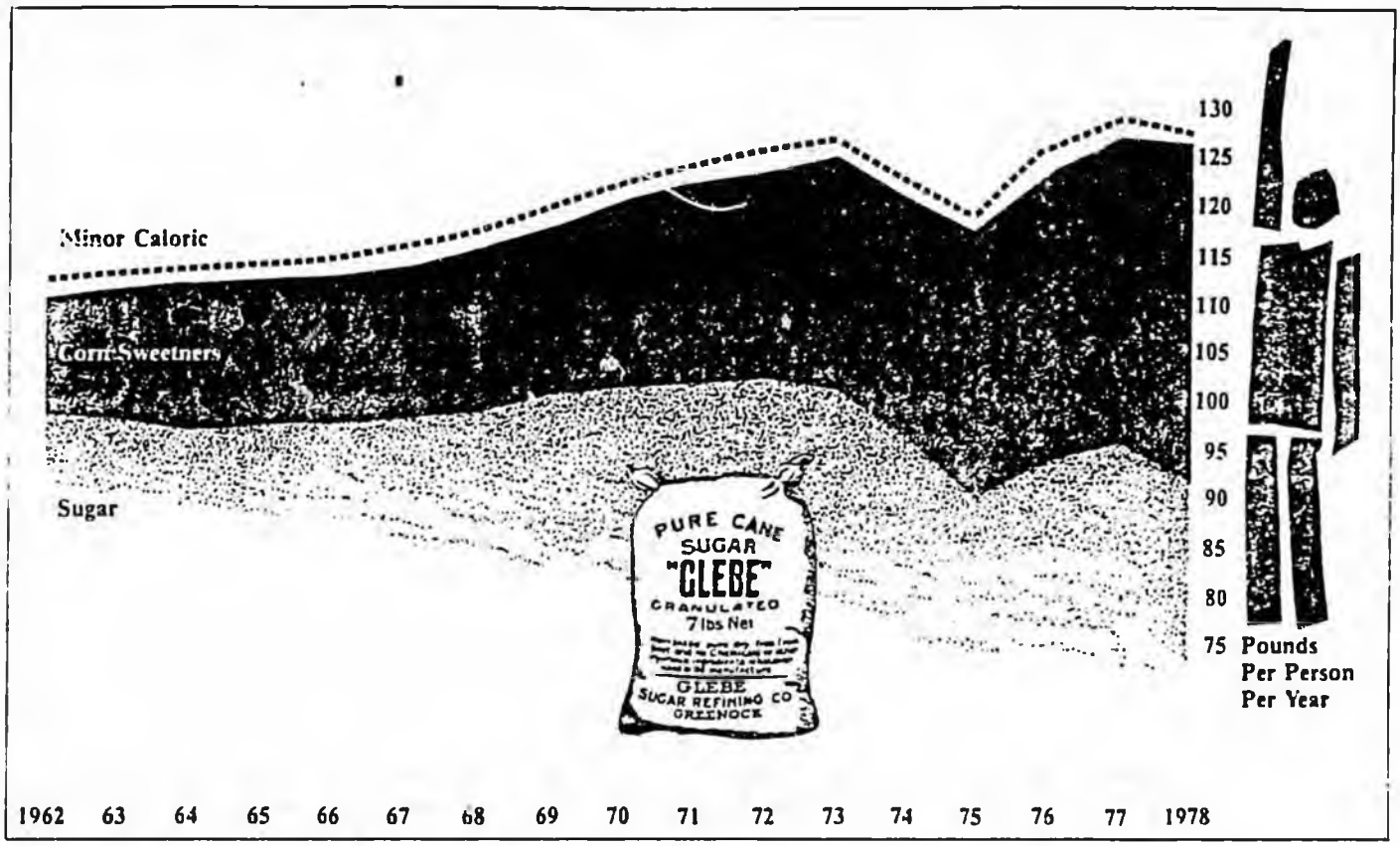
Its point, of course, is that if food is sweetened, people will eat the foods with the nutrients they need. However, many nutritionists and others concerned with American eating habits dispute sugar's value.

In a 1976 evaluation of the health aspects of sucrose as a food ingredient, the Federation of American Societies for Experimental Biology (FASEB) stated in a report to FDA: "Unlike most other foods, sucrose furnishes virtually only energy."

Many nutritionists concur and describe sugar as an "empty Calorie." If sugar is to be part of the diet, they say, it is preferable to get it from fruits, vegetables, and other items where it's a natural part of the product.

As it does with most other carbohydrates, the body converts sugar into glucose, the primary fuel of the body. During digestion it is broken down into equal parts of two simple sugars: glucose (dextrose) and fructose (levulose).

These components enter the bloodstream through the walls of the small intestine, and the blood carries the sugars to the tissues and the liver. There it is used or converted into glycogen and stored until the body needs it. The hormone insulin makes it possible for glucose, or



blood sugar, to enter nearly all the cells of the body, where it is used as an energy source.

When more energy is needed, the liver converts glycogen into glucose, which is then delivered by the bloodstream to other organs or muscle tissue. Glucose not needed by the cells is metabolized in the liver into fatty substances called triglycerides. The body can call upon this stored energy during dieting and fasting.

Because of these energy reserves, nutritionists discount the argument that sugar is useful for quick energy needs before physical activity.

Americans get about 24 percent of their Calories from sugar—of which 3 percent comes in natural form from fruits and vegetables, 3 percent from dairy products, and the balance from sugar added to foods.

If sugar provides about 20 percent of a person's Calories, he must get the other 80 percent by selecting foods that supply the other nutrients his body needs—which is not easy to do, say some nutritionists, if one is trying to lose weight.

For many Americans, weight is a problem. A study released in 1978 by the National Center for Health Statistics indicated that one-third of the population was overweight.

In a study of 13,600 people whose weights between 1971 and 1974 were compared with adults of equivalent height a decade earlier, the Center found that men and women under 45 were, on the average, 3.8 and 4.7 pounds heavier, respectively. Those over 45 had gained an average of 4.8 pounds.

There is no accurate measurement of how much sugar the average American eats. The best available barometer of sugar use is the per capita consumption figures of the U.S. Department of Agriculture (USDA).

Although the per capita figures do not tell how much a person actually eats, they do show the amount of sugar that "disappears" into the marketplace—that is, the amount shipped by sugar producers for industrial, home, and other uses.

Citing USDA figures, sugar industry spokesmen maintain that sugar consumption in the United States has been relatively stable for more than 50 years now, at around 100 pounds a year per person.

However, that figure refers only to the consumption of refined cane and beet sugar. It does not reflect the growing impact of a variety of corn sweeteners now in use. The term "corn sweeteners" includes various corn sirups (high fructose corn sirup, glucose) plus other Caloric sweeteners, such as dextrose, that are derived from corn.

Refined sugar, corn sirup, and corn sugar account for the bulk of the sweeteners consumed in this country. Among the remainder are honey, maple, and other edible sirups.

All of these are Caloric, and when all are taken into account, USDA figures show a rise in per capita consumption from 122 pounds in 1970 to 128 pounds in 1978.

Per capita consumption of just refined sugar hovered around the 100 pounds per year level between 1960 and 1974. Since then, the trend generally has been downward, falling below 93 pounds in 1978, according to USDA. Fred Gray, an agriculture economist for USDA, predicted a further drop of several pounds for 1979.

The decline in refined sugar consumption has been more than offset by the steady rise in corn sweetener usage—from a per capita rate of 19 pounds in 1970 to almost 34 pounds in 1978.

Norris Bollenback, scientific director for the Sugar As-

sociation, said the primary impetus for the increase has come from the growing industrial use of high fructose corn sirups, especially by soft drink producers.

The use of high fructose corn sirups was neglible—less than a pound per capita, on the average—in the early 1970's. The industry was in its infancy then, and food and beverage manufacturers relied almost entirely on cane and beet sugar for their products because those sugars were cheap and plentiful, selling for about 11 or 12 cents a pound wholesale.

The rapid escalation of sugar prices in 1974—up to around 33 cents a pound wholesale—compelled the food and beverage industries to turn to other sweeteners, and the most attractive of them all was the high fructose corn sirups.

By the end of 1975, USDA figures show that per capita consumption of those corn sirups had risen to 5 pounds and 3 years later up to 11 pounds. Gray predicted that high fructose corn sirup usage would reach 15 pounds in 1979 and 18 pounds by the end of 1980.

Bollenback cited figures that showed that high fructose corn sirup producers have maintained their product's price consistently below that of refined sugar—roughly from 3 to 10 cents a pound less at the wholesale level. Last year, the wholesale price of high fructose corn sirup was around 13 cents a pounds compared to 20 cents for refined sugar.

"If (refined) sugar proponents think things will be back the way they were, they are being unrealistic," Bollenback noted.

Things also aren't the way they used to be in how sugar gets to our stomachs. Fifty years ago, two-thirds of the sugar produced went directly into the home, which meant control was directly in the hands of the housewife or individual who bought it. The balance was used mostly by industry.

Now, the reverse is true. Sixty-five percent of the refined sugar produced today is being consumed by the food and beverage industries and only 24 percent is going for home use.

The beverage industry—comprised of soft drink bottlers and beer and wine producers—is the leading industrial user of refined sugar and of high fructose corn sirups. It used 26 percent of the 9.8 million tons of refined sugar shipped in 1978 and about 40 percent of the high fructose corn sirups.

Although there has been a considerable amount of public controversy over the amount of sugar in cereals, the bakery and cereal industries combined used only 13.4 percent of all the sugar produced for food purposes in 1978. USDA figures did not separate the two.

Producers of confectionery products had the next highest usage at 9.2 percent, followed by 7 percent for the processed food and canning industries, and 5.6 percent for dairy products.

The consumer today is confronted by a wide variety of sugars and other nutritive sweeteners, and there is no significant difference in the amount of Calories each provides.

Below is a brief explanation of the more common sugars and sweeteners:

Sucrose, obtained in crystalline form, from cane and beets, is a double sugar or disaccharide and is composed of two simple sugars, glucose and fructose. It is about 99.9 percent pure and is sold in either granulated or powdered form.

Raw sugar, tan to brown in appearance, is a coarse, granulated solid obtained from evaporation of sugarcane juice. FDA regulations prohibit the sale of raw sugar unless impurities—dirt, insect fragments, etc.—are removed.

Turbinado sugar is sometimes viewed erroneously as a raw sugar. Actually, it has to go through a refining process to remove impurities and most of the molasses. It is produced by separating raw sugar crystals and washing them with steam. It is edible if produced under proper conditions. However, some samples in the past have been found to contain contaminants, the Sugar Association warns.

Brown sugar consists of sugar crystals contained in a molasses sirup with natural flavor and color. However, some refiners make brown sugar by simply adding sirup to refined white sugar in a mixer. It has 91 to 96 percent sucrose.

Total invert sugar, a mixture of glucose and fructose, is formed by splitting sucrose in a process called inversion, which is accomplished by the application of acids or enzymes. It is sold only in liquid form and is sweeter than sucrose. It helps prolong the freshness of baked foods and confections and is useful in preventing food shrinkage.

Honey is an invert sugar formed by an enzyme from nectar gathered by bees. Its composition and flavor depend on the source of the nectar. Fructose, glucose, maltose, and sucrose are among its components.

Corn sirups, produced by the action of enzymes and or acids on cornstarch, are the result of hydrolysis of starch. High fructose corn sirup is a derivative of corn. The amounts of fructose vary with the manufacturer. One major producer's sirups contain 42 percent, 55 percent, and 90 percent fructose. Dextrose comprises most of the balance.

Levulose, or fructose, is a commercial sugar, considerably sweeter than sucrose, although its sweetness actually depends on its physical form and how it is used in cooking. Fructose, known as a fruit sugar, occurs naturally in many fruits.

Dextrose, or glucose, is also called corn sugar. It is made commercially from starch by the action of heat and acids, or enzymes. It is often sold blended with regular sugar.

Lactose, or milk sugar, is made from whey and skim milk for commercial purposes. It occurs in the milk of mammals. The pharmaceutical industry is a primary user of prepared lactose.

Sorbitol, *mannitol*, *maltitol*, and *xylitol* are sugar alcohols or polyols. They occur naturally in fruits but are commerically produced from such sources as dextrose. Xylitol is a sugar alcohol made from a part of birch trees. Sorbitol, mannitol, and maltitol are about half as sweet as sucrose; xylitol has a sweetness about equal to sucrose.

Although fructose and the other sugar alcohols are promoted as suitable substitute sweeteners, especially for diabetics, many health scientists question their supposed advantages pending more research and long-term studies. This will be the subject of the next article in this series in FDA CONSUMER.

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at 8 hours, 45 µg/mL at 12 hours, and 25 µg/mL at 16 hours. Following a single 1.6-g oral dose (as two 800-mg tablets) of one commercially available extended-release aspirin preparation in healthy adults in one crossover study, an average peak plasma aspirin concentration of about 1 µg/mL was attained within 2 hours and average peak plasma salicylate concentrations of about 22 µg/mL were attained within 8–12 hours; the plasma salicylate concentration declined to about 15 µg/mL by 24 hours.

Suppositories

In one study in children given a rectal dose of 150–300 mg of aspirin as a suppository, peak serum salicylate concentrations of 20–140 µg/mL generally occurred within 3–4 hours.

DISTRIBUTION

Aspirin is rapidly and widely distributed, apparently into most body tissues and fluids. The volume of distribution of aspirin is approximately the same as that of salicylate and is generally 0.15–0.2 L/kg.

In one study in patients with rheumatic disease who received a single 650-mg oral dose of buffered aspirin, aspirin was detected in synovial fluid within 10–30 minutes and salicylate was detected in synovial fluid within 15–35 minutes. In this study, peak aspirin concentrations in synovial fluid occurred after an average of 1.3 hours and were about 75% of peak blood concentrations; peak salicylate concentrations in synovial fluid occurred after an average of 2.2 hours and were about 60% of peak blood concentrations.

Aspirin is poorly bound to plasma proteins; the unhydrolyzed drug is 33% bound at a serum salicylate concentration of 120 µg/mL. However, aspirin acetylates serum albumin at the ε-amino group of lysine; the acetylation may alter binding of other drugs (e.g., phenylbutazone) to the protein. Acetylation of serum albumin by aspirin is inhibited by salicylate.

ELIMINATION

The elimination half-life of aspirin in plasma is approximately 15–20 minutes. Unlike salicylate, unhydrolyzed aspirin does not undergo capacity-limited metabolism and does not accumulate in plasma following multiple doses.

Following oral administration, aspirin is partially hydrolyzed to salicylate during absorption by esterases in the GI mucosa. Following absorption, unhydrolyzed aspirin is rapidly and almost completely hydrolyzed by esterases principally in the liver but also in plasma, erythrocytes, and synovial fluid; hydrolysis occurs more slowly in synovial fluid apparently because the amounts of esterases in synovial fluid are lower. It has been reported that aspirin may be hydrolyzed more slowly in women because women apparently have lower amounts of plasma aspirin esterases.

Only about 1% of an oral dose of aspirin is excreted unhydrolyzed in the urine. The remainder is excreted in the urine as salicylate and its metabolites.

Uses

Aspirin is used extensively in the treatment of mild to moderate pain, fever, and inflammatory diseases. Aspirin is also used in the prevention of arterial and possibly venous thrombosis. Aspirin, however, should be used with extreme caution, if at all, in patients in whom urticaria, angioedema, bronchospasm, severe rhinitis, or shock is precipitated by other salicylates or other NSAIAs. (See Cautions: Sensitivity Reactions, in the general statement on Salicylates 28:08.04.)

PAIN

Aspirin is used to relieve headache, neuralgia, myalgia, arthralgia, and other low-intensity pain of nonvisceral origin, particularly pain associated with inflammation. Aspirin may also relieve mild to moderate postoperative pain, postpartum pain, oral surgery or other dental pain, dysmenorrhea, or other visceral pain such as that associated with trauma or cancer. Many studies have shown that the analgesic effects of aspirin are greater than those of placebo in the treatment of these types of pain. The drug, however, does not usually relieve severe acute pain of visceral origin. In addition, use of chewing gum tablets or gargles containing aspirin has not been shown to be effective in relieving sore throat pain.

The analgesic effect of aspirin appears to increase with increasing single oral doses up to at least 1.2 g; however, single oral doses of aspirin greater than 650 mg apparently do not result in a greater incidence or degree of pain relief in most patients. Multiple oral doses of aspirin greater than 650 mg each have not been shown to be more effective in relieving pain than multiple oral doses of 650 mg.

When used to relieve postoperative pain, 600-mg oral doses of aspirin appear to be as effective as 60-mg oral doses of codeine or 50-mg oral doses of pentazocine. When used to relieve oral surgery pain, 650-mg oral doses of aspirin appear to be more effective than 30-mg oral doses of codeine, as effective as 650-mg oral doses of acetaminophen, about as effective as 50-mg oral doses of zomepirac, and less effective than 250-mg, 500-mg, or 1-g oral doses of diflunisal or 100-mg oral doses of zomepirac.

In the treatment of postpartum uterine pain, the analgesic effect of 650-mg oral doses of aspirin is about equal to that of 300- or 600-mg oral doses of naproxen or 275-mg oral doses of naproxen sodium and greater than that of 60-mg oral doses of codeine or codeine sulfate. When used to relieve episiotomy pain, several studies have shown that 600-mg to 1.2-g oral doses of aspirin are more effective than placebo; in one study, the analgesic effect of 900-mg oral doses of aspirin was about equal to that of 300- or 900-mg oral doses of ibuprofen. In another study, the analgesic effect of 600-mg oral doses of aspirin was less than that of 500-mg oral doses of diflunisal.

In the treatment of nonspecific pain associated with cancer, 650-mg oral doses of aspirin appear to be at least as effective as 650-mg oral doses of acetaminophen, 65-mg oral doses of codeine, 250-mg oral doses of mefenamic acid, or 50-mg oral doses of pentazocine, and more effective than 75-mg oral doses of ethoheptazine citrate or 65-mg oral doses of propoxyphene hydrochloride. When used to relieve nonspecific pain associated with cancer, 650-mg oral doses of aspirin in combination with oral doses of codeine (65 mg), oxycodone (976 µg), or pentazocine hydrochloride (25 mg) appear to be more effective than 650-mg oral doses of aspirin alone or in combination with oral doses of caffeine (65 mg), ethoheptazine citrate (75 mg), pentobarbital sodium (25 mg), promazine hydrochloride (25 mg), or propoxyphene napsylate (100 mg).

Results of studies comparing aspirin (500–650 mg 4 times daily) with placebo to relieve primary dysmenorrhea have been inconsistent. Although the effects of higher dosages of aspirin remain to be evaluated, most clinicians consider aspirin to be one of the *least* effective NSAIAs currently available for the treatment of primary dysmenorrhea.

In several double-blind placebo-controlled studies with small numbers of patients with migraine, prophylactic therapy with aspirin (650 mg twice daily) alone or aspirin (300 mg twice daily) with dipyridamole (25 mg 3 times daily) has reportedly been effective in reducing the frequency of headache; however, further evaluation is needed.

Aspirin has been used in the treatment of pain in various combinations with acetaminophen, caffeine, opiates, salicylamide, and/or other agents. However, combinations of aspirin with agents such as acetaminophen, caffeine, or salicylamide have not been clearly shown to have greater analgesic effect than an optimal dose of aspirin alone. In addition, there is little evidence that such combinations cause fewer adverse effects than higher doses of the individual agents alone. In one study, the simultaneous administration of 325- or 650-mg oral doses of acetaminophen with 650-mg oral doses of aspirin resulted in increased blood concentrations of unhydrolyzed aspirin compared to 650-mg oral doses of aspirin alone; however, the clinical importance of such an effect remains to be established. Aspirin (650-mg oral doses) in combination with oral doses of an opiate (e.g., codeine, oxycodone) produces greater analgesic effect than that produced by either aspirin or higher doses of the opiate alone. There is also some evidence that aspirin/opiate combinations may cause fewer adverse effects than equianalgesic doses of the individual drugs alone.

FEVER

Aspirin is used frequently to lower body temperature in febrile patients in whom fever may be deleterious or in whom considerable relief is obtained when fever is lowered. However, antipyretic therapy is generally nonspecific, does not influence the course of the underlying disease, and may obscure the course of the patient's illness. For information on salicylates and Reye's syndrome, see Cautions: Pediatric Precautions, in the general statement on Salicylates 28:08.04.

Aspirin and acetaminophen are equally effective as antipyretics. In one study in febrile children, the combination of oral doses of aspirin and acetaminophen was at least as effective in reducing fever as either drug alone, and the duration of fever reduction was longer with the combination than with the individual drugs. However, because of the study design, it could not be concluded that the combination had additive effects. Many clinicians use regimens of alternating doses of aspirin and acetaminophen; however, combined overdosage with both drugs has occurred with such a regimen and the efficacy and safety of these regimens remain to be established.

Several clinical studies have shown that the antipyretic effect of usual dosages of aspirin is about equal to that of usual dosages of mefenamic acid and naproxen, and less than that of usual dosages of indomethacin. However, efficacy of these other NSAIAs as antipyretics remains to be clearly established

and they should not be used for routine treatment of fever because of their potential adverse effects.

INFLAMMATORY DISEASES

Many clinicians consider aspirin to be a drug and the salicylate of first choice for anti-inflammatory and analgesic effects in the initial and/or long-term symptomatic treatment of rheumatoid arthritis, juvenile arthritis, and osteoarthritis. Aspirin may also be useful in the treatment of other polyarthritic conditions (e.g., psoriatic arthritis, Reiter's syndrome, ankylosing spondylitis), systemic lupus erythematosus, and nonarticular inflammation; however, other NSAIAs may be preferred in the treatment of some of these conditions (e.g., ankylosing spondylitis).

Most clinical studies have shown that the anti-inflammatory and analgesic effects of usual dosages of aspirin in the treatment of rheumatoid arthritis or osteoarthritis are greater than those of placebo and about equal to those of usual dosages of fenoprofen calcium, ibuprofen, indomethacin, meclofenamate sodium, naproxen, piroxicam, sulindac, and tolmetin sodium, and somewhat less than those of usual dosages of phenylbutazone. In the treatment of osteoarthritis, aspirin is used principally for its analgesic effect rather than anti-inflammatory effect, although inflammation may be part of the symptomatology. In the treatment of juvenile arthritis, the anti-inflammatory and analgesic effects of usual dosages of aspirin are about equal to those of usual dosages of fenoprofen, naproxen, or tolmetin sodium. Patient response to NSAIAs is variable, however, and patients who do not respond to one agent may be successfully treated with a different agent.

Aspirin has been used in conjunction with other NSAIAs in the treatment of some patients with rheumatoid arthritis, but such combination therapy is generally not recommended because there is inadequate proof that such combination therapy is more efficacious than the individual agents alone. In addition, the potential for adverse reactions may be increased, and there is evidence that aspirin alters plasma concentrations of some other NSAIAs.

Aspirin may be effective in the treatment of some patients with psoriatic arthritis or Reiter's syndrome but usually only when the disease is mild. Aspirin is seldom effective in the treatment of ankylosing spondylitis unless the disease is mild. In one study in patients with ankylosing spondylitis, the anti-inflammatory and analgesic effects of aspirin were less than those of indomethacin or phenylbutazone.

Some clinicians consider aspirin to be a drug of first choice for the treatment of fever, arthritis, pleurisy, and pericarditis in patients with systemic lupus erythematosus (SLE). In one study in patients with SLE, the anti-inflammatory and analgesic effects of aspirin were greater than those of ibuprofen. Aspirin has also been used in the treatment of symptomatic pericarditis following myocardial infarction; in one study, the effects of 2.6 g of oral aspirin daily were comparable to those of 100–200 mg of oral indomethacin daily, with either drug relieving symptoms within 48 hours. The anti-inflammatory and analgesic effects of aspirin may also be useful in the symptomatic treatment of nonarticular inflammation such as bursitis and/or tendinitis (e.g., acute painful shoulder) and fibrositis.

Most clinicians consider aspirin to be the salicylate of choice when salicylate therapy is indicated in the treatment of rheumatic fever. For information on salicylate therapy in the treatment of rheumatic fever, see Uses: Rheumatic Fever, in the general statement on Salicylates 28:08.04.

THROMBOSIS

Since there is considerable clinical and experimental evidence that thrombosis (particularly arterial thrombosis) may result from platelet-mediated processes which can be inhibited by aspirin, the drug has been extensively evaluated in the prevention of arterial and venous thrombosis. However, results are largely conflicting and/or inconclusive. This may be due in part to the complexity of thromboembolic disorders, problems in study design, and the possibilities that the antithrombotic effect of aspirin is dosage dependent and/or sex related. (See Pharmacology: Antithrombotic Effect.) Presently, the most widely accepted indication for prophylactic aspirin therapy is for reducing the risk of recurring transient ischemic attacks (TIAs) and stroke or death in men who have had single or multiple TIAs. Further controlled studies are necessary to determine the safety and efficacy of prophylactic aspirin therapy in many thrombosis-related conditions.

Cerebrovascular Disease

Aspirin has been shown to reduce the risk of recurring transient ischemic attacks (TIAs) and stroke or death in men who have had single or multiple TIAs; however, it has not been established that aspirin prevents stroke. In addition, it is not clear whether aspirin is similarly effective in women. Aspirin is not beneficial in the treatment of completed stroke.

In one study in patients with TIAs, oral doses of aspirin (650 mg twice daily) were more effective than placebo after 6 months of therapy, but only when the occurrence of TIAs, nonfatal cerebral or retinal infarction, and death were considered together as end points. After 2 years of treatment, aspirin was more effective than placebo only in those patients who had multiple TIAs before starting treatment and in those having stenotic lesions of the carotid artery on the side appropriate to their symptoms. In another placebo-controlled trial, aspirin alone (325 mg 4 times daily) was more effective than placebo or sulfinpyrazone alone (200 mg 4 times daily) in reducing the risk of recurring TIAs, stroke, or death in men but not in women; although no interaction between aspirin and sulfinpyrazone was definitely found, a trend favoring the efficacy of the combination was observed in men. No differences in therapeutic response were evident for the vascular site of TIAs (carotid or vertebrobasilar) or for single or multiple TIAs before treatment. When the recurrence of TIAs was considered in combination with stroke and death as end points in both this study and the previous study, there was no sex difference in treatment response; however, it is not clear that reducing the risk of TIAs necessarily reduces the risk of stroke. Results of several other studies have also supported the efficacy of aspirin therapy and suggested that therapeutic benefit may be limited to males.

Combination therapy with aspirin (500 mg twice daily) and dipyridamole (75 mg twice daily) after 2 months of therapy with an oral anticoagulant (e.g., warfarin) has also been reported to reduce the risk of cerebral infarction in patients with TIAs. However, no controlled trials comparing aspirin with an oral anticoagulant have been reported to date.

In men (and possibly in women) who have had TIAs for 2–12 months and are not treated surgically, many clinicians recommend aspirin therapy unless a recent increase in frequency, duration, or severity of TIAs has occurred, in which case an oral anticoagulant is given for 3–6 months followed by aspirin therapy. Patients who have had TIAs for less than 2 months and who are not treated surgically, generally receive an oral anticoagulant (unless contraindicated) for 3–6 months before treatment with aspirin is started. Aspirin therapy is generally continued until the patient has been free of TIAs for 1 year. No specific therapy is recommended for patients who are not treated surgically and have not had a TIA for longer than 1 year. Additional controlled trials evaluating the effect of aspirin alone or in combination with dipyridamole in patients with TIAs are ongoing.

Coronary Artery Disease

The value of prophylactic aspirin therapy in patients surviving a myocardial infarction remains to be clearly determined. In several randomized, placebo-controlled studies, oral doses of aspirin (300 mg once daily or 900 mg to 1.5 g daily in divided doses) were generally shown not to reduce the risk of death, sudden cardiac death, or nonfatal recurrent myocardial infarction. However, a trend favoring the efficacy of aspirin has been observed. In 2 of these studies, aspirin reduced the risk of nonfatal recurrent myocardial infarction. Further studies are needed to determine the efficacy of aspirin alone or in combination with other platelet-aggregation inhibitors in reducing the risk of death and/or recurrent myocardial infarction in patients surviving a myocardial infarction. Although the efficacy of aspirin or oral anticoagulant therapy (compared to placebo) in reducing the mortality of patients surviving a myocardial infarction has not been clearly established, the results of one comparative study indicate that the effect on mortality and recurrent myocardial infarction of aspirin (1.5 g daily) are about the same as those of oral anticoagulants.

Since no therapeutic effects have been unequivocally shown to date and aspirin has potential adverse effects, many clinicians recommend that prophylactic aspirin therapy should not be used routinely in patients surviving a myocardial infarction. Pending further accumulation of clinical data on aspirin, prophylactic therapy with other agents (e.g., β-adrenergic blockers) should be considered.

In one study in men with unstable angina, low doses of aspirin (324 mg once daily) reportedly reduced the risk of nonfatal myocardial infarction, although not conclusively demonstrated, a reduction in mortality was suggested. Further studies are needed to evaluate the efficacy of aspirin in patients with unstable angina.

Thrombosis in Other Arteries and Arteriovenous Communications

Although aspirin has generally been ineffective in preventing thrombosis after arterial catheterization, a single 600-mg oral dose the evening before surgery has been reported to reduce the incidence of thrombosis following

radial-artery catheterization for surgery. Oral doses of aspirin (325 mg to 1.3 g daily) have been given prophylactically alone or in combination with oral doses of dipyridamole (50–75 mg 3 times daily) to prevent thrombosis in patients undergoing percutaneous transluminal angioplasty of the coronary, iliac, femoral, popliteal, or tibial artery; aspirin and/or dipyridamole are usually given for 2–3 days before and for 3–9 months after the procedure.

Oral doses of aspirin (160 mg once daily) have been shown to be safe and effective in reducing the incidence of thrombosis in silastic arteriovenous shunts in patients undergoing hemodialysis.

Microcirculatory Thrombosis

Aspirin has been used as a component of various regimens for the treatment of thrombotic thrombocytopenic purpura, but its therapeutic value in this condition has been difficult to determine. In one study, combination therapy with aspirin and dipyridamole was considered ineffective and patients receiving the combination had an increased risk of severe bleeding complications; therefore, some clinicians have recommended that aspirin no longer be used in the treatment of thrombotic thrombocytopenic purpura. However, other clinicians believe that platelet-aggregation inhibitors (e.g., aspirin) are useful in the treatment of this condition. The combination of aspirin and dipyridamole has been shown to reduce blood concentrations of circulating platelet aggregates and β-thromboglobulin in patients with scleroderma; however, the long-term effect of such therapy on the disease is not known.

Aspirin has been effective in the treatment of some patients with thrombocytosis associated with a syndrome of spontaneous platelet aggregation and symptoms of digital ischemia.

Prosthetic Heart Valves

Because oral anticoagulant therapy alone does not completely prevent thrombosis in patients with prosthetic heart valves, aspirin or dipyridamole has been used in conjunction with an oral anticoagulant to reduce the incidence of thrombosis in these patients. The combinations appear to be more effective than an oral anticoagulant alone. In 2 studies comparing treatment regimens of an oral anticoagulant alone or in combination with 500-mg or 1-g daily doses of aspirin, patients receiving 1 g of aspirin daily had an increased risk of GI bleeding while those receiving 500 mg daily did not. In another study comparing treatment regimens of an oral anticoagulant alone or in combination with aspirin (500 mg daily) or dipyridamole (400 mg daily), the combination regimen with aspirin was associated with an increased risk of bleeding complications compared to the other regimens. Although some clinicians consider the risk-to-benefit ratio of combination therapy with aspirin acceptable, many others do not. Pending further evaluation of the safety and efficacy of therapy with aspirin and an oral anticoagulant, most clinicians recommend therapy with dipyridamole and an anticoagulant. The value of platelet-aggregation inhibitors alone has not been established; however, some clinicians suggest that combination therapy with aspirin and dipyridamole may be useful in patients unable to tolerate an oral anticoagulant.

Venous Thrombosis

The value of aspirin alone or in combination with dipyridamole in preventing venous thrombosis remains controversial.

Although results of many studies suggest that oral doses of aspirin (1.2–1.5 g daily in divided doses) may reduce the incidence of postoperative venous thrombosis (particularly following hip operations), this has not always been found. For the prevention of postoperative venous thrombosis in patients undergoing major abdominal or thoracic surgery, most clinicians recommend low-dose heparin therapy. However, low-dose heparin prophylaxis is usually ineffective in reducing the incidence of thrombosis after orthopedic surgery, including total hip replacement. Some clinicians recommend aspirin prophylaxis in men undergoing total hip replacement. In one well-controlled study, oral doses of aspirin (600 mg twice daily) were more effective than placebo in reducing the incidence of thrombosis in men (but not in women) following total hip replacement. In another study, aspirin prophylaxis appeared to be effective in patients undergoing total knee replacement. However, further studies are needed to establish the efficacy of aspirin for the prevention of postoperative venous thrombosis following these and other types of surgery. Aspirin has also been used in combination with dihydroergotamine for prevention of postoperative deep-vein thrombosis following major abdominal surgery. Although limited data show that the combination may be more effective than aspirin alone, further study is required to determine the safety, efficacy, and dosage of combination therapy with these drugs.

In one placebo-controlled study, oral doses of aspirin (300 mg 4 times daily) given in combination with oral doses of dipyridamole (25 mg 4 times daily) were reportedly effective in reducing the incidence of thrombosis in patients with recurring venous thrombosis who had decreased platelet survival and were refractory to treatment with oral anticoagulants.

Aspirin has been used alone or in combination with dipyridamole to prevent thrombosis in vein grafts in patients who undergo aortocoronary-artery bypass, but results have been conflicting and inconclusive. However, in one study in which treatment with dipyridamole was started before surgery (and continued) and aspirin was added soon after surgery, the combination therapy appeared to effectively reduce the incidence of vein-graft occlusion during the first 6 months after surgery; the long-term effects remain to be established.

OTHER USES

In some patients, aspirin appears to prevent or reduce adverse GI effects (e.g., vomiting, abdominal pain, diarrhea) associated with food intolerance or radiation therapy. Aspirin also appears to reduce intestinal fluid loss in some patients with gastroenteritis; however, further evaluation of aspirin therapy is necessary and fluid and electrolyte replacement remain the principal therapeutic modalities in the management of this condition. Aspirin has also been reported to effectively prevent flushing episodes in one patient with metastatic renal carcinoma. Although the exact mechanism(s) by which aspirin reduces these adverse GI effects or flushing is not clearly established, the drug may inhibit the synthesis and/or release of prostaglandins which mediate or cause these effects.

Aspirin may occasionally be useful for the treatment of hypercalcemia that occurs with certain types of solid tumors associated with prostaglandin-mediated osteolytic activity; however, other therapies (e.g., IV hydration and diuresis) are usually preferred. In one study in hypercalcemic patients with such tumors (lung carcinoma), aspirin therapy (1.8–4.8 g daily for 5–7 days) reduced serum calcium concentrations and urinary excretion of a metabolite of prostaglandin E; both variables returned to elevated levels 3–4 days after aspirin was discontinued.

Because of its ability to inhibit the synthesis of prostaglandins, aspirin has been used in the treatment of patent ductus arteriosus in premature infants and in the treatment of Bartter's syndrome; however, in both of these conditions, other agents (e.g., indomethacin) appear to be more effective.

Some clinicians have observed a decreased prevalence of cataracts in patients with rheumatoid arthritis, with or without diabetes mellitus, who were treated with aspirin (2.3–2.7 g daily for 8–10 years). Therefore, it has been suggested that aspirin may prevent the development of cataracts; however, this has not been clearly established and further studies are needed. There is no evidence to date that aspirin can reverse cataracts that have already formed.

Aspirin, alone or in combination with dipyridamole, is also being evaluated for potential efficacy in preventing progression of diabetic retinopathy in patients with diabetes mellitus.

Dosage and Administration

Aspirin is usually administered orally, preferably with food or a large quantity (240 mL) of water or milk to minimize gastric irritation. In patients unable to take or retain oral medication, aspirin suppositories may be administered rectally; however, rectal absorption may be slow and incomplete. (See Pharmacokinetics: Absorption.) *Aspirin tablets should not be administered rectally since they are likely to cause irritation and erosion of the rectal mucosa.* Aspirin preparations should not be used if a strong vinegar-like odor is present. (See Chemistry and Stability: Stability.)

If an unpleasant taste or aftertaste, burning in the throat, or difficulty in swallowing occurs with uncoated aspirin-containing tablets, these effects may be reduced with film-coated tablets. Although specific data are not available, these effects are also likely to be reduced with enteric-coated tablets. If gastric irritation and/or symptomatic GI disturbances occur with uncoated aspirin-containing tablets, these effects may be reduced with enteric-coated tablets or extended-release tablets. If a liquid dosage form of aspirin is desired for short-term treatment of pain, an oral solution may be prepared from commercially available effervescent tablets (Alka-Seltzer®). Dosage must be carefully adjusted according to individual requirements and response, using the lowest possible effective dosage.

PAIN AND FEVER

Aspirin should not be used for *self-medication* of pain for longer than 10 days in adults or 5 days in children, unless directed by a physician, since pain of such intensity and duration may indicate a pathologic condition requiring medical evaluation and supervised treatment. Aspirin chewing gum/tablets should not be used for *self-medication* of sore throat pain for longer than 2 days

in adults or children, unless directed by a physician, since prolonged use could cause mucosal erosions in the mouth. Aspirin or buffered aspirin preparations should not be chewed before swallowing for at least 7 days following tonsillectomy or oral surgery because of possible injury to oral tissues from prolonged contact with aspirin particles. In addition, aspirin or buffered aspirin tablets should not be placed directly on a tooth or gum surface because of possible injury to tissues.

Aspirin should not be used in adults or children for *self-medication* of marked fever (greater than 39.5°C), fever persisting longer than 3 days, or recurrent fever, unless directed by a physician, since such fevers may indicate serious illness requiring prompt medical evaluation.

To minimize the risk of overdosage, no more than 5 doses of aspirin should be administered to children for analgesia or antipyresis in any 24-hour period, unless directed by a physician.

For analgesia or antipyresis in adults or children older than 11 years of age, the usual oral or rectal dosage of aspirin is 325–650 mg every 4 hours as necessary, but should not exceed 4 g daily; higher single doses (e.g., 975 mg or 1 g) may be useful for analgesia in some patients. If a rapid response is required, the more slowly absorbed dosage forms (i.e., enteric-coated, extended-release tablets) should not be used. In children 2–11 years of age, the usual oral or rectal dosage for analgesia or antipyresis is 1.5 g/m^2 daily or 65 mg/kg daily, administered in 4–6 divided doses; total daily rectal dose should not exceed 2.5 g/m^2. Alternatively, children may receive the following *approximate* oral or rectal doses every 4 hours as necessary: children 11 years of age, 480 mg; children 9–10 years of age, 400 mg; children 6–8 years of age, 325 mg; children 4–5 years of age, 240 mg; and children 2–3 years of age, 160 mg. Dosage in children younger than 2 years of age must be individualized. Chewable aspirin tablets may be chewed, crushed, and/or dissolved in a liquid, or swallowed whole, followed by approximately 120 mL of water, milk, or fruit juice immediately after administration of the drug.

The usual dosage of aspirin (as chewing gum tablets) for analgesia in adults and children older than 11 years of age is 454 mg, repeated as necessary; total daily dose should not exceed 3.63 g. The chewing gum tablets should be thoroughly chewed for about 15 minutes to ensure adequate dosing and then the gum should be expelled from the mouth and discarded. Children 6–11 years of age may be given 227–454 mg, repeated as necessary, not to exceed 1.82 g daily unless directed by a physician. Children 3–5 years of age may be given 227 mg, repeated as necessary, not to exceed 681 mg daily. Aspirin chewing gum tablets should not be used in children younger than 3 years of age unless directed by a physician; dosage must be individualized.

The usual oral dosage of aspirin as a highly buffered effervescent solution (Alka-Seltzer®) for analgesia in adults and children older than 11 years of age is 648 mg every 4–6 hours as necessary; total dose in any 24-hour period should not exceed 2.59 g. Because of the high sodium content of this preparation (approximately 24 mEq of sodium per 324 mg of aspirin), it should be used with extreme caution, if at all, in patients in whom excessive amounts of sodium may be harmful. The solution is prepared by adding each tablet for oral solution containing 324 mg of aspirin to approximately 90 mL of water; the entire solution must be ingested to ensure adequate dosing. If the solution is not ingested immediately, it should be refrigerated. (See Chemistry and Stability: Stability.) The usual oral dosage for patients 60 years of age or older and children 6–11 years of age is 324 mg every 4–6 hours as necessary, not to exceed 1.3 g in any 24-hour period. Children 3–5 years of age may receive 162 mg every 4–6 hours as necessary, not to exceed 648 mg in any 24-hour period. The preparation should not be used in children younger than 3 years of age unless directed by a physician; dosage must be individualized. In addition, higher than usually recommended dosages of this preparation should not be used unless directed by a physician.

The usual oral dosage of aspirin (as 650-mg extended-release tablets) for analgesia in adults is 650 mg to 1.3 g every 8 hours as necessary, not to exceed 3.9 g daily. For patients who have difficulty swallowing the 650-mg tablets whole, the tablets may be gently broken or crumbled before administration (or in the mouth), but they must *not* be ground up if they are to retain the property of extended release. An 800-mg extended-release aspirin tablet is also commercially available but is indicated for use only in the symptomatic treatment of inflammatory disease; the 800-mg tablet *cannot* be broken or crumbled and must be swallowed whole. Most clinicians believe that extended-release aspirin tablets offer no therapeutic advantage over other types of aspirin tablets; this is particularly true at high dosages since the elimination half-life of salicylate is dose dependent and prolonged at high dosages. However, symptomatic GI disturbances and/or occult GI bleeding may be reduced with extended-release tablets.

INFLAMMATORY DISEASES

For the symptomatic treatment of rheumatoid arthritis, osteoarthritis, or other polyarthritic or inflammatory conditions, the usual initial adult dosage of aspirin is 2.4–3.6 g daily, administered in divided doses. When necessary, dosage is generally increased by 325 mg to 1.2 g daily no more frequently than at weekly intervals. The usual adult maintenance dosage is 3.6–5.4 g daily; however, higher dosages may be necessary. Dosage should be adjusted according to the patient's response, tolerance, and serum salicylate concentration.

For the symptomatic treatment of juvenile arthritis, the usual initial dosage is 60–90 mg/kg daily in children weighing 25 kg or less, or 2.4–3.6 g daily in children weighing more than 25 kg, administered in divided doses. Alternatively, some clinicians recommend an initial dosage of 1.5 g/m^2 daily, administered in divided doses. When necessary, dosage is generally increased by 10 mg/kg daily no more frequently than at weekly intervals. The usual maintenance dosage is 80–100 mg/kg daily; up to 130 mg/kg daily may be required in some children. Although some clinicians have reported a high incidence of chronic intoxication in children receiving 90–100 mg/kg daily, this has not been found by many others. However, it appears that dosages of 100 mg/kg daily or greater should not be used in children weighing more than 25 kg. Based on body surface area, dosage should generally not exceed 3 g/m^2 daily. Dosage should be adjusted according to the patient's response, tolerance, and serum salicylate concentration. In addition to potentially reducing adverse GI effects, some clinicians suggest that enteric-coated tablets may be swallowed more easily by children and may therefore result in increased compliance.

Because of the prolonged elimination half-life of salicylate at high dosages, at least 5–7 days are generally required to achieve steady-state serum salicylate concentrations in the treatment of inflammatory diseases. Therefore, some clinicians have suggested that loading-dose regimens of aspirin may be useful to more rapidly attain serum concentrations associated with an anti-inflammatory effect. In one small study, healthy individuals were given oral doses of 650 mg of aspirin every 4 hours for 4 days (conventional-dose regimen) or two 1.3-g doses 4 hours apart followed 2 hours later by initiation of a maintenance dosage of 650-mg oral doses every 4 hours through 4 days (loading-dose regimen). In this study, the time required to reach a serum salicylate concentration of 150 µg/mL was approximately 15 hours with the loading-dose regimen and approximately 48 hours with the conventional-dose regimen; serum salicylate concentrations were higher during the first 36 hours with the loading-dose regimen. However, the actual clinical importance of any difference between these regimens in patients with inflammatory diseases is not known; further evaluation of loading-dose regimens in such patients is needed.

RHEUMATIC FEVER

For the symptomatic treatment of rheumatic fever, dosage and duration of aspirin therapy are generally determined by the severity and duration of acute manifestations. For maximal suppression of acute inflammation, the usual initial dosage of aspirin is 4.9–7.8 g daily in adults and 90–130 mg/kg daily in children, administered in divided doses every 4–6 hours. Patients with only polyarthritis and fever usually respond to lower dosages. Subsequent dosage should be adjusted according to the patient's response, tolerance, and serum salicylate concentration. The initial dosage is generally administered for up to 1–2 weeks, then decreased to approximately 60–70 mg/kg daily for 1–6 weeks or as long as necessary, and then gradually withdrawn over 1–2 weeks. Various aspirin regimens have been suggested depending on the severity of acute manifestations, and the clinician should consult published protocols for more information on specific dosages and schedules of administration.

In patients with carditis and cardiomegaly or congestive heart failure who are treated with corticosteroids, aspirin therapy is usually initiated as steroid therapy is gradually withdrawn. In these patients, some clinicians recommend an aspirin dosage of 60 mg/kg daily, administered in divided doses. High dosages should be used with caution in patients with carditis since congestive heart failure or pulmonary edema may be precipitated. Aspirin is usually administered for approximately 2–4 weeks after steroids are discontinued. Only extremely severe clinical rebounds of rheumatic activity require reinstitution of therapy, in which case aspirin is administered in the usual dosage for 3–4 additional weeks.

THROMBOSIS

For reducing the risk of recurring transient ischemic attacks (TIAs) and stroke or death in men (and possibly in women) who have had single or multiple TIAs, the usual oral dosage of aspirin is 1.3 g daily, administered in 2 or 4 divided

doses. Only uncoated or film-coated, plain aspirin or buffered aspirin tablets or capsules should be used since differences in the bioavailability of unhydrolyzed aspirin might theoretically affect antithrombotic efficacy; however, no data are available comparing different preparations in this regard. Lower dosages may also be effective (e.g., 40–150 mg every 24–48 hours), but further evaluation is needed.

Aspirin has also been used in varying dosages alone or in combination with other platelet-aggregation inhibitors (e.g., dipyridamole) or oral anticoagulants for prophylaxis of other thrombosis-related conditions. (See Uses: Thrombosis.)

For further information on chemistry and stability, pharmacology, pharmacokinetics, uses, cautions, chronic toxicity, acute toxicity, drug interactions, laboratory test interferences, and dosage and administration of aspirin, see the Salicylates General Statement 28:08.04.

Preparations

ASPIRIN

Oral

Capsules

325 mg

A.S.A.® Pulvules®, Lilly

Capsules (containing enteric-coated aspirin particles)

325 mg

Ecotrin® Duentric®, Menley & James; *Encaprin®*, Norwich Eaton

500 mg

Ecotrin® Maximum Strength Duentric®, Menley & James; *Encaprin® Maximum Strength*, Norwich Eaton

Tablets

324 mg*

325 mg*

A.S.A.®, Lilly; *Empirin®*, Burroughs Wellcome; *Norwich® Aspirin*, Procter

487.5 mg

Hipirin®, Blaine

500 mg*

Norwich® Aspirin Extra Strength, Procter

650 mg*

Tablets, chewable

65 mg

Aspirin Children's, Lannett

81 mg

Bayer® Children's Chewable Aspirin, Glenbrook; *St. Joseph® Aspirin for Children*, Plough

Tablets, chewing gum

227 mg

Asperguin®, Plough

Tablets, enteric-coated

324 mg*

325 mg*

A.S.A. Enseals®, Lilly; *Cosprin® 325*, Glenbrook; *Ecotrin® Duentric®*, Menley & James

500 mg*

APF® Arthritis Pain Formula®, Whitehall; *Ecotrin® Maximum Strength Duentric®*, Menley & James

650 mg*

A.S.A. Enseals®, Lilly; *Cosprin® 650*, Glenbrook

975 mg

Easprin®, Parke-Davis

Tablets, extended-release

650 mg

Arthritis Bayer® Timed-Release Aspirin (scored), Glenbrook; *Measurin®*, Winthrop-Breon; *Vetin®*, Verex

800 mg

Zorprin®, Boots

Tablets, film-coated

325 mg

Bayer® Aspirin, Glenbrook

500 mg

Bayer® Aspirin Maximum Strength, Glenbrook

Rectal

Suppositories

60 mg*

65 mg*

120 mg*

125 mg*

130 mg*

195 mg*

200 mg*

300 mg*

325 mg*

A.S.A.®, Lilly

600 mg*

650 mg*

A.S.A.®, Lilly

1.2 g*

*available in unspecified dosage

ASPIRIN WITH BUFFERS

Oral

Capsules

324 mg with buffers

Bufferin®, Bristol-Myers

500 mg with buffers*

Bufferin® Extra-Strength, Bristol-Myers

Tablets

324 mg with buffers*

Asperbuf®, Bowman; *Bufferin®*, Bristol-Myers

325 mg with buffers*

Ascriptin®, Rorer; *Ascriptin® A/D*, Rorer; *Bufferin®*, Mallard; *Speedrin®*, Columbia

486 mg with buffers*

Arthritis Pain Formula®, Whitehall; *Bufferin® Arthritis Strength*, Bristol-Myers

500 mg with buffers*

Bufferin® Extra-Strength, Bristol-Myers

650 mg with buffers

Salagen® (scored), Lannett

Tablets, film-coated

500 mg with buffers

Cama® Inlay-Tab®, Dorsey

Tablets, for oral solution

324 mg

Alka-Seltzer® Effervescent Pain Reliever and Antacid (with citric acid and sodium bicarbonate 1.9 g), Miles

*available in unspecified dosage

ASPIRIN COMBINATIONS

Oral

Capsules

250 mg with Acetaminophen 250 mg and Caffeine 65 mg

Excedrin®, Bristol-Myers

325 mg with Butalbital 50 mg and Caffeine 40 mg

Fiorinal® (C-III), Sandoz

325 mg with Butalbital 50 mg, Caffeine 40 mg, and Codeine Phosphate 30 mg

Fiorinal® with Codeine No. 1 (C-III), Sandoz

325 mg with Butalbital 50 mg, Caffeine 40 mg, and Codeine Phosphate 15 mg

Fiorinal® with Codeine No. 2 (C-III), Sandoz

325 mg with Butalbital 50 mg, Caffeine 40 mg, and Codeine Phosphate 30 mg

Fiorinal® with Codeine No. 3 (C-III), Sandoz

325 mg with Propoxyphene Hydrochloride 65 mg

Darvon® with A.S.A.® Pulvules® (C-IV), Lilly

356.4 mg with Caffeine 30 mg and Dihydrocodeine Bitartrate 16 mg

Synalgos®-DC (C-III), Ives

356.4 mg with Caffeine 30 mg

Synalgos®, Ives

380 mg with Caffeine 30 mg and Codeine Phosphate 30 mg

A.S.A.® and Codeine Compound No. 3 Pulvules® (C-III), Lilly

ALASKA STATE LEGISLATURE
HOUSE OF REPRESENTATIVES
RESEARCH AGENCY

P.O. Box Y, State Capitol
Juneau, Alaska 99811-3100
Mail Stop 3100
(907) 465-3991

P

March 3, 1987

TO: Representative Pat Pourchot

FROM: Penelope Weyhrauch
Legislative Analyst

RE: The Physiological Effects of Marijuana, Alcohol, Tobacco, Aspirin, and Salt
Research Request 87.155

Please check the appropriate box and return to Mail Stop 3100 or the above mailing address.

( ) I approve the release of this information.

( ) I approve the release of this information, but remove my name.

( ) Keep Confidential.

_____ _____
Date Signature

To assist us in improving the quality of our research services, we would appreciate your response to the following questions. Please be assured that we will take your comments seriously in performing future research for you.

Was the information objective?

Was it clearly written?

Did it provide answers to (or, at least, useful information on) all the questions you posed?

Was the research completed and delivered to you in a timely manner?

TABLE 2
A Comparison of the Ingredients and Effects of Marijuana and Alcohol

	Marijuana	Alcohol
Active constituent	delta-9-tetrahydrocannabinol (THC)	ethyl alcohol (ethanol)
Excretory product	dihydroxy-THC and others	$C0_2$ and H_20
Pharmacologic class	sedative-hallucinogen	sedative-anesthetic
Half life	24-52 hours	½-2 hours
LD_{50}	human	500 ml, human
Solubility	lipophilic	hydrophilic
Tolerance	proven	proven
Psychological dependence	proven at high doses	proven
Physical dependence	slight	proven
Heart rate	increased	unchanged
Respiration	unchanged	unchanged
Blood pressure	slight decrease	unchanged with acute use, chronic use elevates
Temperature	slight decrease	slight decrease at high doses
Brain	intoxication at high doses	intoxication at high doses
Blood vessels	variable dilation	dilation
Lungs	irritant, contains carcinogens	no effect
Heart	no known effect	toxic, chronically
Gastrointestinal tract	no effect	inflammatory changes
Liver and pancreas	no effect	inflammatory changes
Endocrine glands	variable	variable
Gonads	changes reported	changes reported
Conjunctiva (white of eyes)	reddening	slight reddening
Nerves	unchanged	injury with chronic use
Adrenals	release of corticotropins	release of corticotropins
Pupil size	slight constriction	no effect
Teratogenic effect	not known	fetal alcohol syndrome
Intraocular pressure	reduced	no effect
Memory	impaired immediate recall	impaired transfer to long term memory on high dose
Time perception	overestimation	no effect
Food intake	may increase	increase or decrease
Food value	no effect	7 calories/gram
Speech	blocking	slurred
Sleep pattern	blocks REM sleep	blocks REM sleep
Driving skills	impaired	impaired

Source: Sidney Cohen, "Marijuana and Alcohol," American Council for Drug Education, 1982, pp. 11-12.

ALASKA STATE LEGISLATURE
HOUSE OF REPRESENTATIVES
RESEARCH AGENCY

P.O. Box Y, State Capitol
Juneau, Alaska 99811-3100
Mail Stop 3100
(907) 465-3991

March 3, 1987

MEMORANDUM

TO: Representative Pat Pourchot

ATTN: Jeannie Larson

FROM: Penelope Weyhrauch
Legislative Analyst

RE: **The Physiological Effects of Marijuana, Alcohol, Tobacco, Aspirin, and Salt**
Research Request 87.155

You asked for a comparison of the physiological effects of marijuana, alcohol, tobacco, aspirin, and salt. I was unable to find a clinical comparison of these substances; this memorandum discusses each of the substances on which you requested information and compares the effects and/or ingredients of marijuana to tobacco and alcohol.

Marijuana

Acute Short-Term Effects. Marijuana affects the intellectual and psychomotor processes of humans. Intellectual impairment has been documented in tests of: reading comprehension; concept formation; speech; choice reaction time (a reaction-time task in which the response depends on rapidly discriminating between choices); and the ability to repeat in forward and backward order a succession of digits, and to mentally make a succession of repeated subtractions. There is evidence that suggests that marijuana use impairs driving ability and related skills.[1] Marijuana also produces some acute short-term effect on the cardiovascular and respiratory systems.

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[1] "Marijuana Research Findings: 1980", Research Monograph Series 31, National Institute on Drug Abuse, pp. 15, 16.

Chronic Effects. There is no substantial evidence which exposes the possible long-term effects of marijuana. The National Research Council stated: "We agree with the conclusion that long-term heavy marijuana use will be shown to result in measurable damage to health, just as long-term chronic tobacco and alcohol use have proven to cause such damage. At this time, however, our judgment as to behavioral and health-related hazards is that the research has not established a danger both large and grave enough to override all other factors affecting a policy decision."[2]

Pulmonary Effects. There is no direct evidence that links the smoking of marijuana with lung cancer. Recent studies, however, showed that when cannabis residuals are applied to the skin of animals, the cannabis "tar" produced tumors. Marijuana has also been found to contain larger amounts of cancer-producing hydrocarbons than tobacco smoke. Benzopyrene, a known cancer-producing chemical found in tobacco smoke, has been reported to be 70 percent more abundant in marijuana smoke. Several clinical studies of marijuana users have reported symptoms similar to those of laryngitis, cough, hoarseness and bronchitis. These symptoms resembled those experienced by heavy tobacco smokers.[3]

Reproductive and Chromosomal Effects. According to the National Institute on Drug Abuse (NIDA), "...the evidence is consistent--cannabis causes decreases in the weight of organs such as testes and ovaries, as well as altering various hormone levels that are involved in reproduction and lactation." The NIDA also stated that "...although there were early reports of increases in chromosomal breaks and abnormalities in human cell cultures, more recent results have been inconclusive."[4]

Other Effects. Studies have found that a significant increase in heart rate occurs after smoking. Changes found in the functioning of the heart, however, appeared to be temporary and were free of adverse consequences. Additional evidence showed that "...in patients with already impaired heart functions, use of marijuana may precipitate chest pain more rapidly and following less effort than tobacco cigarettes." Virtually all the studies completed up to 1979 showed no evidence of chronically impaired neuropsychologic test performance.[5]

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[2]"An Analysis of Marijuana Policy," National Research Council, Committee on Substance Abuse and Habitual Behavior, Commission on Behavioral and Social Sciences and Education, 1982, pp. 5, 6.

[3]"Marijuana Research Findings: 1980," pp. 18, 19.

[4]"Marijuana Research Findings: 1980," p. 23.

[5]"Marijuana Research Findings: 1980," pp. 22, 25.

Tobacco

There is conclusive evidence that cigarette smoking is the most prominent cause of lung cancer, and is also a major factor in deaths from heart disease, chronic bronchitis, emphysema, and other diseases. There is also evidence of increased illness and a notable shortening of life expectancy among smokers.[6] According to the National Organization for the Reform of Marijuana Laws, tobacco was responsible for more deaths (in 1979) than alcohol, aspirin, caffeine and marijuana put together (Attachment A).

Both marijuana smoking and tobacco smoking draw smoke into the lungs, where it can harm the cells that line the airways (trachea, nasopharynx, bronchi, and alvoloi) and impair such cells as lung macrophages, which are part of the immune system. While continued exposure to tobacco smoke has been proven to cause a high risk of chronic bronchitis and/or carcinoma of the lungs, there is no substantial evidence that the smoking of marijuana presents similar risks.[7] Contemporary information that exists in regard to marijuana's effects on the lungs is confounded by the fact that most marijuana smokers are also tobacco smokers.[8]

The materials in tobacco cigarette and marijuana cigarette smoke are compared in Table 1. Toxic substances, such as carbon monoxide, hydrogen cyanide, and nitrosamines occur in similar concentrations in tobacco and marijuana smoke; so do the amount of the particulate material known as "tars." According to the study which accompanies Table 1, "...It is not easy to compare the toxicity of a given number of marijuana cigarettes to a given number of tobacco cigarettes. There are general similarities in the composition of the smoke, but the variations in composition of both tobacco and marijuana cigarettes and differences in smoking techniques make simple extrapolations of risks of tobacco versus marijuana smoking not valid."[9]

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[6]Edward M. Brecher and the Editors of Consumer Reports, "Licit and Illicit Drugs," the Consumers Union Report on Narcotics, Stimulants, Depressants, Inhalants, Hallucinogens and Marijuana--including Caffeine, Nicotine and Alcohol, 1972.

[7]"An Analysis of Marijuana Policy," 1982, p. 5.

[8]"Marijuana and Health," Report of a Study by a Committee of the Institute of Medicine, Division of Health Sciences Policy, 1982, p. 57.

[9]"Marijuana and Health," p. 27.

TABLE 1

TABLE 3 Marijuana and Tobacco Reference Cigarette Analysis of Mainstream Smoke

	Marijuana Cigarette (85 mm)	Tobacco Cigarette (85 mm)
A. Cigarettes		
Average weight, mg	1115	1110
Moisture, percent	10.3	11.1
Pressure drop, cm	14.7	7.2
Static burning rate, mg/s	0.88	0.80
Puff number	10.7	11.1
B. Mainstream smoke		
I. Gas phase		
Carbon monoxide, vol. percent	3.99	4.58
mg	17.6	20.2
Carbon dioxide, vol. percent	8.27	9.38
mg	57.3	65.0
Ammonia, ug	228	199
HCN, ug	532	498
Cyanogen $(CN)_2$, ug	19	20
Isoprene, ug	83	310
Acetaldehyde, ug	1200	980
Acetone, ug	443	578
Acrolein, ug	92	85
Acetonitrile, ug	132	123
Benzene, ug	76	67
Toluene, ug	112	108
Vinyl chloride, ng[a]	5.4	12.4
Dimethylnitrosamine, ng[a]	75	84
Methylethylnitrosamine, ng[a]	27	30
pH, third puff	6.56	6.14
fifth puff	6.57	6.15
seventh puff	6.58	6.14
ninth puff	6.56	6.10
tenth puff	6.58	6.02
II. Particulate phase		
Total particulate matter, dry, mg	22.7	39.0
Phenol, ug	76.8	138.5
o-Cresol, ug	17.9	24
m- and p-Cresol, ug	54.4	65
Dimethylphenol, ug	6.8	14.4
Catechol, ug	188	328
Cannabidiol, ug	190	-
Δ^9-Tetrahydrocannabinol, ug	820	-
Cannabinol, ug	400	-
Nicotine, ug	-	2850
N-Nitrosonornicotine, ng[a]	-	390
Naphthalene, ug	3.0	1.2
1-Methylnaphthalene, ug	6.1	3.65
2-Methylnaphthalene	3.6	1.4
Benz(a)anthracene, ng[a]	75	43
Benzo(a)pyrene, ng[a]	31	21.1

[a]Indicates known carcinogens.
SOURCES: Hoffmann et al., 1975, 1976; Brunnemann et al., 1976, 1977.

Source: "Marijuana and Health," Report of a Study by a Committee of the Institute of Medicine Division of Health Sciences Policy, 1982, page 17

Alcohol

Alcohol is a central nervous system depressant. Although its occasional use appears to be relatively harmless, excessive or long-term use can be harmful and even deadly. Alcohol accounts for roughly 75,000 deaths annually in the United States. About two-thirds of these are caused by trauma (accidents, suicide, and homicide) and one-third are caused by acute and chronic alcohol-related illness.[10]

Alcohol users have an increased risk for liver cirrhosis, acute pancreatitis, and cancers of the liver, esophagus, larynx, and mouth. Damage from alcohol abuse can occur in the brain and in the peripheral nerves. Alcohol also has an effect on the endocrine system and has properties which can cause genetic and birth defects.[11]

A comparison of some of the effects of alcohol and marijuana is provided in Table 2.[12] Matt Felix, Coordinator of the State Office of Alcoholism and Drug Abuse, said that the detrimental effects of marijuana are innocuous as compared with the effects of alcohol. He said that alcohol is more acceptable in the United States because it has been around longer.

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[10]"Medicine for the Layman," United States Department of Health and Human Services, Public Health Service, National Institute of Health, p. 20.

[11]"Medicine for the Layman," pp. 21-24.

[12]Sidney Cohen, M.D. and Phyllis J. Lessin, "Marijuana and Alcohol," Neuropsychiatric Institute, Center for the Health Sciences, University of California at Los Angeles, American Council for Drug Education, 1982.

Aspirin

Aspirin can cause heartburn, dyspepsia, stomach discomfort, nausea and vomiting. It can also cause stomach ulcers, erosion of and bleeding from the lining of the stomach, kidney dysfunction, and gastrointestinal hemorrhage. When aspirin is taken over a long period of time, there is sometimes enough loss of blood in the lining of the stomach to cause iron-deficiency anemia. Studies have also shown that aspirin may pose special risks for certain groups--including pregnant women, people with bleeding disorders, those with ulcers and children with viral illnesses.[13] Aspirin leads over-the-counter drugs as a cause of adverse reactions leading to hospitalization and is a major cause of child poisoning.[14]

Excessive amounts of ingested aspirin is considered a possible cause of malformations in fetuses and is believed to create the danger of infant mortality. A study of Australian women showed that the infants of aspirin users had significantly lower birth weights and were more likely to die around the time of birth. Studies also associate the use of aspirin with significant increases in post maturing (the birth of an overdeveloped infant), length of time spent in labor, the likelihood of a complicated delivery, and increased hemorrhaging in both mothers and newborn infants.[15]

Caffeine

Caffeine stimulates the central nervous system, makes the heart beat faster, speeds up metabolism, promotes secretion of stomach acid, and steps up the production of urine. It also widens some blood vessels, narrows others, and increases the capacity of muscular work. Studies show that coffee (decaffeinated as well as regular) can stimulate stomach-acid secretion, thus, physicians commonly advise ulcer patients to avoid its consumption.[16] Caffeine is also addictive, producing withdrawal effects at some dosages. These effects include headaches, irritability, inability to work effectively, nervousness, restlessness and lethargy.[17]

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[13]Children with viral illnesses such as chicken pox and the flu are susceptible to Reyes Syndrome if they take aspirin. Reyes Syndrome causes the brain to swell, causes a fatty infiltration of the liver and can cause death.

[14]Flora Taylor, "All About Aspirin," Consumers Research Magazine, August 1984, p. 21.

[15]"All About Aspirin," p. 22.

[16]"Is Coffee Safe to Drink?," Consumer Reports Magazine, May 1985, pp. 267-268.

[17]"Licit and Illicit Drugs," p. 22.

According to Consumer Reports Magazine, although studies suggest that coffee can contribute to higher blood cholesterol levels, there is as yet no evidence that reducing coffee consumption will help lower cholesterol levels or prevent them from rising. Researchers in a study conducted in 1985 noted that "...the preponderance of current evidence 'fails to support' a relationship between coffee and coronary disease." Consumer Reports also stated that no well-controlled studies of human birth defects have linked any common malformations to caffeine intake, and that studies linking coffee consumption with cancer have produced inconsistent and conflicting findings.[18]

Salt

Research has linked excessive consumption of salt to hypertension (high blood pressure) and its potentially fatal consequences, heart and kidney disease and strokes. The main precipitant of hypertension is the mineral sodium, which is 40 percent of the substance of salt. Hypertension afflicts an estimated 34 million Americans, usually producing no symptoms until the signs of permanent organ damage suddenly appear as a chronic illness or death.[19]

I hope this information is helpful to you. If you have any questions or would like additional information, please contact our agency.

Attachment

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[18]"Is Coffee Safe to Drink?," pp. 267-268.

[19]Jane Brody, "Jane Brody's Nutrition Book--A Lifetime Guide to Good Eating for Better Health and Weight Control by the Personal Health Columnist of the New York Times," 1981, p. 199.

ATTACHMENT A

"HOW DANGEROUS IS MARIJUANA . . . IN *COMPARISON* TO OTHER SUBSTANCES?"

According to World Almanacs, Life Insurance Actuarial (death) Rates, and the last 12 years of the U.S. Surgeon General's Reports, Americans DIE, directly or primarily, from the following *(selected)* causes per year Nationwide. *(Figures are for 1979 from the Federal Government's Bureau of Mortality Statistics, and NIDA, the last complete year at the time of this writing.)*

TOBACCO . . . . . 200,000 to 300,000

ALCOHOL *(not including 50% of all highway deaths and 65% of all murders)* . . . . . 18,951 to 130,000

ASPIRIN *(including deliberate overdose)* . . . . . 180 to 1,000 plus

CAFFEINE *(from stress, ulcers, and triggering irregular heartbeats, etc.)* . . . . . 1,000 to 10,000

OVERDOSE *(deliberate or accidental) from prescribed legal or patent medicines and/or mixing with alcohol e.g., Valium/alcohol* . . . . . 7,101 to 21,000

OVERDOSE *(deliberate or accidental) from all illegal drugs* . . . . . 981 to 3,600

MARIJUANA *(including overdose)* . . . . . — 0 —

Marijuana users also have the same or lower incidence of murders and highway deaths and accidents than the general non-marijuana using population as a whole. *Crancer Study, UCLA;* U.S. Funded *($6 million),* Jamaican Study(s) 1st and 2nd, 1968 to 1974; Costa Rican Studies, 1980 to 1982; et al.

LOWEST TOXICITY

100% of the studies done at dozens of American universities and research facilities show pot toxicity does not exist. Medical history does not record anyone dying from an overdose of marijuana *(UCLA, Harvard, Temple, etc.)*

Official Actions

American Psychiatric Association

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Position Statement on Psychoactive Substance Use and Dependence: Update on Marijuana and Cocaine

This statement is an adjunct to the position statement on substance abuse published in the June 1981 issue of the American Journal of Psychiatry, *which emphasizes diagnosis and treatment. It replaces the position statement on marijuana laws published in the May 1979 issue of the* American Journal of Psychiatry. *The statement was prepared by the Committee on Drug Abuse[a] of the Council on Psychiatric Services and was approved by the Assembly in November 1986 and by the Board of Trustees in December 1986.*

The misuse of psychoactive substances is the nation's foremost public health challenge. The use and abuse of alcohol, cigarettes, illicit drugs (heroin, cocaine, marijuana, etc.), and licit drugs (sedatives and tranquilizers) are by far the largest cause of preventable and premature illness, disability, and death in our society. The annual economic cost of alcohol and drug abuse has been estimated to be $136 billion, over four times that of cancer and nearly a third greater than that of cardiovascular disease (1). Illicit drug use has increased so rapidly over the past 25 years that it may be difficult for someone over age 50 to comprehend the extent to which drugs have permeated our society. Experience with illicit psychoactive drugs was restricted to 2% or less of the population in most areas of the country in the early 1960s (2). In contrast, the 1982 household survey (3) found that almost a third of the household population in the United States age 12 and older had had some experience with illicit drugs. Almost 60 million household residents had tried marijuana, and an estimated 20 million were current users. In 1982, it was estimated (4) that over 20 million had tried cocaine and over 4 million were current users. The prevalence of cocaine use and abuse has increased dramatically in the ensuing 4 years (4).

Illicit drug use is most prevalent in young adults. Typically, children begin experimenting with drugs of abuse by trying alcohol and cigarettes in early adolescence. By the time they complete secondary school, they have established attitudes toward drugs and patterns of use that will carry them through much of their lives. Most adults addicted to nicotine through smoking cigarettes established regular smoking in their teens. Adult users of cocaine and opiates generally began drug use in adolescence and may have been heavy marijuana users (5). In addition to exposing themselves to the risks of drug use (automobile accidents, overdose, or impaired physical, emotional, and psychological development), adolescents are establishing attitudes toward and actual patterns of use that have profound long-term consequences on health. By the time they graduate, more than half (54%) of high school seniors have tried marijuana and a fourth (26%) are current users. Cocaine use tends to begin a few years later than marijuana use, and heavy marijuana use is an important risk factor for cocaine use. Nevertheless, cocaine use now is increasing among our high school population. In the 1985 national survey of high school seniors (6), it was found that 17% had tried cocaine and almost 7% were current users.

In addition to statistics on the prevalence of use, there are now data from National Institute of Mental Health (NIMH) catchment area studies (7) on the lifetime prevalence of substance abuse disorders, which was found to vary from 15.0% to 18.1% among the three sites reported. These rates were significantly higher than the lifetime prevalence of any other group of disorders (except for phobic disorders at one site).

SOCIAL CONSEQUENCES OF USE OF MARIJUANA AND OTHER DRUGS

Young people may use drugs in an attempt to alleviate problematic family relationships. Over the short term, drugs may allow the young person temporarily to ignore intrafamilial strife, including developmental adjustments between child and parents and among siblings. Regular or heavy drug use undermines the adolescent's ability to work through these problems with other family members, thereby exacerbating family problems over the long term. The heavy drug user may withdraw socially from other family members, refuse to consider their needs and concerns, and put his or her own needs above those of the family. Theft from other family members (to obtain drugs) and lying (to hide drug use) undermine the trust necessary for coexistence within the family. Angry outbursts, property destruction, and intrafamily violence can ensue. Alienation of the drug user from the family, once present, is difficult to repair (8). Adult substance abusers also exert powerful effects on their families. Families react variably but often go through stages of denial, overprotection, personal mental illness, and family disruption. The effects on children in such families have been so profound that a national movement, the Adult Children of Alcoholics, has recently emerged to provide support and understanding (9–11).

Heavy drug use can precipitate financial problems in two ways. First, drugs themselves cost money; drug expenses are proportional to the cost of the drug, frequency of use, and dose consumed. Such costs mount as tolerance develops, habitual use becomes established, and larger amounts of drug are consumed more often. A second source of financial problems is unemployment or job loss. Early drug use may seem to facilitate work by alleviating fatigue or boredom or helping the user tolerate work-related stresses. Eventually, continued drug use undermines the person's energy, ambition, concentration, problem-solving abilities, performance, productivity, and social skills in dealing with co-workers and supervisors. Drug-induced paranoia, if present, further exaggerates interpersonal dissensions. In addition to individual financial loss, theft and unpaid loans from other family members can cause financial difficulties for the entire family.

The heavy drug user may resort to criminality to financially support the drug habit. Theft and illicit drug selling are the most

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common illegal activities, but prostitution, robbery, and drug smuggling also occur. Easy money from criminal behavior impedes later rehabilitation, since the youthful person has been learning criminality rather than a licit occupation during this critical development period. Learning a job skill or profession requires hard work, willingness to make a commitment and risk failure, and learning responsibility, tasks not easily accomplished. Frustration, anxiety, and fear result to a greater or lesser extent, feelings that marijuana, cocaine, and other drugs can alleviate temporarily. Continued drug use undermines the persistence and industriousness needed to succeed at this developmental task. Drug intoxication and, later, withdrawal, impair the ability to concentrate, synthesize, and organize material, learn new material, apply general principles to specific problems, exert judgment in complex tasks and situations, and make timely decisions (12).

In developing friendships and, later, intimacy with persons of the opposite sex, most youthful persons experience anxiety, embarrassment, and fear of rejection. They may believe that drugs can relieve these aversive feelings as well as alleviate premature ejaculation (in males) and vaginismus (in females). However, prolonged heavy use can reverse these temporary gains in sexual performance, leading to anhedonia, amenorrhea, impotence, and rejection by a sexual partner (13). The lack of judgment seen in young drug and alcohol users often results in teenage pregnancy.

Adolescence is the time to acquire hobbies, sports, and other avocations that may last decades, even a lifetime (14). By and large, drug use does not enhance these activities. Drug use may in fact lead to abandonment of these pursuits and may intensify social isolation. Instead, the drug user pursues activities that focus on the drug use experience and that tend to be banal and boring if done without drug use. Thus, without drugs, the chronic user may be bored and at a loss for stimulating and rewarding activities. Recreational pastimes usually require a period of learning and acquiring skills, another lengthy process that is abandoned with drug use. Drug use during activities involving rapid psychomotor coordination, speed, and judgment (e.g., driving a car or motor boat, water or snow skiing) places the intoxicated person at risk of harming self or others.

In the process of becoming an adult, an adolescent learns to accept responsibility and cope with adversity. Maturation demands a focus outside oneself, task orientation, and the ability to delay gratification for a time. This personality development is impaired by the use of drugs, which furthers an egocentric and present-oriented attitude. If regular drug use began early in adolescence and was continued over several years, the recovering abuser often has the personality characteristics and maturation level of a much younger person (15). It is important to note that alcohol and cigarettes are "gateways," predecessors of marijuana use, which is in turn a predecessor of other drug use and abuse (16).

CONSEQUENCES OF MARIJUANA USE

General Medical Consequences

Two distinguished independent scientific groups separately have reported on marijuana in the past 6 years. The Institute of Medicine, National Academy of Sciences, prepared a report on marijuana and health that was published in 1982 (17). The Addiction Research Center, World Health Organization, prepared a report on the Conference of Adverse Health and Behavioral Consequences of Cannabis, which was published in 1981 (18). Both reports concluded that cannabis has both known and suspected health hazards that should be of serious national concern.

The health consequences of chronic marijuana use depend to some extent on the frequency, duration, and intensity of use, the age at which use begins, and biopsychosocial characteristics of the user, which may contribute to risk in still unspecified ways. For example, not all individuals who smoke tobacco cigarettes will go on to develop carcinoma of the lung, but the risk of this disorder is much greater among smokers, and the relative risk increases with the intensity, frequency, and chronicity of use.

Since the two aforementioned studies were published, further evidence of the harmful effects of marijuana has been established. In particular, the clearest evidence for harmful changes in physical health involves the pulmonary system (19–22 and a December 1979 report of the AMA Council on Scientific Affairs). Bronchitis and related inflammatory changes have been shown repeatedly. More recently, it has been shown that marijuana smoking causes a significant reduction in the gas-diffusing capacity of the lung. Moreover, there is considerable evidence to suggest that long-term use, like tobacco smoking, may lead to pulmonary cancer. Indeed, marijuana has up to 50% more aryl hydrocarbons in its smoke than tobacco, and high levels of these are associated with susceptibility to bronchogenic carcinoma. Many marijuana smokers also smoke tobacco, and it is postulated that the combined effects of smoking both substances may substantially increase the risk of cancer. Most important are the profound acute and chronic psychosocial, cognitive, and behavioral effects associated with marijuana use by youth. Acute toxicity is accompanied by negative effects on learning and memory, as well as psychomotor impairment. The typical effects of cannabis resemble a transient acute brain syndrome; they include deficits in attention span, concentration ability, short-term memory, information processing, and the performance of complex perceptual motor tasks. Thus, accidental injury to persons driving motor vehicles, piloting airplanes, or operating heavy machinery while intoxicated with marijuana is of special concern.

Even when marijuana use is discontinued, the memory loss continues for 3 to 6 months. This particularly affects adolescents who have been having difficulties in school. This consequent negative reinforcement leads them to return to marijuana use.

Specific Psychiatric Concerns

Psychiatrists have described three general complications associated with cannabis: acute adverse reactions, flashbacks, and prolonged reactions. Acute reactions are characterized by errors in judgment and confusion, which may be followed by an amnesic period. These are dose related and fall within the general category of deliria (23, 24). Anxiety may progress to acute pain reaction with overwhelming anxiety and a fear of losing control in response to drug-induced symptoms. Factors related to setting and/or personality may lead to severe anxiety.

Flashbacks refer to brief, spontaneous recurrences of mental states experienced during marijuana intoxication that occur sometime after the last drug use. At this writing, the exact mechanism for flashbacks is uncertain.

Prolonged reactions secondary to marijuana use include psychotic and nonpsychotic reactions. Marijuana smoking may trigger a schizophrenic reaction in vulnerable individuals. Descriptions of long-lasting cannabis-induced psychoses appear mainly in medical journals in Asia and North Africa, where individuals may use cannabis at substantially higher doses than in the United States. Descriptions of cannabis psychoses vary by culture, and most reports suggest a persistent delirium, which includes bizarre behavior and the potential for violence and panic feelings in the absence of a "typical" schizophrenia-like psychotic state. There is fairly general agreement that persons suffering from marijuana psychosis do not develop psychotic thoughts or symptoms characteristic of schizophrenia. Most reports describe cannabis psychosis as lasting 1–6 weeks among very heavy users of high doses of cannabis. However, some reports describe longer-lasting marijuana psychoses in which the psychotic episodes do not clear in the usual time but persist in residual form. Repeated intoxications may result in recurrent psychotic episodes. There has been a problem in relating marijuana psychosis to the experience in Western countries because of differences in smoking patterns in the East and the West, the difficulty of translating the psychiatric symptom picture from one body of literature and culture into another, and the impossibility of generalizing from cases that come to psychiatric attention to the overall marijuana-using population.

Nonpsychotic prolonged adverse reactions have also been described. Chronic anxiety states, depressive symptoms, and changes in life style (including an "amotivational syndrome") have been linked to chronic marijuana use by a number of observers. The amotivational syndrome includes apathy, loss of effectiveness, and diminished capacity or willingness to carry out complex long-term

plans, endure frustration, concentrate for long periods, follow routines, or successfully master new materials. Verbal facility often is impaired both in speaking and in writing. Such individuals experience greater introversion, become totally involved with the present at the expense of future goals, and demonstrate a strong tendency toward regressive, childlike, magical thinking. It remains unclear whether those who are attracted to heavy marijuana use already were inclined toward an amotivational syndrome, of which the marijuana use was symptomatic, or whether the amotivational syndrome developed as a consequence of the chronic marijuana use. What is clear is that chronic marijuana smokers who develop amotivational patterns of behavior need to stop marijuana use if they are to be rehabilitated.

Finally, the question of marijuana's dependence-producing capability is raised frequently. Laboratory animals do not self-administer Δ^9-tetrahydrocannabinol as they do opioids, sedative hypnotic drugs, alcohol, and stimulants. Nevertheless, compulsive patterns of cannabis consumption do develop in human beings, and heavy use of marijuana in humans is associated with the development of a dependence syndrome. Moreover, heavy users of marijuana appear to be at substantially greater risk for other forms of drug abuse than persons who do not use marijuana. Finally, the long persistence of cannabinoids in the body after ingestion (up to 9 days after a single dose) raises the additional prospect of toxicity due to accumulation of the drug and its metabolites in the brain and other lipid-containing organs.

CONSEQUENCES OF COCAINE USE

The growing popularity of cocaine, as a drug of both use and abuse, is testimony of the willingness of human beings to consume psychoactive substances without regard to their effects on the brain or other body organs.

The adverse effects of cocaine on health may be divided into the general medical, specifically psychiatric, and social sequelae of acute and chronic use. The probability that adverse effects will occur is, in turn, related to factors such as dose, route of administration, and frequency and duration of use. Changing routes of cocaine administration (such as "free basing" or using "crack") increases the severity of health consequences. Frequent administration, even over short periods of time, leads to the accumulation of cocaine in plasma and presumably in brain tissue and increases the risk of adverse medical and psychiatric sequelae. Cocaine rapidly depletes endogenous neurotransmitters, leaving the user in a depressed state. Individual tolerance and vulnerability to the physical and psychological effects of the drug also play a role.

General Medical Consequences

Some sequalae of cocaine use stem from the drug's local anesthetic properties, its direct effects on small capillaries, and its ability to stimulate sympathetic nervous system activity. Other medical complications are the indirect result of the drug-using life style.

Until the upsurge of smoking crack cocaine, 80% of all cocaine use was by nasal inhalation (snorting). The direct effects of the drug on mucous membranes are responsible for a number of medical complications. These include rhinitis, erosion of the mucous membranes, and in severe cases, perforation of the nasal septum (25). Intravenous cocaine use, favored by some for the rapidity of onset and intensity of drug effects, is associated with all of the complications that one might expect with any type of unregulated intravenous drug use. These include skin abscess, thrombophlebitis, septicemia, hepatitis B, acquired immune deficiency syndrome (AIDS), and tetanus (26). Smoking the basified extract of cocaine (free basing or crack smoking) delivers the drug into the pulmonary capillary bed, where it is rapidly absorbed and results in a dramatically intense effect and a more rapid onset of addiction. Free basing and crack smoking have been associated with the development of chronic bronchitis and impairment in pulmonary diffusing capacity (27).

Cocaine's ability to stimulate the sympathetic nervous system may result in elevated heart rate and increased susceptibility to premature ventricular beats and, in some vulnerable individuals, ventricular fibrillation, respiratory arrest, and death (28). Acute elevations of blood pressure, with headache and the potential for cerebral hemorrhage, also have been described (29). Increased body temperature due to failure of the brain mechanisms controlling heat regulation, coupled with vasoconstriction and hyperactivity, has led to some deaths from hyperthermia (30).

Another untoward effect of cocaine is the development of status epilepticus. This may occur either as an acute response to high-dose use or as a result of a sensitivity to cocaine developed during chronic administration. The latter may be due to a so-called "kindling" phenomenon, in which brain neurons become increasingly sensitized to the effects of cocaine and fire in response to even relatively low doses of the drug (30).

All of the adverse medical complications of cocaine use are far more likely after acute administration of large doses. In many instances overdose is unintentional, since the user has little knowledge of the purity or even the amount of the drug consumed. Overdose deaths have occurred after the first use in apparently healthy individuals with no preexisting illness. In addition, repetitive use is associated with increasing sensitivity in some of the excitatory effects of cocaine. Finally, a small number of individuals suffer from a congenital lack of the enzyme pseudocholinesterase and thus are unable to metabolize the drug. In these individuals, even small doses can produce dramatic effects. The medical complications of cocaine use are more likely to occur in persons with preexisting heart or respiratory disease, hypertension, seizure disorders, or compromised immune function and in those who are taking other drugs whose effects are potentiated by cocaine.

Specific Psychiatric Complications

The acute subjective response to cocaine is characterized by euphoria, insomnia, increased energy, enhanced mental acuity and alertness, and an increase in sensory awareness. However, some individuals become hyperexcitable, while others, particularly those with underlying depressive disorders, experience dysphoria. Anxiety, concentration difficulties, decreased attention span, and memory problems also have been reported after use of cocaine. In individuals with underlying panic disorder, the drug can precipitate panic attacks. Some cocaine users may misperceive reality and/or experience auditory, visual, and tactile hallucinations. Flight of ideas, distractibility, pressured speech, restlessness, impulsivity, and poor judgment are common. Paranoia and delusions of persecution, coupled with profound irritability and grandiosity, may lead to assaultive and/or homicidal behavior by some cocaine abusers. These alterations in thinking, mood, and behavior may last a short time or, in certain vulnerable individuals, may persist long after the drug has been metabolized (31, 32).

Chronic cocaine use also is associated with untoward effects on psychological health. Several studies have demonstrated a direct relationship between cocaine dose, chronicity of use, and the development of cocaine-related psychopathology. Chronic cocaine users frequently complain of fatigue, headaches, impairment of recent memory, concentration difficulties, and sexual indifference. They also are more likely to develop a cocaine psychosis (described previously).

In some individuals the powerfully reinforcing effects of cocaine lead to increased frequency of use, escalation of dose, and the eventual development of psychological and physical dependence. The onset of dependence is particularly rapid with the use of crack. The primary reinforcing effects of the drug are probably mediated through the limbic system mechanisms responsible for the perception of pleasure—specifically, those neural circuits that use norepinephrine and dopamine as neurotransmitters. Other factors that contribute to the development of dependence include psychological variables, peer pressure, drug availability, and (perhaps) some sort of underlying biological vulnerability.

The tendency toward repetitive use is further enhanced by the occurrence of a cocaine withdrawal syndrome characterized by depression, lethargy, fatigue, feelings of guilt, anxiety, and feelings of helplessness, hopelessness, and worthlessness. In some individuals, particularly those with preexisting underlying depression, transient suicidal thoughts may emerge.

The cocaine withdrawal syndrome is particularly marked after chronic high-dose use. The signs and symptoms usually last 12–36 hours. In some individuals, however, the depression may last up to several weeks. To avoid withdrawal, some chronic users will self-administer the drug every 20–30 minutes. This pattern of use is more likely to be associated with the development of cocaine psychosis. The serious psychosocial consequences of cocaine use include loss of job and problems with one's family, friends, and finances.

In summary, both acute and chronic cocaine use are associated with adverse effects on health. In addition to medical and psychiatric sequelae, chronic cocaine use also is associated with the hazards of a drug-using life style. These include anorexia and associated weight loss, malnutrition and vitamin deficiencies, accidents, and a greater likelihood that one will be the perpetrator or victim of violence.

ROLE AND RESPONSIBILITY OF PSYCHIATRISTS

Psychiatrists should exercise a leadership role in drawing attention to the major public and mental health consequences of substance abuse in our society. Psychiatrists have a responsibility to educate the public about how ubiquitous drug abuse is and how it is both the cause and consequence of emotional problems. We must be aware that drug and alcohol abuse are often the primary problem among patients who present themselves to psychiatrists. Psychiatrists should take leadership responsibility in assuring that adequate training in substance abuse occurs at all levels of medical education and in influencing physician attitudes and behaviors as part of this training process. Psychiatrists also should interface with nonmedical care givers, such as educators, the clergy, counselors, and self-help groups, in imparting an understanding of the psychiatric implications of substance abuse. The psychiatrist's role in working with the family is essential.

Evidence has accumulated over the past decade that there is a significant association between psychopathology and substance abuse. In some instances, substance abuse has resulted from psychopathology and in other cases has been the cause of it. In either case, for most individuals regular reliance on drugs is incompatible with a life of meaningful relationships, productivity, and satisfaction. Substances of abuse are dangerous because they exert powerful deleterious effects on human emotions and behavior. Mind-altering drugs, including alcohol, create illusions that emotional distress can be avoided, that desired states or behaviors can be augmented, and that performance can be enhanced or improved. During adolescence, when particularly intense emotions, behaviors, and performance concerns loom large, this is a seductive and dangerous effect of drug use. However, these dangers also apply to other phases of life, when other developmental challenges are encountered and need to be mastered.

Psychiatrists should address the emotional and mental health needs of substance abusers. Psychiatrists should educate themselves and the public about how substance abuse affects the psychological and social functioning of individuals and their families and should take active roles in developing and establishing guidelines and protocols for the assessment and management of substance abuse problems. Psychiatrists should provide the public with information on the hazards of substance abuse through the media, public education campaigns, and contacts with other care providers and professional associations. Psychiatrists should take the initiative in developing guidelines and procedures for quality assurance and assessment of treatment outcome for substance abuse treatment programs. Finally, psychiatrists, through the American Psychiatric Association, should exercise an ongoing leadership role to assure nondiscriminatory reimbursement practices for substance abuse treatment services.

Each psychiatrist has a responsibility to understand and learn about substances of abuse; their psychoactive, toxic, and withdrawal effects; and how they interact with human emotions and behavior. Practicing psychiatrists must routinely obtain drug and alcohol histories, focusing not only on duration, amounts, and patterns of use but also on the effects that patients seek and obtain from the drugs they choose. Similarly, family histories of drug use and misuse patterns also should be obtained routinely. Psychiatrists should routinely consider whether their patients with psychiatric conditions suffer from concomitant substance abuse disorders and whether patients presenting with substance abuse disorders also might be suffering from coexistent treatable psychiatric problems. Psychiatrists should be cognizant of the life-threatening aspects of substance abuse as background for emphasizing the importance and necessity of obtaining control and abstinence at the onset of treatment. Accordingly, psychiatrists must learn how to use appropriate hospital and other residential treatment, support groups (e.g., Alcoholics Anonymous and Narcotics Anonymous), pharmacological treatment, and psychotherapeutic modalities (33).

Psychiatrists involved in the treatment of children and youth presenting with behavioral and emotional problems should be alert to the possibility that drug use may be a contributing factor. Close cooperation between psychiatrists, primary care providers, parents, and educators is needed to overcome the serious problems of alcohol and other drug abuse among our youth.

Finally, psychiatric practitioners are well suited to work with primary care providers in assessing and managing substance abuse patients in both outpatient and inpatient settings. They also are able to work with and interface with nonmedical caregivers, especially in consulting with self-help programs and drug counselors and helping them appreciate the mental health needs and psychiatric disabilities of their clients. The psychiatrist has a substantial contribution to offer in the management of the substance abuser. The psychiatrist can provide a dynamic understanding of the patient and can plan individualized multidisciplinary treatment and its implementation. It is the responsibility of the psychiatrist to emphasize the danger of drug use. To adopt a more neutral stance toward drug use by youth and refrain from warning of the dangers to mental health is to fail to fulfill an important public health responsibility of our profession.

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ALASKA STATE LEGISLATURE
HOUSE OF REPRESENTATIVES
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April 15, 1983

MEMORANDUM

TO: Representative Ramona Barnes

FROM: Betty Barton BB
Research Staff

RE: Driving Under the Influence of Drugs
Research Request No. 83-120

You requested information regarding procedures and methods that can be used "in the field" to test individuals driving under the influence of drugs other than alcohol. You also asked that we research the legal implications of such tests.

To respond to your questions, we contacted Mr. Joseph Gormley, of the International Association of the Chiefs of Police, Dr. Kurt Dubowski, a national authority on toxicology at the University of Oklahoma, and Mr. Robert Reeder, an expert on DWI law at Northwestern University's Traffic Institute. Within Alaska, we spoke with Gayle Horetski, in the Criminal Division of the Department of Law, Mr. Charles Smith, who administers the Alaska Highway Safety Program, and Major Mike Korhonen, with the Alaska State Troopers.

Based from our conversations with these individuals, we have found that although there is substantial research in progress pertaining to drugs and driving, no methods have been established for on-site, roadside chemical testing of drug intoxications. Further, forensic scientists project that technology of this nature will not be developed for a number of years. Qualitative and quantitative testing of intoxicating substances other than alcohol is a complex issue that is the subject of continuing research. Consequently, even laboratory-based chemical analysis pertaining to the effects of intoxicating substances other than alcohol is in its developing stages.

Unlike alcoholic beverages which all share a common ingredient, ethyl alcohol, other drugs have varied chemical properties that make them difficult to identify and isolate. As a result, standardized measures of these types of controlled substances are difficult to develop as is the development of any drug equivalencies for "blood alcohol concentrations."[1]

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[1] Blood alcohol concentration, often referred to as BAC, is the standard measurement of impairment. It is generally accepted that a BAC of .10 percent is the level where most individuals become impaired by the intoxicating effects of a substance. A few states, however, have set BAC levels of .08 percent.

Besides the absence of adequate qualitative and quantitative data, forensic scientists lack sufficient experiential research regarding drivers who are under the influence of drugs. Oklahoma, for example, is one of four states that is authorized to conduct experiments on the effects of drugs on human subjects. However, all of the testing occurs in laboratory settings, which can alter the outcome of experiments. The measured effects that drugs would have on a person's decision-making abilities while in a secure, laboratory setting would be much different than they would be, say, for a drugged driver who is being pursued by police. Consequently, while this type of laboratory research is significant, it is of limited value.

Chemical analysis of drugs also can be very costly. Unlike alcohol, where chemical tests can be conducted with relatively inexpensive and portable breathalyzer equipment, the presence of drugs in an individual's blood stream can only be detected by chemical analysis of blood plasma or, in some cases, urine.[2] Equipment for this type of analysis costs between $100,000 and $200,000. Additional expenditures, of course, are incurred from laboratory fees; because of the expertise involved in this type of testing, analysis is often done in special laboratories.

In light of these factors, according to Dr. Kurt Dubowski, forensic methods are rarely used in court as the basis for DWI charges pertaining to drugs. Instead, prosecuting attorneys typically rely on several key issues in developing their cases:

- the officer's probable cause for arrest;
- the demonstrated indication of the driver's impairment;
- the chemical test results that indicate the absence of sufficient alcohol concentration in an individual's system to have caused impairment; and
- the presence or evidence of drugs within the defendant's motor vehicle at the time of the arrest.

In Alaska, DWI cases pertaining to drug intoxication currently represent a very small percentage of the court's caseload. Gayle Horetski commented that this is partially due to the fact that the State has placed greater emphasis on improving its capabilities in alcohol-related cases. However, Ms. Horetski added that the drug-impaired driver is harder for officers to

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[2] Dr. Dubowski noted that urine anlysis is limited because it is not possible to determine whether there was a sufficient concentration of the drug at the time of formal charges.

detect unless there are visible signs of impairment. Ms. Horetski believes that the State's abilities to apprehend and convict drivers who are under the influence of drugs would improve if the technology existed for roadside analysis.

The Alaska Department of Public Safety currently has two gas chromatographs, which can be used for qualitative and quantitative analysis of certain drugs. However, according to Charles Smith, the equipment was purchased and is used primarily to test the alcohol levels of individuals who have died in motor vehicle accidents. According to Major Korhonen, drug testing is not currently emphasized within the Department because generally chemical tests in Alaska cases indicate the presence of alcohol. The costs that would result from additional laboratory testing to determine whether other drugs were also present is viewed to be an unessential added expense.[3]

In light of the limited technology in drug testing, state governments have considered other methods as a means of improving capabilities for enforcement of highway safety laws. In several states, including Maryland and New York, roadblock or checkpoint programs have been established as a means of checking for drunk or drugged drivers as well as other offenders. Officers briefly question drivers and look for symptoms such as slurred speech or indications of blurred vision.

In Westchester County, New York, local police recently set up a roadblock on a parkway for eight hours on a Friday night and early Saturday morning. Three-thousand-two-hundred motor vehicles passed through the checkpoint; 95 drivers were detained on suspicion of DWI. Of these, twelve were arrested, one of whom was charged with driving while impaired by drugs.

Not only can this approach potentially increase the police's abilities to approach impaired drivers, but also can help to give highway safety officers a more visible presence. Westchester County's Deputy Commissioner of Public Safety commented that checkpoints assist in conveying "a message that we're going to be out in full force from time to time; so if you're going to drink, don't drive."[4] According to some professional opinions,

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[3] Charles Smith added that excessive alcoholic consumption among Alaska's driving population appears to be a larger problem than drug intoxication. According to Mr. Smith, between April 1977 and March 1978, the Municipality of Anchorage Police Department administered involuntary blood tests on individuals who had refused breathalyzer examinations. During this period, 254 persons were administered tests. Of these, the average blood alcohol content was .26 percent and 35 cases had alcohol levels of .300 or higher. While some these individuals may have been under the combined influence of drugs and alcohol, in only two cases were impaired conditions solely attributed to drug intoxication.

the impact that this type of message may have on the drinking driver is significant. In recent testimony presented before the Alaska Senate State Affairs Committee, Dr. Laurence Ross, a national authority on the deterrent effect of DWI penalties, stated that highway safety laws, regardless of the level of penalty imposed, tend to lose their effectiveness as a preventive measure because most people recognize that the likelihood of their being caught is low. However, if enforcement capabilities measurably increase, individuals may weigh the risks of apprehension more seriously.

While the checkpoint method does appear to offer some promise in terms of enforcement and prevention, public support for this type of program is often limited. The courts have ruled that roadblocks do not violate constitutional protections against search and seizure as long as all vehicles are checked and certain measures are followed by the police.[5] Nonetheless, this type of program is perceived by some as placing an undue hardship on lawabiding drivers.

We hope this information has assisted you. If you would like us to provide you with additional information regarding the checkpoint system or other enforcement methods, please let us know.

BB/bb

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4 Lena Williams, "Three Thousand Two Hundred Cars Halted in a Check on Drunken Drivers," New York Times, March 27, 1983, P. 1.

5 Delaware v. Prouse Supreme Court, 47 US Law Week 4323 1979. Guidelines for police are established in State v. Hillesheim 291 NW 2nd 314, Iowa Supreme Court, 1980.

Andrew P. Mason,[1] *B.S. and Arthur J. McBay,*[2] *Ph.D., DABFT*

Cannabis: Pharmacology and Interpretation of Effects

REFERENCE: Mason, A. P. and McBay, A. J., "*Cannabis:* Pharmacology and Interpretation of Effects," *Journal of Forensic Sciences*, JFSCA, Vol. 30, No. 3, July 1985, pp. 615-631.

ABSTRACT: A selective introductory review of the *Cannabis* literature is presented. Subjects reviewed include the relative psychoactivities of *Cannabis* constituents, the disposition and distribution of THC and its metabolites, the relative psychoactivities of THC metabolites, and the use of cannabinoid concentrations in physiological fluids in interpretations of the significance of *Cannabis*-induced effects. The pharmacology of cannabinoids in humans is emphasized.

KEYWORDS: toxicology, marijuana

Marijuana and other *Cannabis* products are used by a significant proportion of people in our society. When smoked or ingested, these substances produce perceptual, cognitive, affective, and behavioral changes in the user. The *Cannabis* constituent that is responsible for the production of the majority of this psychoactive response is (−)-trans-delta-9-tetrahydrocannabinol or THC [*1*]. There has been great concern that the psychoactive response experienced by marijuana users has a detrimental effect on the performance of complex coordinated psychomotor skills. Naturally, the impairment of performance would be of greatest concern in those individuals with direct responsibility for the health and safety of others and in individuals whose impaired actions could potentially be dangerous to themselves or to others near them. Motor vehicle operators, pilots, air traffic controllers, law enforcement or emergency aid personnel, military personnel, and industrial workers are all good examples of people whose impaired performance could potentially be dangerous.

During the last decade, remarkable progress has been made in the ability to analyze biological samples for cannabinoid compounds. This ability was developed as a prerequisite for, and was instrumental in the acquisition of data concerning the pharmacology, pharmacokinetics, metabolism, behavioral effects, and toxicology of *Cannabis* constituents. These analytical methods and the knowledge derived from their use in basic research on cannabinoids are now being used in attempts to interpret the significances of cannabinoid concentrations found in forensic science specimens. The frequency with which these analytical methods are used and the frequency with which forensic scientists are required to provide estimates of the probable significances of *Cannabis*-induced effects or the degree of impairment experienced by a *Cannabis* user based on cannabinoid concentrations in biological specimens are both expected to increase. Use of these methods and in-

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Andrew P. Mason,[1] *B.S. and Arthur J. McBay,*[2] *Ph.D.; D.A.B.F.T.*

Ethanol, Marijuana, and Other Drug Use in 600 Drivers Killed in Single-Vehicle Crashes in North Carolina, 1978–1981

REFERENCE: Mason, A. P. and McBay, A. J., "Ethanol, Marijuana, and Other Drug Use in 600 Drivers Killed in Single-Vehicle Crashes in North Carolina, 1978–1981," *Journal of Forensic Sciences*, JFSCA, Vol. 29, No. 4, Oct. 1984, pp. 987–1026.

ABSTRACT: Although the use of ethanol, marijuana, and other drugs may be detrimental to driving safety, this has been established by direct epidemiological evidence only for ethanol. In this study, the incidences of detection of ethanol (and other volatile substances), delta-9-tetrahydrocannabinol (THC), barbiturates, cocaine and benzoylecgonine, opiates, and phencyclidine were determined in an inclusive population of 600 verified single-vehicle operator fatalities that occurred in North Carolina in 1978 to 1981. The incidence of detection of amphetamines and methaqualone were determined for drivers accepted for study during the first two years ($n = 340$) and the last year ($n = 260$), respectively. Blood concentrations of 11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid (9-carboxy-THC) were determined in THC positive drivers. EMIT cannabinoid assays were performed on blood specimens from all drivers accepted for study during the third year, and the feasibility of using the EMIT cannabinoid assay as a screening method for cannabinoids in forensic blood specimens was investigated. The incidence of detection of ethanol (79.3%) was far greater than the incidences determined for THC (7.8%), methaqualone (6.2%), and barbiturates (3.0%). Other drugs were detected rarely, or were not detected. Blood ethanol concentrations (BECs) were usually high; 85.5% of the drivers whose bloods contained ethanol and 67.8% of all drivers had BECs greater than or equal to 1.0 g/L. Drug concentrations were usually within or were below accepted therapeutic or active ranges. Only a small number of drivers could have been impaired by drugs, and most of them had high BECs. Multiple drug use (discounting ethanol) was comparatively rare. Ethanol was the only drug tested for that appears to have a significantly adverse effect on driving safety.

KEYWORDS: toxicology, motor vehicle accidents, alcohol, marijuana

It is accepted that ethanol use has a detrimental effect on the performance of drivers because it impairs sensory input and perception, judgement and cognition, motor control, and their integration and coordination. It is also known that the use of ethanol is strongly associated with traffic fatalities. Nationally, between 40 and 55% of all drivers involved in fatal crashes have blood ethanol concentrations (BECs) greater than or equal to 1.0 g/L [1],[3] the

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[3]1.0 g/L = 100 mg/dL = 100 mg% = 0.10%.

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Cover: A young marijuana plant glistens with crystals rich in psychoactive delta-9-tetrahydrocannabinol. Although marijuana has been used for millennia as a medicinal, the U.S. government says it has no accepted medical value. Proponents of pot-by-prescription are taking their case to court. (Photo: Ed Rosenthal)

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Letters

Hail and Farewell

As a poet delighted not only by the discoveries of physics but also by its serendipitous and colorful nomenclature, I have been surprised by the reticence of those probing for new fundamental forces to name them.

As I was reading "Evidence for New Force — May Be No. 6" (SN: 12/19&26/87, p.388), Hail and Farewell struck me as apt designations: the former for the attractive Force 6, apparently dominant from a few feet to hundreds of yards over the repulsive Force 5, its influence more circumscribed to a range approximating distances habitual for conversation. The gladiatorial allusion, too, has much to recommend it, given their contention for supremacy, however transitory.

Less abstract than the equally anthropocentric Beauty and Charm, Hail and Farewell have the further advantages of the balance and tangential anthropomorphism of Sunrise and Sunset.

Daniel Zimmerman
Metuchen, N.J.

The chicken, or the egg?

Re your report on new research supporting the old Air Force myth that fighter pilots are more likely to sire daughters than sons ("What do you suppose B-forces make?" SN: 12/12/87, p.377): Is it possible that cause and effect are reversed here? Could it be that that type of occupation attracts a certain type of man, and that that type may in some way be more likely to sire daughters?

[illegible] Hellman
Leonia, N.J.

Some years ago, while employed at NASA at a randomly selected division, I surveyed all the bosses to determine the sex of their children. The result of my small survey showed that of 19 bosses contacted, 9 had all girls while only 3 had all boys, and the ratio of all the girls of the bosses to all the boys was over 2:1. This, of course, did not mean that being a boss made one have girls.

Since I assumed the rest of the employees had the then-prevailing average ratio of girls to boys (100:94), my conclusion was that girls gave their fathers a lot of self-esteem, which is a characteristic required not only to seek a boss's job but also to seek a fighter pilot's job. Thus there is a strong possibility that men become fighter pilots because of having more girls rather than the other way around.

[illegible]d characteristic I noticed is that [illegible] married males tend to sire children [illegible]one sex. Since fighter pilots must be [illegible]iant to cope with all the tin-soldier rules and regulations and safety precautions, any second or third children born during training or while on active duty would tend to be also girls.

A. P. Sabol
Lewisburg, N.C.

TAKE TWO PUFFS AND CALL ME IN THE MORNING

Proponents of marijuana's medical benefits take their case to court

By RICK WEISS

Once a month, Robert Randall strolls into his neighborhood pharmacy in Washington, D.C. He chats with the pharmacist while his prescription is filled, and a few minutes later walks out the door with a 30-day supply of the medicine he needs — 300 prerolled marijuana cigarettes.

Such has been Randall's routine for the past 10 years, ever since he won a court order that recognized his medical need to smoke marijuana. Marijuana lowers the pressure that builds up in his eyes as a result of his having glaucoma. He is the only glaucoma patient in the United States to have won such an order. But if he and others have their way — that is, if Federal Administrative Law Judge Francis Young Jr. rules in their favor later this year — thousands of patients may get easier access to the drug for a variety of ailments ranging from chemotherapy-induced nausea to spasticity.

Such a decision would be the climax of a tedious, decade-long battle by a coalition of groups convinced that pot's therapeutic potential has been unjustly ignored. "It's been like a play by Ionesco with footnotes by Kafka," Randall says of the unusual legal struggle. "It's been absurd, venal and bizarre."

Such surrealism is not a part of his everyday experience, Randall assures. Although he smokes eight to 10 "joints" per day, he says he developed a tolerance to marijuana's psychoactive effects many years ago. Meanwhile, he says, a "fixation" on marijuana as a drug of abuse has kept the Drug Enforcement Administration (DEA) from appreciating the drug's medical merits.

Marijuana (*Cannabis spp.*) is classified by the DEA as a "Schedule 1" drug — one that has "no currently accepted medical use as a treatment in the United States" and is considered unsafe even under medical supervision. A prescription version of delta-9-tetrahydrocannabinol (THC), the primary active ingredient in marijuana, is less tightly restricted and was approved by the Food and Drug Administration in 1985 as an antinausea agent for cancer patients. But its effectiveness is hotly disputed; many patients and physicians claim that purified THC is not nearly as effective as a puff of pot.

As part of a campaign to reverse what they believe is a political bias against marijuana, the Alliance for Cannabis Therapeutics and the National Organization for the Reform of Marijuana Laws, both based in Washington, D.C., have challenged the drug's Schedule 1 status. The groups contend that, at minimum, marijuana should be classified as a Schedule 2 drug — a status that would keep it illegal but would ease the restrictions on research into its medical applications. Although researchers can apply for permission to perform human trials with Schedule 1 drugs, few applications are ever granted. Proponents of reform say a schedule change would speed the recognition, acceptance and availability of marijuana as medicine.

In one of the final stages of the rescheduling challenge, completed earlier this month, court-ordered hearings were held in New Orleans, San Francisco and Washington, D.C. Closing briefs are now being prepared by attorneys on both sides and should be completed by May. After reviewing the briefs and scores of volumes of testimony, Judge Young is expected to make a recommendation to the chief administrator of the DEA before the end of the year.

But even then the battle may not be over. The DEA is not bound by the judge's recommendation, and in either case the DEA's decision can be appealed.

The case may get even more complicated because the DEA is expected within the next few weeks to announce its decision in a similar case involving MDMA — an illegal drug that some believe has potential as an adjunct to psychotherapy. Last year, after lengthy hearings, Judge Young recommended that the DEA drop MDMA from Schedule 1 to Schedule 3. Schedule 3 drugs are illegal to possess except with a DEA license, but are acknowledged as having medical potential.

Illustration of Cannabis *from the works of Dioscorides, a first-century physician.*

The DEA ignored that recommendation, kept MDMA in Schedule 1 and was subsequently sued by one of the drug's proponents, Harvard psychiatry professor Lester Grinspoon. Grinspoon claimed that Schedule 1 was an overly restrictive status for a drug that had, he said, "been taken in a therapeutic setting by thousands of people, apparently with few complications." Grinspoon won his case in the U.S. Court of Appeals and the DEA is now reconsidering its stand. Among other things, the case is forcing the DEA to redefine some of its schedule definitions, which may have an impact on the marijuana decision.

A central issue in both cases is the DEA's definition of the "no accepted medical use" clause that relegates a drug to Schedule 1 status.

"The original definition was that in order for a drug to have an accepted medical use it had to be lawfully marketed in the United States under the Food, Drug and Cosmetic Act," says Charlotte Mapes, a DEA attorney. "What the court said [in the MDMA case] is that the administrator cannot rely exclusively on lack of marketing approval as a condition

for no accepted medical use."

Indeed, proponents of rescheduling say a simple lack of FDA approval hardly counterbalances marijuana's long record as a therapeutic agent. Chinese herbal catalogues have listed the plant as an aid to digestion for thousands of years, and as many as 30 marijuana preparations were listed in the *U.S. Pharmacopoeia* as recently as 1937. "It appears that every society that encounters marijuana acknowledges its therapeutic properties," says Alice O'Leary, a cofounder of the Alliance for Cannabis Therapeutics.

In the United States, researchers have been most interested in marijuana's usefulness as an anti-emetic for cancer patients suffering from chemotherapy-induced nausea. Several FDA-approved Investigational New Drug studies have demonstrated its value as such, and in some cases its advantages over THC pills.

"Never mind the absurdity of giving an oral medicine to someone who is throwing up all the time," Randall says of the FDA-approved pills. The tablets have negative side effects of their own, he says, adding that in one study "50 percent of the patients said they'd rather throw up."

According to testimony by John Morgan, a professor of medicine at City College of New York, "Marijuana's use in reducing nausea appears to be quite widespread and generally, albeit discretely, accepted within the oncologic community and among patients. Physicians confront profoundly difficult ethical, legal and moral questions because of marijuana's inappropriate classification."

Marijuana may also be useful for reducing some of the neurological complications inherent to multiple sclerosis, Parkinson's disease and paraplegia. Preliminary studies show that it seems to work quickly and effectively against severe episodes of muscle spasticity, according to testimony by Denis Petro, director of clinical research at Fidia Pharmaceuticals, a major Italian drug company that specializes in neurological therapeutics. Other studies have suggested that marijuana may be useful in the treatment of asthma, anxiety and eating disorders and for improving the quality of life in terminally ill patients.

The DEA says that most such studies have been poorly designed, are fraught with subjective errors and represent little more than collections of anecdotal evidence. Proponents of rescheduling concede that few case-controlled, double-blind studies have been performed on marijuana in its natural form. However, they add, that shortage exists in large part because it is so difficult to get research approval for Schedule 1 drugs.

In addition to the controversy over marijuana's "accepted medical use," there is considerable debate over the issue of its safety and how to apply the "lack of accepted safety" clause in the Schedule 1 definition.

"Marijuana has not killed anyone in 5,000 years," Randall says flatly. But the DEA is not convinced.

"Our perception of safety is different from theirs," DEA attorney Mapes told SCIENCE NEWS. "They're saying it's safe because nobody's died. We're saying that it has to be shown to be safe."

Fitz Hugh Ludlow Memorial Library

Broadsides such as this one characterized the campaign against marijuana in the 1930s and 1940s.

Research has suggested that marijuana can suppress the body's immune system (SN: 7/18/87, p.46), and deficits in short-term memory among users have been reported. According to the most thorough U.S. examination of the health-related effects of marijuana, a 15-month study by the Institute of Medicine of the National Academy of Sciences published in 1982, "marijuana impairs motor coordination and affects tracking ability and sensory and perceptual functions important for safe driving and the operation of other machines." However, the report adds, "we have no convincing evidence thus far of any effects persisting in human beings after cessation of drug use. . . ."

Perhaps most significantly, marijuana has a variety of psychological effects. Depending on the individual, the dose and the setting, it has been known to produce everything from sensory enhancement and euphoria to intense anxiety and paranoia.

"Most doctors do not want to give a psychoactive drug to someone when they can give a nonpsychoactive one that is more effective," says Madeleine Shirley, a DEA attorney working with Mapes in the current case. With so many new drugs being created, she says, "Frankly, there's not a lot of interest in marijuana any more."

The debate goes on. The government says marijuana is notoriously variable in potency, containing dozens of active ingredients in unpredictable concentrations. Randall counters that the marijuana he buys at his local pharmacy – grown on a government pot plantation in Oxford, Miss. – is routinely blended to a uniform potency, tested and certified by the National Institute of Drug Abuse.

In addition, the DEA claims that smoking is a poor way to get a measured dose of a drug, since depth of inhalation and the length of time before exhaling can affect the amount of drug that gets into the bloodstream. But other experts note that inhalation has many benefits as a means of drug delivery, providing rapid absorption and avoiding gastric complications (see related story, p.120).

Given the lack of scientific consensus on such issues, the discussion ultimately turns to politics. Statements from the Alliance for Cannabis Therapeutics clearly suggest that the government's hard line on marijuana is motivated by political considerations.

But if Alliance members believe there is a federal cabal aimed at nipping marijuana research in the bud, federal officials are equally suspicious of the reformers' motivations.

"I think this whole thing has got more to it than meets the eye," says Paul Leber, director of the FDA's division of neurological and pharmacological drug products. "I'm not interested in suppressing a drug just because somebody says it's bad. But I do have to ask myself, 'Is it likely to benefit the patient? Or is this being used by someone in an unscrupulous attempt to foster some nonsense?' "

Proponents of reform note that pot would still be illegal and tightly controlled under Schedule 2 or 3. Rescheduling would simply encourage much-needed research, they say, and might open the door to "compassionate use." Under its compassionate use rule, the FDA allows unapproved drugs to be prescribed when effective alternatives are not available. In addition, if the number of studies begins to increase, hundreds of patients might gain long-sought access to the drug as subjects in licensed studies.

In any case, neither of the parties to the marijuana dispute foresees immediate or widespread availability of the drug. Even if the current rescheduling effort is successful, the government may still be slow to approve new research and to appropriately scale up its marijuana accounting and distribution mechanisms. Because of marijuana's potential for abuse, says the DEA, it would be important to keep careful inventories of the drug.

Happily, sighs Shirley, drug approval and distribution are not the DEA's responsibilities. "We just decide what schedule it's in. Getting the drug to the people is the FDA's problem."

ENCLOSED ARTICLES ON THC

Dear Mr. Nordlund,

I have enclosed selected articles on the toxic effects of Marijuana. There are at probably 2-3000 articles on the toxic effects of this drug since the Alaska Supreme Court decision.These I selected are from refereed journals and have been authenicated prior to publication. I want to emphasize the effects on the immune system and birth defects. Also the records of cardiac deaths from Marijuana smoking are significantly relevant. The birth defects and immune system are problems that affect the whole of society and surpass the rights of the individual to get stoned at home and get stoned, while damaging his or her brain and risking lung cancer. The society cannot tolerate an agent that is producing birth defects. Driving under the influence of THC is plain foolish.

Articles:

1. Marijuana effects on Immunity 1986
2. The new Immunomodulator 1987 Nicotine and Marijuana
3. Developmental effects of cannabis 1986
4. Marijuana Use by pregnant women 1981
5. Cannabinoid Exposure: Effects on Development 1986
6. Induction of sister-chromatic exchanges in marijuana-cannabis 1981
7. Effect of Marijuana use in pregnancy on fetal growth,1986
8. Maternal Marijuana Use and neonatal Outcome 1985
9. Perinatal Cannabinoid Exposure 1985
10. The effects of Alcohol , Marijuana and the combination on driving about
11. The effects of Marijuana and alcohol on actual driving performance.
12. Epidemiology of road accidents involving Marijuana
13. The clinical syndrome of marijuana dependence 1986
14. Effects of Long term Marijuana use
15. The addictive potential of cannabis, 1980
16. Marijuana 1987
17. Health aspects of cannabis 1982
18. Marijuana: an overview 1987
19. Marijuana's effects on Human Cognitive functions etc 1986
20. The chronic cerebral effects of cannabis 1986
21. Pulmonary hazard of smoking marijuana 1988
22. Fatal coronary artery thrombosis associated with cannabis smoking 1984
23. Myocardial infarction during marijuana smoking in a young female, 1985

You can see from these dates that I am more current with my information than some of the opponents of the bill who testified. It is clear that the witness selection was biased. Please try to correct that error by making copies of this literature available to the committee members.

Sincerely yours,

Jeanne F. Stein, M.D.

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MARIJUANA EFFECTS ON IMMUNITY: SUPPRESSION OF HUMAN NATURAL KILLER CELL ACTIVITY BY DELTA-9-TETRAHYDROCANNABINOL

STEVEN C. SPECTER, THOMAS W. KLEIN, CATHERINE NEWTON, MARLENE MONDRAGON, RAYMOND WIDEN and HERMAN FRIEDMAN

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(*Recieved* 18 *November* 1985 *and in final form* 17 *February* 1986)

Abstract—Delta-9-tetrahydrocannabinol (THC), the major psychoactive component of marijuana, was tested for its ability to modulate human natural killer (NK) cell function. THC was toxic for peripheral blood lymphocytes at 20 μg/ml but not at 10 μg/ml or less. This component of marijuana also was inhibitory for NK activity against K562, a human tumor cell line at concentrations down to 5 μg/ml when pre-incubated with the effector cells. Suppression of NK function was dependent upon the concentration of THC and the length of time of pre-incubation but was independent of the ratio of effector to target cells. Prostaglandins were not involved in suppression of NK activity.

The psychoactive effects of marijuana, as well as some of the physiological and biochemical effects of this drug, are well documented. There is considerably less information, however, concerning the ability of marijuana and its components, such as delta-9-tetrahydrocannabinol (THC), to influence various aspects of the immune system. Acute or chronic exposure of human or mouse peripheral blood leukocytes (PBL) to marijuana have yielded equivocal results when these cells were exposed to specific (antigens) or nonspecific (plant mitogens) stimuli (Matsuyama & Jarvik, 1977; Munson & Fehr, 1983; White, Brin & Janicki, 1975). A number of reports have appeared indicating that marijuana has detrimental effects on immunity, suppressing antibody responses (Levy, Farrar, Harris, Dewey & Munson, 1975; Levy & Heppner, 1981; Rosenkrantz, Miller & Esber, 1975), cell-mediated immune responses and macrophage function (Huber, Pochay, Pereira, Shea, Hinds, First & Sornberger, 1980; Levy & Heppner, 1979; Nahas, Suciu-Foca, Armand & Morishima, 1974), but there are a number of other reports indicating no effects of THC on these responses (Lau, Tubergen, Barr, Domino, Benowitz & Jones, 1976; Peterson, Graham & Lemberger, 1976; Rachelefsky, Opelz, Mickey, Lessin, Kiuchi, Silverstein & Stiehm, 1976).

Natural killer (NK) cells, which are recognized as being important in host defenses against tumor cells and microbial infections, have not been examined for their susceptibility to modulation by THC. These cells are considered a first line of defense against infections and often inhibit tumors before they can become well established. NK cell function has been demonstrated to be influenced by a variety of substances which inhibit or enhance imunologic responsiveness (Brunda, Herberman & Holden, 1980; Droller, Schneider & Perlman, 1978; Henney, Kuribayashi, Kern & Gillis, 1981; Oehler, Lindsay, Nunn, Holden & Herberman, 1978). Prostaglandins and corticosteroids clearly inhibit NK function, while interferons and interleukins enhance activity. Considering the importance of NK cells in host resistance, it was of interest to examine the effects, if any, of THC on NK activity. The results of the present study indicate that THC suppresses human NK cell activity *in vitro*.

EXPERIMENTAL PROCEDURES

Blood donors

Healthy donors who denied a history of marijuana use served as a source of PBL for these studies. Thirty ml blood were collected by venepuncture and

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Table 1. Cytotoxicity of THC over a 3 h time period for human peripheral blood leukocytes

Addition to cultures*	Mean percent cytotoxicity after treatment for† 30 min	60 min	120 min	180 min
Medium	4.0‡	6.7	10.5	13.9
DMSO (0.1%§)	4.2	8.4	9.7	16.5
THC (μg/ml)				
20	21.9	36.6	40.5	51.4
10	4.3	7.0	8.5	14.6
5	3.7	5.8	7.1	11.3
2	4.0	6.5	6.6	15.3
1	3.9	6.0	7.6	—

*Cells incubated in THC at indicated concentration, washed twice in medium to remove excess THC and tested for cytotoxicity at the times indicated.

†Mean percent cytotoxicity = $\frac{\text{counts/min experimental}}{\text{counts/min maximum release}} \times 100$

measured by ^{51}Cr release from three separate cultures using 2×10^4 cells/well. Variation between replicates was always less than 5% of the counts/min. Representative experiment from one patient.

§Concentration of DMSO equivalent to that used to dilute THC to 20 μg/ml.

Table 2. Suppression of natural killer cell activity by THC as function of time of exposure

Addition to cultures	Percent specific cytotoxicity after incubation with THC for* :8 h	4 h	3 h	2 h	1 h	0 h
Control (medium)	31.0	43.0	32.5	57.3	48.5	54.0
DMSO (0.1%)†	36.0	40.6	33.0	47.5	46.4	39.7
	(116.3)‡	(94.4)	(101.5)	(82.9)	(95.7)	(73.5)
THC (20 μg)	—	0.6	0.5	4.0	4.3	55.3
		(1.4)	(1.5)	(7.0)	(8.9)	(102.4)
(10 μg)	0.6	15.6	8.6	26.4	28.17	47.4
	(1.8)	(36.3)	(26.5)	(46.1)	(59.2)	(87.8)
(1 μg)	—	41.7	35.5	52.3	45.2	50.3
		(97.0)	(109.2)	(91.3)	(93.2)	(93.1)

*Cells incubated in THC at times indicated, washed twice in medium to remove excess THC and tested in 4 h NK assay against K562 target cells.

†Concentration of DMSO equivalent to that used to dilute THC to 20 μg/ml.

‡Percent of control.

PBLs separated by Ficoll–Hypaque centrifugation for use in the NK assay. Cells were adjusted to 1.1×10^6/ml RPMI 1640 medium supplemented with 10% fetal bovine serum and antibiotics and distributed into 12 × 75 mm plastic tubes (0.9 ml per tube).

THC treatment

Tetrahydrocannabinol (THC) was obtained from the National Institute on Drug Abuse, Research Technology Branch, Rockville, MD and reconstituted at 20 mg per ml in dimethyl sulfoxide (DMSO). This stock was diluted in RPMI 1640 medium immediately prior to addition to cultures. DMSO was also diluted in a similar RPMI 1640 and included as controls. THC was added to tubes in 0.1 ml amounts to yield final concentrations of 20, 10, 5, 2 and 1 μg/ml. Control cultures were incubated in either medium only or DMSO diluted in medium to a final concentration of 0.1%. Cells were incubated with THC for various times, ranging from 1 to 18 h at 37°C, in a humified atmosphere of 5% CO_2, 95%

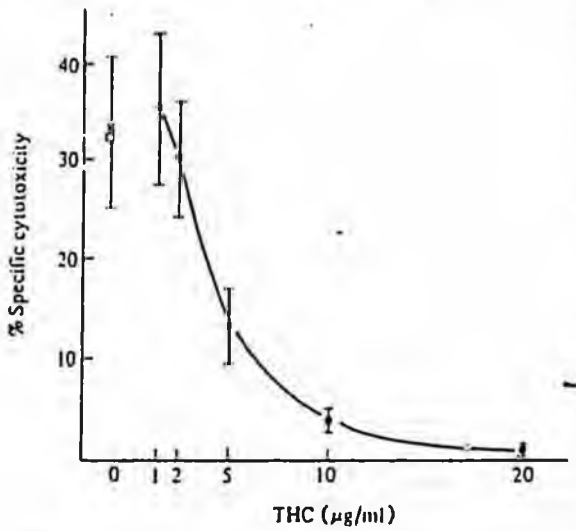

Fig. 1. Effect of THC on human natural killer cell activity. Effector cells were incubated in increasing concentration of THC (●), DMSO (○) or RPMI 1640 medium (X) for 3 h, then washed and incubated with 5 × 10^3 target cells at a ratio 50:1. Each point represents the mean of seven experiments ± S.E.M.

air. After incubation, cells were suspended in 5 ml RPMI 1640 to dilute the THC; then centrifuged at 500 *g* for 10 min at 4°C. The supernatant fluid was removed, the pellet was resuspended in 5 ml RPMI 1640 and centrifuged again to remove unbound THC. Supernatant fluid was again removed and cells were resuspended in RPMI 1640 and adjusted to 2.5 × 10^6 viable cells/ml, as assessed by trypan blue dye exclusion.

Natural killer cell assay

Target cells were the NK sensitive K562 erythroleukemia cell line which is commonly used to assess human NK activity. Cells were labelled with chromium-51 (Na_2 $^{51}CrO_4$) as described previously (Moody, Specter, Bendinelli & Friedman, 1984). Cells were washed free of execess chromium and adjusted to 5 × 10^4/ml RPMI 1640. 0.1 ml was added to wells of a 96 well round bottom microtiter plate for the assay. Effector cells were added to wells in 0.1 ml medium so that 2.5 × 10^6 cells/ml yielded an effector: target ratio of 50:1. The microtiter plate received also target cells only or target cells plus 0.1 ml medium. The former were used to measure maximum release and the latter spontaneous release. The plates were centrifuged at 250 g for 2 min and then incubated for 4 h at 37°C. Maximum release was attained by lysing target cells with 0.1 ml 10% sodium dodecyl sulfate, mixing well and removing 0.1 ml of the mixture. The remaining cells in the plates were then centrifuged at 500 g for 10 min and 0.1 ml supernatant fluid removed and placed in 7 × 35 mm glass tubes for counting in a gamma counter (United Technologies, Downers Grove, IL). Specific cytotoxicity was calculated using the formula

$$\% \text{ specific cytotoxicity} = \frac{\text{experimental release} - \text{spontaneous release}}{\text{maximum release} - \text{spontaneous release}}$$

Toxicity of the THC for lymphocytes was measured using lymphocytes labelled with ^{51}Cr. As can be seen in Table 1, when cultured for up to 3 h in THC lymphocytes were killed by the 20 μg/ml dose but not lower doses ranging from 10 to 1 μg/ml. The DMSO control was not substantially different from leukocytes incubated in culture medium alone. Visual counting for viability using trypan blue dye exclusion confirmed these results. On the basis of these findings cells were always readjusted after incubation in THC so that cell counts reflected the number of viable cells at the time of initiation of the NK assay.

RESULTS

Pretreatment of leukocytes with THC in doses ranging from 1 to 20 μg/ml for up to 18 h revealed that there was a direct relationship between the time of exposure and the resulting suppression of NK activity (Table 2). Virtually all NK activity was lost upon exposure to 20 μg/ml THC for 3 h and 10 μg/ml for 18 h. Incubation for 1 or 2 h resulted in proportionately less suppression, whereas addition of THC directly into the 4 h NK assay (time 0) had no appreciable effect even at 20 μg/ml.

Additional experiments were performed using a pre-incubation of 3 h in THC, then removal of the drug for the NK assay. As can be seen in Fig. 1, as little at 5 μg/ml THC had a marked suppressive effect on NK function. However, 2 or 1 μg/ml had no noticeable effect. Suppression was highly dose dependent with a stronger effect noted as the dose increased to 20 μg/ml. The NK depressive effects of THC were observed over a broad range of effector to target cell ratios. However, examination of percent reduction of cytotoxicity vs positive controls revealed that a consistent suppressive effect of THC at 10 and 20 μg/ml is achieved at all E:T ratios (Table 3).

Table 3. Effect of THC on natural killer cell activity at difference effector to target cell ratios

Additions to cultures	Percent specific cytoxicity 50:1*	25:1	12:1	6:1	3:1
Control (medium)	49.1†	38.8	22.2	12.1	7.0
DMSO (0.1%)	65.8	47.1	31.2	17.3	10.3
	(134.0)‡	(121.4)	(140.5)	(144.2)	(147.1)
THC (20 μg)	0.9	0.0	0.8	0.2	0.0
	(1.8)	(0)	(3.6)	(0.2)	(0)
(10 μg)	9.8	5.0	3.4	2.8	1.3
	(20.0)	(12.9)	(15.3)	(12.2)	(18.6)
(1 μg)	53.0	38.4	23.9	12.8	7.9
	(107.9)	(99.0)	(107.7)	(106.7)	(112.9)

*Effector:target.
†Mean of two individuals.
‡Percent of control.

DISCUSSION

The data presented demonstrate that delta 9-THC, when added to human peripheral blood leukocytes, decreases their ability to function in the 4 h NK cell cytotoxicity assay. This activity was dependent upon the length of time the effector cells were exposed to THC and the dose of THC. Killing was independent of the effector to target cell ratio over a wide range. Although THC was cytotoxic for PBL at a dose of 20 μg/ml, this cannot be the explanation for the suppressive effects of the drug since cells were readjusted at initiation of the NK assays. Lower doses, i.e. 10 μg/ml and 5 μg/ml, were also highly suppressive for NK cell function but did not have any effect on effector cell viability.

The mechanism by which THC is capable of suppressing NK activity is as yet unclear. Preliminary experiments to delineate this mechanism have shown that indomethacin has no effect in reversing this suppression (unpublished data). Thus suppression cannot be attributed to induction of prostaglandins, since indomethacin is known to inhibit prostaglandin synthesis (Brunda *et al.*, 1980). This is an important observation since prostaglandins have been shown to suppress NK function in other systems (Brunda *et al.*, 1980; Droller *et al.*, 1978; Kendall & Targan, 1980). It is also possible that the lipophilic nature of THC results in an interference with ion channels in the NK cell membrane. Recently, a preliminary report has appeared (Schlichter & Sidell, 1985) demonstrating a suppression of NK killing by potassium and calcium channel blockers. This reduced NK activity in THC exposed PBL may be a highly significant observation since THC has been implicated, in experimental infection models, in enhancement of susceptibility to infection (Bradley, 1984; Juel-Jenson, 1972; Morahan, Klykken, Smith, Harris & Munson, 1979). Such enhanced susceptibility could be due to suppressed NK activity.

Interestingly, other psychoactive agents have recently been reported to alter NK cell function. Two separate reports indicate that either endorphins (Kay, Allen & Morley, 1984) or enkephalin (Faith, Liang, Mungo & Plotnikoff, 1984) can enhance NK activity. Conversely, morphine and "opioid stress" resulted in depression of NK cytotoxicity (Shavit, Lewis, Terman, Grale & Liebeskind, 1984). While these data do not allow any generalization about psychoactive agents and NK activity, they do lead to speculation about possible mechanisms for the immunomodulatory activities. Suppression of NK function could be generated indirectly by THC by stimulating the release of immunosuppressive hormones like adrenocoritcosteroids, which are known to inhibit NK activity (Cox, Holbrook, Grasso, Specter & Friedman, 1982; Hochman & Cudkowitz, 1979); or by inhibition of interferon synthesis. Morphine, for example is known to depress interferon levels (Hung, Lefkowitz & Geber, 1973). While the mechanism of THC induced suppression remains to be determined, the results generated by other psychoactive agents have yielded clues as to how this may be pursued.

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MINIREVIEW

IMMUNOMODULATION BY MORPHINE AND MARIJUANA

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Summary

The immunomodulatory effects of morphine and the active components of marijuana, particularly tetrahydrocannabinol, on various aspects of the host immune parameters include alterations in humoral, cell-mediated and innate immunity. Most studies have shown immunosuppressive effects due to use of these abused substances, although there are reports that they may not produce any deletrious effect and may even enhance some aspects of host immunity. They reduce resistance to cancer growth and microbial pathogens in animals.

Morphine and marijuana have profound effects on the immune parameters of their users. The adverse effects of morphine can lead to various immune dysfunctions including increased susceptibility to infections and neoplasms. Similarly, the widespread use of marijuana for recreational purposes have raised concerns about its' cardiac complications, psychomotor impairment, genetic hazards, psychopathological conditions and immune suppression (1). Ironically, delta-9-tetrahydrocannabinol (THC), the major psychoactive ingredient in marijuana has been shown to be an antiemetic drug in cancer patients. The combination of these factors has made THC an actively investigated drug. Human and animal studies have revealed a myriad of effects attributed to THC (2). This review summarizes studies that have been performed in man and animals to understand morphine and marijuana modulation of immune responses.

Morphine-Induced Immune Alterations in Man.

Several studies have drawn a parallelism between morphine abuse and immune inhibition. In vitro studies showed that polymorphonuclear cells (PMN) and monocytes from patients subjected to morphine treatment were severely depressed in their phagocytic and killing properties, as well as their ability to generate superoxide (3). Opiate addiction also caused alterations in the frequencies of T and null lymphocytes in human peripheral blood. A study by McDonough et al showed that as a result of opiate addiction there was a significant decrease in the number of T lymphocytes that form rosettes with sheep red blood cells (SRBC). This decrease was accompanied by a concurrent increase in the number of null cells. However, there was no significant change in the number of B lymphocytes. These alterations in T and null cell

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Table 1.. Summary of the effects of morphine or marijuana on various aspects of the immune system.

Immune Response	MORPHINE			MARIJUANA OR THC		
	Suppressed	Enhanced	Not Altered	Suppressed	Enhanced	Not Altered
Resistance to:						
C.albicans	10*			61		
L.monocytogenes						
K.pneumoniae	10					
Tumor	14					
Viral infections				60,61,62		
Phagocytosis	3,10,20			33,51,54		42
Phagocyte killing	3,20					
Superoxide generation	3,10,20					
Antibody levels				31,49,50		46
Primary antibody response	11			49,53,54		
Secondary antibody response				49		
Interferon levels	15,16			55,57,59		
Blastogenic response to:						
PHA	4			26,27		37,38,39
Con A	21,22			51		
LPS				51		
PWM				52		40
Lymphocyte frequencies:						
T cells	4	6		28,29,30		
Null cells	4	6				
NK cell activity	13,17	12		32,52,58		
Cellular immunity	18,19			39,49,50		36,41

*Numbers indicate reference(s) in which the observations were reported.

frequencies were reversed by treatment of the lymphocytes in naloxone, a morphine antagonist. This reversal was paralleled by an increase in the ability of these lymphocytes to be stimulated by phytohemagglutinin (PHA) (4). Subsequently, it was shown that the decrease in SRBC-rosetting was due to a morphine-induced depression of SRBC receptor levels on T cells (5). In contrast to the results of these studies, Bocchini et al showed that incubation of normal human lymphocytes in either morphine or naloxone caused an increase in the frequencies of these cells as well as their response to PHA stimulation (6).

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There is also convincing evidence of the presence of opioid receptors on various types of human immune cells. Wybran et al were the first to provide evidence of receptors specific for morphine on normal human T lymphocytes (7). This observation has been confirmed by other workers (4,8). Subsequently, the presence of opioid receptors have been demonstrated on human PMN and monocytes (9), and platelets (8). The presence of opioid receptors on immune cells may allow for modulation of specific immune functions in the presence of exogenous opiates.

Morphine-Induced Immune Alterations in Animals

Studies have been performed in animals to elucidate the mechanisms by which morphine affects the immune system. Morphine administration in mice caused a profound increase in susceptibility to bacterial and fungal infections. Various administration schedules were shown to potentiate infections due to Klebsiella pneumoniae and Candida albicans (10). The increased susceptibility was partly due to a decreased reticuloendothelial system activity as well as a reduction in the number of phagocytes and not due to a direct cytotoxic effect of the drug. A reduced capacity to produce superoxide was also observed. These observations are in agreement with altered disease resistance in man (3).

Chronic administration of morphine also inhibited the primary antibody response of mice to SRBC, and the spleen:body weight ratio. These effects were antagonized by naloxone indicating that morphine inhibits the immune system in a specific manner via its interaction with opioid receptors (11).

Other studies in animals have shown that morphine can affect natural killer (NK) cell activity (12,13,17) perhaps yielding reduced resistance to tumors (14). Interferon (15,16) and a variety of other cell-mediated reactions are also altered (18-23). The effect of morphine on NK cell activity in animals is not well defined. The drug has been shown to enhance the activity of these cells in mice (12) but a suppression was observed when similar experiments were performed in rats (13,17). The ability of animals to mount a response to tumor challenge was also affected by morphine treatment. Rats given injections of morphine either before or after challenge with a mammary ascites tumor showed a significant decrease in survival time and percent survival. It was postulated that morphine enhances the susceptibility to tumor via its inhibition of NK cell activity (14). Reduced phagocytic or cytotoxic actions of monocytes could also affect cancer resistance. In vitro studies using cells from morphine-treated mice have demonstrated that PMN and mononuclear cells from these animals were reduced in their ability to phagocytize and kill C. albicans and also in their generation of superoxide (20).

In vivo studies in rats revealed that animals chronically- treated with morphine exhibited an inability to produce a tuberculin reaction (18), a measure of cell-mediated immunity (CMI), as well as a depressed ability to produce an inflammatory reaction in response to carrageenan (19). This effect was dose-dependent and inhibited by naloxone. Reduced mitogenesis may also be important in disease resistance functions associated with inflamation. Lymphocytes from morphine-treated mice (21) and guinea pigs (22) were decreased in their mitogenic response to stimulation with Concanavalin A (Con A).

Such changes, which can also include morphine suppression of spleen and body weight, and plaque-forming cells of mice (23), show evidence of significant changes in immune functions. A reduction in number and size of splenic germinal centers, total spleen cellularity and thymic size was

observed. Histological examination revealed that there was a loss of peripheral definition of splenic follicles (23). There is limited information on morphine and production of immunological proteins. Another adverse effect of morphine is the depression of serum interferon titers. Mice that were treated with morphine had depressed levels of serum interferon following injection with polyinosinic: polycytidylic acid (poly I:C) (15,16).

These studies have shown that there is a strong parallelism between host susceptibility to diseases as a result of exposure to morphine and alterations in the physiology and functions of immune cells.

Effects of THC on Human Immune Systems

Several approaches have been used to study the effects of marijuana or its active component, tetrahydrocannabinol (THC), on human immune systems. These include using cells isolated from chronic marijuana smokers, cells from normal volunteers exposed to marijuana smoke or using cells from normal donors and exposing these cells to THC in vitro. Results obtained from human studies have been equivocal. Several studies have found THC to be immunosuppressive while others have been equivocal.

A survey of 51 chronic marijuana smokers showed that the response of their cells to stimulation with allogeneic cells or PHA was depressed. These observations were supported by in vitro studies which showed that normal human lymphocytes incubated in THC were depressed in their blastogenic response to similar stimuli (26,27). Peripheral blood lymphocytes from chronic marijuana smokers contained reduced number of T lymphocytes that form rosettes with SRBC (28-30). A similar reduction could also be achieved by in vitro incubation of normal lymphocytes in THC (28). Although marijuana use was able to interfere with T lymphocyte function as measured by rosetting and PHA-stimulation, this effect was transient and varied between individuals (30).

However, several other studies have shown that marijuana smoking or THC is not immunosuppressive. The skin responses of 22 chronic marijuana smokers against 2,4-dinitrochlorobenzene (DNCB) showed no significant difference from those of normal controls (36). The blastogenic response of cells from chronic marijuana smokers to PHA (37-39) and pokeweed mitogen (PWM) (40) were also similar to those of cells from normal controls. An evaluation of the immune status of 12 healthy chronic marijuana smokers revealed that while there was an initial depression of various immune parameters in several subjects, these values returned to normal over time (41). The values in the other subjects were not significantly different from normal. The authors concluded that marijuana smoking did not produce any significant impairment of either humoral or cell-mediated immunity (41). Functional comparisons of macrophages from marijuana smokers and non-smokers showed that these cells have similar capacities to phagocytose C. albicans (42) although marijuana smoking has been shown to be more injurious to the lungs than cigarette smoking (43).

Other immune alterations that have been associated with marijuana or THC include significantly reduced serum IgG levels in chronic smokers (31), inhibition of NK cell activity (32), inhibition of phagocytic activity (33), elevation of serum IgD levels (31), decreased T:B cell ratio as a result of reduced T cell numbers (29,33) and inhibition of leukocyte migration (34). THC also inhibited DNA, RNA and protein syntheses in PHA-stimulated normal human lymphocytes (35).

Results from human studies have thus shown many inconsistencies. The findings probably reflect how various parameters may affect the outcome of any study. Factors such as sex, age, hormonal balance, nutritional status, length

of exposure to the drug as well as its quality, and other drugs may have had a significant influence on the outcome of these investigations. Some studies may be suspect if carried out in the past six years in areas where rates of infection with human immunodeficiency virus (HIV) were significant in intravenous drug users, as the virus is immunosuppressive.

Effects of THC on the Humoral Immune System of Animals

Studies performed in animals have produced more consistent findings than those in humans. In most cases THC is associated with immunosuppression of various immune parameters. The greater consistency observed in animal studies probably reflects the influence of genetic factors, consistent dosage levels, controlled diets, and use of other drugs.

Several studies have shown an immunosuppressive effect of THC on the humoral immune response of animals. Administration of THC prior to or post immunization of mice with SRBC significantly reduced the number of plaque forming cells in their spleens (44-48) as well as hemagglutinin titers (49,50). A concurrent loss of germinal centers and follicular definition, together with a reduction of splenic lymphocytes, and reduced spleen and body weights were observed in mice treated with THC either before or after immunization with SRBC (44,45). Although THC caused an inhibition of the primary anti-SRBC response, it did not suppress the secondary response if THC was given together with the secondary antigenic challenge. However, if THC was given during primary immunization, the response to secondary challenge was suppressed indicating an inhibition of the memory aspect of humoral immunity (49). A study by Levy and Heppner (46) found that THC only changed the kinetics of plaque forming cell production. Mice treated with THC were shown to produce peak plaque forming cell numbers 24 - 48 hours later than control mice while the numbers did not vary significantly. In contrast to the finding of other investigators, they did not observe any significant reduction in hemagglutinin titers in THC-treated mice.

In vitro observations that support other findings of THC-induced suppression of humoral immunity include demonstration of a reduced blastogenic response of splenic lymphocytes to Escherichia coli lipopolysaccharide (51) or PWM (52), which are both B cell mitogens, and a depressed in vitro primary-like immune response of mouse splenocytes against SRBC (53,54). THC was suppressive if it was present during the entire 6 day culture period or for the first 24 hours following antigenic stimulation. This indicates that the presence of THC during the period following antigenic stimulation was critical for an immunosuppressive effect (53).

Effects of THC on Cell-Mediated Immunity of Animals

The immunomodulatory effect of THC on the CMI of animals has also been demonstrated. In vitro and in vivo measures of CMI that have been studies in relation to THC-induced immune modulation include delayed type hypersensitivity (DTH) to SRBC (39,47), rosette-forming T cell numbers (45), blastogenic responses of lymphocytes to PHA (51) and Con A (54), skin graft survival (50), mixed lymphocyte reaction and migration inhibition factor activity (55). Most of these studies revealed an immunosuppressive effect of THC. For example, the DTH response to SRBC was significantly lowered in mice treated subcutaneously with THC at a dose of 100 mg/kg for 4 days (49), or in mice fed THC perorally at a dose of 30 mg/kg (39). Skin graft survival was increased in mice as a result of treatment with THC (50). This indicates a suppression of the cellular mechanism involved in graft rejection. Finally, the blastogenic response of lymphocytes to PHA and Con A, which are both T

cell mitogens, was depressed in mice treated with THC (51), and in monkeys administered marijuana smoke (52).

Other studies have demonstrated an immunosuppressive effect of THC on other mechanisms involved in immunity. These include inhibition of phagocytic function (54,56), interferon production (55,57) and NK cell activity (52,58). THC, at levels that are attainable by smoking marijuana, inhibited macrophage spreading and phagocytic function (51). In vitro and in vivo interferon production were also depressed by THC. Mice treated with THC produced lower titers of interferon in response to stimulation with poly I:C or Herpes simplex Type 2 virus (57). Splenocytes from normal mice also produced less interferon in in vitro cultures in the presence of THC (59).

These studies have thus been able to provide strong evidence of the immunosuppressive effects of THC particularly in animals. Such effects were clearly demonstrated by studies that showed that animals exposed to THC were more susceptible to infections. THC is capable of exacerbating viral infection, as has been shown in mice (60,61) and guinea pigs (62), as well as reducing resistance to bacterial pathogens (61,63). The resistance of mice to Listeria monocytogenes, which is used as a measure of CMI, was inhibited by THC in a dose dependent manner (61). Thus, these findings reflect an inhibition of CMI by THC, supporting in vitro observations.

There are thus obvious differences in the susceptibility of man and animals to the immunomodulatory effects of marijuana and THC. Clearly animals studies show that THC is immunosuppressive and reduces disease resistance. Whether such changes occur regularly in man is less clear due to fewer studies and problems of determining dose. Due to these differences it is very difficult to make definitive conclusions on the suppressive effects of this drug on the human immune system. They may have significant relevance due to the current AIDS epidemic, where immunomodulation of T cells would be expected to alter the growth of the virus, and possibly its infectivity.

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Developmental Effects of Cannabis

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Cannabis preparations (Marihuana, Hashish) have become the most frequently used illicit drug in the United States and the Western World. Besides the chemical euphoriant Delta-9-Tetrahydrocannabinol which Cannabis contains, 60 other cannabinoids have been identified as well as 360 other compounds such as Sterols, Terpenes, Flavinoids, Furan derivatives and alkaloids. Marihuana smoke of a marihuana cigarette contains in its gas phase: Carbon Monoxide, Acetaldehyde, Acrolein, Toluene, Nitrosamine, Vinyl Chloride and in its particulate phase: Phenol, Cresol, Methyl. It also contains twice as much Napthalene and Carcinogens (Benzanthracene and Benzopyrene) than in a tobacco cigarette of the same weight.

Available evidence indicate that Cannabis exerts significant effects in all phases of reproduction and development in members of both sexes in all species which have been studied: these include fish, birds, rodents (mice, rats, hamsters) rabbits, dogs, horses, monkeys and homo sapiens. Several reviews have been written on the subject (Nahas 1984, Rosenkrantz 1985).

Experimental studies have reported that negative developmental effects can be caused by Cannabis in three ways:

1. Preconception exposure with resulting damage to the gametes, sperm or ovum (gametotoxicity).
2. Prenatal exposure with resulting damage to the embryo and to the fetus during organogenesis.
3. Postnatal exposure through maternal milk, with resulting damage to the growing offspring, and behavioral toxicity.

PRECONCEPTION EXPOSURE

Cannabis may be gametotoxic in male and female.

Evidence in the male.

Administration of delta-9-THC or crude marihuana extract (CME) decreases testicular size in pigeons (Vyas and Singh, 1976), rodents (Dixit et al., 1974), and dogs (Dixit et al., 1977). This organ is sensitive to Cannabis preparations in many different routes (Bloch et al., 1978). Immature and mature animals are equally affected. Fujimoto et al. (1978) reported that adult rats treated with CME (15 and 75 mg/kg orally) for 77 days presented a significant reduction in prostate, seminal vesicle, and epididymal weight. Oligospermia in the epididymis was also present.

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Thirty days after cessation of treatment, testicular function and organ weight appeared to return to control levels. Abnormal forms of sperm were reported in mice treated for 5 days with delta-9-THC (5-10 mg/kg, i.p.) or CBD (10-25 mg/kg) (Zimmerman et al., 1979), and in rats exposed to marihuana smoke for 75 days (Huang et al., 1979). CBD decreased testicular size and spermatogenesis (at all stages) in rhesus monkeys (30-300 mg orally) (Rosenkrantz et al., 1981).

Hembree et al. (1976) observed 16 patients in a hospital ward before, during, and after a 4-week period of marihuana smoking (5-20 cigarettes a day, equivalent to 100-400 mg delta-9-THC). Marihuana administration was associated with decreased sperm count, sperm motility, and an increased incidence of abnormally non-ovoid shaped sperm cells (Fig.1). These changes were most marked 4 weeks following onset of smoking and 1 week after the smoking period had terminated, indicating that effect of the cannabinoid is exerted on spermiogenesis since hormonal suppression of spermatogenesis takes longer than a month and is usually not associated with an increase in abnormal form and decrease in motility. Hembree et al. (1979) concluded that the inhibitory effect of Cannabis smoke on spermatogenesis was also exerted directly on the testicular germinal epithelium (besides the possible indirect effect of THC on spermatogenesis through gonadotropin suppression). Many experiments reviewed elsewhere (Rosenkrantz, 1985) and beyond the scope of this paper have been carried out to clarify the mechanism causing morphological changes in sperm: THC exerts its effects on the hypothalamo-pituitary axis and also with other non-psychoactive cannabinoids directly on testicular cells. All of these alterations of gonadal function in the male have not been associated in man with an increased incidence of developmental defects in his offspring.

However male preconception exposure to Cannabis has been associated in mice with developmental defects of his offspring. Dalterio et al. (1982) treated male mice orally with large doses of CME (25 mg/kg for 5 days, or a single dose of 50 mg/kg), and with CBN or THC (single 100 mg/kg dose). Such treatment was associated with a reduction in fertility, increased pre- and post natal losses, and reduced litter size persisting several weeks after discontinuation of treatment. Cytogenetic studies of sperm cells indicated increased frequency of chromosomal abnormalities including ring translocations and nondisjunction. These same effects were observed in 30% of the F1 offspring of the treated mice. Major teratology was recorded in three of these F1 offspring. Dalterio et al. (1982) conclude that cannabinoids can be gametotoxic.

Evidence in the female.

Henrich et al. (1983) have reported that 30-day old female mice were given 0.1 mg THC i.p. for 21 days. Ovulation was indu-

FIG. 1. Top: Normal ovoid shape human spermatozoa sampled from tobacco smoker and moderate alcohol drinker. Bottom: Non-ovoid and immature form present among ovoid shape human spermatozoa sampled from daily marihuana smoker. (From Hembree et al., 1978, with permission.)

ced by FSH and chorionic gonadotropin, injected to the treated females and controls, which were then mated and sacrificed 24 to 48 hrs later. THC treated animals presented a higher incidence of abnormal fertilized ova in their early stage of development than untreated mice. Such studies suggest that chronic THC administration may have a significant effect on ovarian oocyte or on early embryonic development of the mice.

In the nonhuman female primate, THC acutely inhibits FSH, LH and prolactin, and disrupts ovarian cycles and ovulation (Smith 1979). Tolerance to these effects develops (Smith et al. 1983). In women smoking marihuana, a disruption of the mensrual cycle has been reported. Tolerance to these effects also develops (Mendelson et al., 1985). Possible gametotoxic effects of THC in the human female needs to be ascertained.

PRENATAL EXPOSURE

Radioactive delta-9-THC crosses the placenta to accumulate in the fetus of pregnant mice (Freudenthal et al., 1972; Harbison and Mantilla-Plata, 1972; Kennedy and Waddell, 1972; Pace et al., 1973) hamsters, (Idänpän-Heikkila et al., 1969) and dogs (Martin et al., 1976). The drug deposits in yolk sac, fetal tissues, and amniotic fluid. Martin et al. (1977) reported that radioactive delta-9-THC was concentrated in the brain of the dog fetus 20 min after injection into the mother. There is a THC concentration gradient of mother → placenta → fetus (Bloch, 1983). Loss of delta-9-THC from fetus and placenta was lower than that found in the mother, which may prolong fetal exposure to the drug (Mantilla-Plata and Harbison, 1976 a,b).

As is the case with other xenobiotics that cross the placenta embryotoxicity, teratogenicity and fetotoxicity have all been reported in different pregnant animals of different species treated with cannabinoids. Incidence of either of these three developmental defects is dependent upon time and length of administration, dose administered, or nature of substance administered, and route of administration and species studied (Rosenkrantz, 1979; Bloch, 1983). The higher the dose, the more likely one of these defects will occur.

Embryotoxicity. Oral doses of delta-9-THC of 5 to 50 mg/kg in mice and of 12 to 50 mg/kg in rats during day 6 to 15 of pregnancy increases incidence of resorption (Rosenkrantz, 1979). Optimal susceptibility to embryotoxicity occurred between days 7 and 9 of gestation. When doses administered were increased from 450 to 600 mg/kg, 21 to 100% fetal resorption was observed. Mice exposed to inhalation of marihuana (0.8-3.8 mg/kg) during the same period of gestation also displayed an increased incidence of fetal resorption. These findings are in agreement with those of Joneja (1976, 1977) and of Mantilla-Plata and Harbison, observed in mice, and of Fried (1976) who reported increased resorption of rat fetus expo-

sed to marihuana smoke from day 1 to 14 of gestation.

The mechanism of embryotoxicity of the cannabinoids has not been identified but Rosenkrantz (1979) noted that there was a correlation between midgestation vaginal bleeding and excessive fetal resorption. This observation suggested a possible direct effect on the endometrium and associated development of feto-placental circulation. A similar result could also have been caused by the effect of these substances on maternal control of neuropeptides and hormones required for maintenance of normal pregnancy.

Fetotoxicity. The growth of the fetus was also impaired by prenatal administration of crude marihuana extract or THC in mice, rats, rabbits, and hamsters. The same dose given orally that increased resorptions (5-30 mg/kg) resulted in retardation of growth, smaller weight, and reduced survival of the fetus (Banerjee et al., 1975; Harbison et al., 1977; Joneja, 1977; Mantilla-Plata and Harbison, 1976 a.b; Soffia, 1979; Wright, 1976). Nahas et al. (1982) reported that oral administration of CME (not exceeding 25 mg/kg of cannabinoid) from day 6 to 19 of gestation was associated with decreased fetal and placental weights (Table 1). Szeto and Cook (1983) administered 5 mg THC, i.v., to a pregnant ewe, with measurable THC. Decrease in heart rate and disruption of sleep cycle were observed in fetus and ewe with measurable THC.

Table 1.

Effects of Cannabis Extracts on Fetal Development in the New Zealand Rabbit (mean litter data)

Group	Number of animals	Number of viable fetuses ♂	♀	total	Number of resorptions early	late	total	Imp. placta	Corpora lutea	% Loss pre-implantation	% Fetal loss	Litter weight (g)	Fetus weight (g)	Total placental weight (g)	Placenta weight (g)
4[a]	14	3.8	4.6	8.4	0.5	0.5	1.0	9.4	11.2	16.5	10.9	363.4	45.26	47.7	5.94
5[b]	14	4.2	5.2	9.4	0.9	1.0	1.9	11.3	11.9	5.1	19.3	330.7	37.02***[d]	43.2	4.91***[d]
6[c]	14	3.8	5.2	9.0	0.5	0.3	0.8	9.8	11.2	12.7	8.0	351.6	39.90*[d]	43.4	4.98*

[a]Control treated by subcutaneous injection of 1 ml/kg of isotonic solution containing 1% Tween 80.
[b]Treated by subcutaneous injection of 1 ml/kg of cannabis extract dissolved in the preceding solution and containing 5 mg of THC, 0.65 mg of CBD + CBC, and 0.45 mg of CBN.
[c]Treated by intragastric administration of 1 ml/kg of cannabis extract in sesame oil and containing 5 mg THC, 0.65 mg of CBD and CBC, and 0.45 mg of CBN.
[d]* $p < 0.05$ (Kruskal-Wallis test).
** $p < 0.01$ (Kruskal-Wallis test).
*** $p < 0.001$ (Kruskal-Wallis test).

from Nahas et al. (1982)

Blood concentration in both for 8 hours. The fetotoxicity and embryotoxicity related to Cannabis exposure and reported in rodents has also been observed in primates (Sassenrath et al., 1979). A group of female rhesus monkeys given an oral daily dose of 2.4 mg/kg to 4.8 mg/kg delta-9-THC for 1 to 4 years had no decrease in number of conceptions but presented a 42% loss of the products of conception at all stages of development, from first trimester to early infant death. There was no specific, consistent congenital

anomaly. The reproductive loss in the control group was 8 to 11%. Surviving male infants had a reduced birth weight and showed altered autonomic and behavioral responsiveness to visual, auditory, and social environmental stimuli. There was no evidence of a deficit related to drug exposure of the sperm of delta-9-THC fathers. Also, evidence for a contribution of direct damage to the ova was lacking. These studies did not suggest any cumulative effect over sequential pregnancies in individuals drugged females. Sassenrath states that "the absence of frank specific teratology and the nonspecific nature of pregnancy interruption and morphological changes suggest that the drug might have impaired the maternal support of the fetus", e.g., placental circulation and function, a conclusion similar to that reached by Rosenkrantz (1979).

Teratogenicity. "High doses of crude marihuana extract or of delta-9-THC are teratogenic in animals" (Marihuana and Health, IOM Report 1982). One might add in certain species. Gerber and Schramm (1969) reported that subcutaneous injection of crude marihuana extracts greater than 200 mg/kg in hamsters and 250 mg/kg in rabbits were teratogenic (runting, encephalocele). Bloch (1978, 1983) has evaluated the conflicting reports concerning the teratogenic potential of Cannabis, and found evidence of a clear teratogenic response in mice (Mantilla-Plata et al., 1973, 1975; Mantilla-Plata and Harbison, 1976 a,b; Harbison et al., 1977; Joneja, 1976; Kostellow et al., 1978). The most frequently described lesion was cleft palate and exencephaly. As reported by Joneja (1976) in mice treated orally with 400 mg/kg of THC, 12% of live fetuses were deformed. Other investigators have found congenital defects in dental developments in rats (delta-9-THC, 3-20 mg/kg/day) including impaired incisor eruption (Fried, 1976) and maxillary asymmetry (Siegel et al., 1977).

Furthermore, substances such as phenobarbital which interact with delta-9-THC metabolism will enhance the teratogenic potential of this drug in mice (production of cleft palate, Harbison et al., 1977). Zebrafish (Thomas, 1975) placed in a medium containing 10 ppm of delta-9-THC produced offspring with curved spine and bulbous tails.

Other species of rodents, such as hamsters and rats, are less sensitive than the mice to the teratogenic effects of large doses of delta-9-THC or Cannabis extract, and several investigators (Harley et al., 1973; Wright et al., 1976) have failed to duplicate the early observations of Persaud and Ellington (1968) who reported malformations in rats treated intraperitoneally with Cannabis resin.

Other studies failed to demonstrate teratogenicity of 1 to 250 mg/kg of THC administered per oz or subcutaneously to rats from gestation day 5 to 15 (Borgen et al., 1971, 1974; Pace et al., 1971; Uyeno, 1975; Banerjee et al., 1975; Vardaris et al., 1976; Wright et al., 1976). The large amounts of cannabinoids

sed to marihuana smoke from day 1 to 14 of gestation.

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[d]** $p < 0.05$ (Kruskal-Wallis test).
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required to produce their effects in animals make it doubtful that these xenobiotics could be grossly teratogenic in man. They might however, facilitate the teratogenicity of other teratogens by lowering the threshold at which these exert their effects (Harbison, 1977). Despite the lack of uniformity of aberrations of Cannabis-evoked teratogenic effects, a common observation has been that of a dose-related increased incidence of embryotoxicity and fetotoxicity (Rosenkrantz, 1979) in all species studied, mice, rats, hamsters, rabbits and primates. These toxic effects on embryo and fetus development occur with delta-9-THC doses which are comparable to those of chronic marihuana use in man.

PERINATAL EFFECTS

Dalterio et al. (1981) have reported that maternal exposure in mice to delta-9-THC or CBN the day before parturition, and for 6 days postpartum, produced long-term alterations in body weight regulation, pituitary-gonadal function, endocrine responsivity to females and adult copulatory behavior. Effects of perinatal exposure did not become apparent until just before puberty.

Milk production in pregnant and lactating rodents treated with marihuana extracts or THC was markedly inhibited (Borgen et al., 1971; Szepsenwol et al., 1979).

The passage of delta-9-THC into mother's milk where it is concentrated because of its elevated fat content was first documented by Jacubovic et al. (1973) in the rat given a single intravenous injection of 0.2 to 1 mg/kg dose, and confirmed by Chao et al. (1976) in the squirrel monkey. Radioactivity was also present in urine and feces of suckling infants. Similar findings were reported in two women smoking marihuana (Perez-Reyes et al., 1982) who were feeding their infants. Their milk contained elevated concentrations of the cannabinoids which were eliminated in feces and urine of the infants.

POSTNATAL DEVELOPMENT

Borgen et al. (1971) using a cross-fostering technique, reported that offspring of rats given delta-9-THC on days 10 to 12 of gestation were retarded in the development of visual-placing reflexes and cliff avoidance. Other similar studies of learning defects in offspring of rats injected with cannabinoids (Gianustos and Abbatiello, 1972; Vardaris et al., 1976) have been reviewed earlier.

Marihuana and its purified components administered prenatally impair development process in experimental animals. Learning deficits were demonstrated in 21 to 65 day old pups from rats treated with Cannabis extracts or delta-9-THC during gestation (Gianustos and Abbatiello, 1972; Vardaris et al., 1976). Luthra

(1979) reported that THC 10 to 15 mg/kg administered to gestating and lactating rats by the oral route produced significant decrements in RNA, DNA and protein concentration in the developping brain of the offspring. These findings may be important in the light of the role of protein and nucleic acids in learning and memory (Barondes, 1970; Glassman, 1969). Dalterio et al. (1982) reported that maternal exposure of mice to cannabinoids either 2 or 4 days before parturition reduced brain amine concentration (dopamine, norepinephrine in the adult male offspring).

Sassenrath et al. (1979 a) have also reported behavioral anomalies in offspring of the THC treated rhesus monkeys which display: 1. enhanced responsivity - both autonomic and behavioral - to visual and auditory stimuli, 2. less fear and avoidance behavior in a novel environment, and 3. overstimulation and assertiveness in response to peer serialization.

CLINICAL REPORTS OF DEVELOPMENTAL EFFECTS OF CANNABIS

The use of Cannabis has been mentioned in six clinical reports describing congenital anomalies in offspring of mothers who had consumed the drug during pregnancy (Bogdanoff et al., 1972; Carakushanky et al., 1969; Geleherter, 1979; Hecht et al., 1968; Jacobson and Berlin, 1972; Qazi et al., 1985). In the first five reports, the use of Cannabis was associated with that of other psychoactive drugs (LSD, amphetamines, barbiturates) and major malformations were reported. In the report of Qazi et al., the mothers admitted smoking marihuana daily during pregnancy, while categorically denying use of alcohol and other psychoactive substances. The five resulting infants displayed symptoms of intrauterine growth retardation - lower birth weight, shorter height, smaller head circumference, abnormal neurological manifestations and facial anomalies. These anomalies are similar to those described in the fetal alcohol syndrome, which was first scientifically documented in 1968 (Lemoine et al.), confirming observations made since recorded history.

Two other reports appeared in 1982. In the first, Greenland et al. (1982) report a prospective study on the effects of marijuana use, with the exclusion of other drugs, in 35 pregnancies. Infants born to users exhibited significantly more meconium staining (a condition that doubles the risk of neonatal death). Users had a higher proportion of protracted or arrested labor and of precipitate labor, as well as a higher proporiton of abnormal fetal rests. In the second study, on a cohort of 1,690 mother/child pairs (Hingson et al., 1982), marihuana use during pregnancy (n=181) was associated with infants who were 300g. lighter than infants of non-users ($p < .001$), and controlling for confounding variables lighter by 103g ($p < 0.01$). Compared with non-users, women who had used marihuana during pregnancy delivered smaller infants, as

well as infants who were nearly five times more likely to have features compatible with the fetal alcohol syndrome.

Qazi et al. (1985) reported in five cases abnormalities in offspring associted with prenatal marihuana exposure in Tables 2 & 3. "The weight of evidence indicates that Cannabis is damaging to the fetus and the newborn" concluded Finnegan and Fehr in their 1983 report to the World Health Organization - Addiction Research Foundation on the Health Hazards of Cannabis.

Table 2.

Parental information of 5 cases

	Case No.				
	1	2	3	4	5
Mother					
Age, years	21	20	20	19	20
Previous pregnancies	0	1	1	1	4
Pregnancy complications	0	0	0	0	0
Alcohol	0	0	0	0	1 pint rum/week
Cigarettes, packs/day	–	¼	¼–½	–	1
Other drugs	0	0	0	0	cocaine once in 2 weeks
Marihuana, joints/day	2	2–3	2	14	5–6
Weight gain during pregnancy	?	≈ 10 lbs	–	9 lbs	–
Father					
Age, years	27	29	18	29	20
Marihuana	+	+	?	+	?
Alcohol	+	+	?	–	?
Other drugs	?	–	?	–	?

from Qazi et al. (1985) with permission

Table 3.

Summary of abnormal findings of 5 infants prenatally exposed to marihuana

	Case No.				
	1[a]	2	3	4	5[b]
Gestation, weeks	35	40	38	36	40
Birth weight, g	1,560	2,310	2,116	1,630	2,340
Birth length, cm	29.5	45.5	48	?	?
Small head	+	+	+	+	–
Tremors	+	+	+	?	+
Epicanthus	+	+	+	+	+
Posteriorly rotated ears	+	+	+	–	+
Long philtrum	+	+	+	+	–
High-arched palate	+	–	–	+	+
Abnormal palm creases	+	–	+	–	+
Age at postnatal examination, months	3	2	1	13	11
Percentiles					
Length	<5	5	5	5	<5
Weight	<5	5	5	5	<5
Head circumference	<5	5	<5	<5	5

[a] Died.
[b] Mother also used cocaine and alcohol.

from Qazi et al. (1985) with permission

This conclusion should be brought to the attention of the public, in view of the widespread use of marihuana among child bearing women and prospective fathers. Blackard (1984) reports in The New England Journal of Medicine, the presence of THC or of its metabolite in maternal plasma and umbilical cord blood sampled from ten women who delivered their babies in two Denver general hospitals and admitted having smoked marihuana daily during the third trimester of pregnancy.

Furthermore, systematic epidemiological studies should be undertaken to determine, in man, the extent of incidence of neonatal and postnatal morphological, neurological and behavioral anomalies associated with prenatal marihuana exposure.

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(4)

Marihuana Use by Pregnant Women and Effects on Offspring: An Update

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FRIED, P. A. *Marihuana use by pregnant women and effects on offspring: An update.* NEUROBEHAV. TOXICOL. TERATOL. 4(4) 451–454, 1982.—This report is based on a previously described sample of 291 mothers-to-be and on an additional 129 subjects. Among these 420 predominantly middle class pregnant women, approximately 3 percent used marihuana regularly during pregnancy. For assessing the effect of marihuana on pregnancy variables and the offspring, the mothers-to-be were matched in terms of nicotine and alcohol use. Marihuana use was associated with a shorter gestation period and a decreased maternal weight gain. No effect on birth weight, length of labor or difficulty in birth were observed. Consistent with the earlier report, babies born to women who smoked more than five joints per week during pregnancy demonstrated marked tremors and startles and altered visual responsiveness at 2–4 days of age. These symptoms had attenuated by 30 days and no developmental impairments were observed in any of seven babies who had reached one year of age born to women who had smoked 2 joints or more per week during pregnancy.

Marihuana Pregnancy Development Neurobehavior

THE present report is a brief update of aspects of an ongoing study started in 1978 involving the department of Psychology of Carleton University and the Ottawa Civic and Ottawa General hospitals. The purpose of the investigation is to examine, in a prospective fashion, the pattern of use of social levels of alcohol, cigarettes and marihuana during pregnancy and the effects of these drugs on the offspring. Details of the procedure and epidemiological information on approximately 200 subjects have been presented previously [4] and birth data and the results of behavioral testing of babies up to 4 days of age born to the marihuana users among 291 subjects in the Ottawa study have also been described elsewhere [3].

METHOD

The present report is based on a sample consisting of 420 subjects and includes several more infants born to marihuana users. As both the demographic data on the mothers and the results of the newborn are essentially the same as those found in the original cohort [3], the data will be described very briefly. Since the original report, a number of offspring of the marihuana users have been followed up and been examined using the Prechtl neurological examination [5] at nine (±1) and 30 (±2) days and the Bayley Scale of Infant Development [1] at 12 months. Although it is obvious, it must be emphasized that the sample size is small and these longitudinal results have to be viewed as quite preliminary.

Mothers-to-be were informed of the study by their obstetrician or notices in the public media and upon volunteering to participate were interviewed one during each of the trimesters remaining in their pregnancy. Information obtained included the volume and variability of alcohol consumption, cigarette smoking habits and marihuana intake for the year before pregnancy and each trimester of pregnancy. In addition to this "soft" drug report a general health history, previous pregnancy details, a 24-hour dietary recall and socio-demographic data were obtained.

The categorization for marihuana use for each of the four time periods (year before pregnancy and each of the trimesters) was: non-user; irregular user—one joint or less per week or exposure to the exhaled smoke of others; moderate user—two to five joints per week and; heavy user—more than five joints per week.

RESULTS

The socio-demographic characteristics of the new sample is essentially the same as that of the cohort described previously [4] and therefore will not be dealt with separately. Among the total sample of 420 women the average family income was $29,250±$13,050 and the average age and parity was 29±4 and 0.7±0.9, respectively. The economic profile was very similar to that of the general population of the Ottawa area reported by Statistics Canada and the age and parity figures were consistant with all the women giving birth in 1979 in the participating hospitals. Ninety-four percent of the women had at least a high school diploma and 63 percent had continued their education beyond high school.

In Table 1 the marihuana habits of the original 291 subjects [3] are compared to the additional 129 subjects making up the 420 subjects described in this report. As can be seen,

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TABLE I

PROPORTION OF WOMEN IN DIFFERENT CATEGORIES OF MARIHUANA USE BEFORE AND DURING PREGNANCY IN TWO PHASES OF STUDY

Marihuana category (joints/week)	Pre-pregnancy (%)		First trimester (%)		Second trimester (%)		Third trimester (%)	
	Phase 1 n=291	Phase 2 n=129	Phase 1 n=291	Phase 2 n=129	Phase 1 n=291	Phase 2 n=129	Phase 1 n=291	Phase 2 n=129
Non-user	80	84	90	92	91	92	91	95
Light (<1)	14	11	6	6	6	7	6	4
Moderate (2–5)	2	2	1	1	1	0	1	0
Heavy (>5)	4	3	2	2	3	1	3	1

the percentages during pre-pregnancy and during each trimester for the two sub-samples are quite consistent. Among the overall 420 subjects, during the year before pregnancy 82% of the women reported that they did not use any marihuana, 13% were irregular users, 2% were moderate users and 3% were heavy users. Of the 14 women in the latter category, 10 women smoked between 6 and 45 joints per week whereas the remaining four exceeded 100 joints per week. Of the 344 women who reported not using marijuana prior to pregnancy, three did report irregular use during pregnancy. Of the 54 women categorized as irregular users before pregnancy, approximately 58% became non-users in the first trimester and the proportion that changed their marihuana habit remained constant throughout pregnancy. Of the seven women categorized as moderate users prior to pregnancy, all became irregular users or abstainers in the first trimester and remained so throughout pregnancy. Of the 14 subjects categorized as heavy users before pregnancy, one abstained from marihuana throughout the pregnancy. Of the remaining 13, four became moderate users during the first trimester. In the second and third trimesters, nine women continued to be categorized as heavy users.

In both the sample described in the previous report and in the present subsample the women who smoked marihuana to either a moderate or heavy extent were different from the remainder of the sample in a number of ways that might have an adverse effect on the development of the offspring, e.g., lower socio-economic level, less formal education, and increased cigarette smoking. Alcohol was not statistically associated with categories of marihuana use although among the women categorized as heavy marihuana users, the average daily amount consumed was significantly greater than that consumed by the other subjects.

In terms of age, before pregnancy only 3 subjects of the 75, who reported any use of marihuana, were over 32 years and during pregnancy, whereas no moderate and only one heavy user was older than 32.

In order to examine pregnancy variables and the data of the offspring, a matched control procedure was utilized in which the mother-to-be who used marihuana to either a moderate or heavy extent was paired with a non-user with comparable nicotine and alcohol habits.

Marihuana users revealed no differences in rate of miscarriages, complications at birth, length of labour, medicated versus non-medicated type of birth. Among the women in the heavy category (the eight women who smoked more than five joints per week during all three trimesters) both maternal weight gain and length of gestation was less than matched controls in all but one case (Wilcoxon T; $p<0.02$ and $p<0.05$ respectively). Among the 8 heavy marihuana users, 4 had a weight gain of less than 10 kg, whereas none of the matched controls had weight gains of less than 11 kg. Whereas only one control mother had a gestation length of less than 40 weeks, 5 of the heavy marihuana users had gestation lengths of 39 weeks or less.

Taking into account gestational age, no effect of marihuana was seen in terms of the newborn's weight, length or head circumference. Interestingly, the four heaviest users (more than 40 joints a week before pregnancy and more than 10 joints per week during each trimester) all gave birth to males. Neither Apgar status nor haemglobin or hematocrit counts differed among the various groups of offspring.

The results of the assessment, 60–80 hours post-partun, of the newborn's capacity to interact and adjust to its environment (2) revealed group differences. Smoking marihuana regularly during pregnancy was associated with a marked decrease in the likelihood of the offspring responding to a light repeatedly directed at their eyes. Among the nine heaviest marihuana users, five failed to respond to the light and two who did respond failed to habituate. Thus seven of the nine offspring had an altered response. Data, although incomplete, on the matched controls tested so far revealed that, out of seven babies examined, only two failed to respond and all responders habituated.

In terms of general behavior using the matched controls for comparison, the finding described in the earlier report, i.e. of a tendency of the babies born to heavy marihuana users to be less successful at self-quieting than controls, was not confirmed. However, as reported previously, the infants were readily consoled and, in fact, even somewhat more cuddly than controls in the sense of grasping rather than resisting being held. The marihuana babies were not more irritable.

Tremors and startles were significantly heightened among the babies born to women who smoked marihuana regularly during pregnancy. These behaviours, frequently interpreted as symptomatic of nervous system immaturity, were the most consistent and visible consequences of regular heavy marihuana consumption. Interestingly, the babies of four subjects, who reduced their intake from heavy prior to pregnancy to lesser categories as the pregnancy progressed, all had babies that did no display the marked tremors.

Neither degrees of activity nor alertness differentiated among the different categories of users. The same lack of

effect was seen in laterality of handedness.

Finally, at this testing age, a high-pitched cry was noted among a third of the regular marihuana users and was not observed among the controls. This *cri de chat* [6] has been reported among neonates undergoing narcotic withdrawal [7].

The Prechtl [5] neurological examination given at 9 and 30 days was administered to 6 babies born to heavy users during pregnancy and to four babies born to women who were heavy users prior to pregnancy, two of whom became moderate users and two of whom became irregular users during pregnancy. The trend for diminished responsiveness to visual stimuli, seen at 4 days of age, persisted in half of the heavy users and one of the moderate users at 9 days but was not seen in any of the matched controls. However, at 30 days responsiveness was equal in both marihuana offspring and matched controls. Rate of habituation did not differ among any of the groups tested.

The tremors that were so marked during the first few days of life persisted in about half of the babies of the heavy users at nine days of age but were not different from controls at 30 days of age. The *cri de chat* was present in 3 babies; one was born to a woman categorized as a heavy user during pregnancy and the other two were born to women who were heavy users prior to pregnancy and had reduced their pregnancy intake to a moderate and irregular level. No *cri d chat* was heard among any of the matched controls. Analysis of the muscular components of the Prechtl examination is presently underway.

The Bayley Scale of Infant Development [1], consisting of mental, motor and behavioral scales, has been administered to the 12-month-old offspring of 4 heavy users and 3 moderate users. In comparison to both matched controls and normative scores, the data from these few babies did not suggest any negative effects associated with marihuana use during pregnancy. Among the offspring of the heavy users, the range of scores on the mental scale was from 98–120 and the range among the babies of the moderate users was from 97–122. On the motor scale the ranges were 99–120 and 98–111 among the heavy and moderate offspring, respectively. The Bayley Infant Behavior Record, which provided an evaluation of the babies' attitudes, interests and temperament, also failed to discriminate between the children of the marihuana users, matched controls or normative scores.

Physical measurements of growth taken at the time of this test did not differentiate the babies in any of the groups.

DISCUSSION

The demographic data obtained from the present updated sample is very consistant with that found in the initial reports [3,4]. The heavy and moderate marihuana users tended to be younger, have less formal education, a lower family income, a greater likelihood to smoke cigarettes and, on the average, drink more alcohol than irregular and non-users.

These data represent a two-edged sword. Although it is very important to know the characteristics of regular marihuana users who are pregnant many of these characteristics make the interpretation of the effects of marihuana quite difficult. Like virtually all observational studies in which membership in particular groups is defined by an attribute of subject rather than by random assignment, the role of background variables that may influence the dependent variables being considered is a major problem. Due to the extensive information collected during pregnancy, some attempt can be made to identify the influence of these "nuisance" variables in the present study.

The sample size of the marihuana groups prevents the use of such statistical procedures as multiple regression or canonical correlations for this purpose. What has been used in the present report as a preliminary step to focus in on the role of marihuana is to match the others in terms of nicotine and alcohol before and during pregnancy. Other approaches have been used in the previous report [3].

From the use of the matched-control procedure, two birth data results emerged that were not found in the original report; heavy marihuana use was associated with a shorter gestation period and a reduced maternal weight gain. However, as originally reported, no association between marihuana and birth weight, birth abnormalities or difficulties at birth were observed. The relationship reported previously between marihuana and aspects of neurological neonatal behavior such as increased tremors and startles and altered visual responsiveness remained a consistant finding in the 60–80 hour old babies.

However, based on a limited number of babies, these effects were less striking at nine days and by 30 days, no longer distinguished the offspring of the heavy marihuana users. Further, at one year of age no motor, mental or general behavioral attributes appeared to characterize the offspring of the marihuana users.

Thus the very preliminary results suggest that the measurable correlates in newborns of regular marihuana use during pregnancy diminishes with age. Whether this is because the neurologicgal abnormalities present at birth are overcome or compensated for with maturity, or whether the tests used and the later ages have a decreased discriminatory sensitivity to subtle differences that may exist can only be answered by increasing the sample size and further follow-up of the infants. Both of these steps are presently being taken.

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Cannabinoid Exposure: Effects on Development

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DALTERIO, S. L. *Cannabinoid exposure: Effects on development.* NEUROBEHAV TOXICOL TERATOL 8(4) 345–352, 1986.—The literature concerning the teratologic effects of cannabinoids is reviewed, and some methodological issues associated with perinatal cannabinoid exposure are discussed. The long-term consequences of perinatal cannabinoid exposure on brain, endocrine, immune, and hepatic functions are considered. In our studies, perinatal cannabinoid exposure affected the long-term development of body weight regulation, neuroendocrine function, and adult sexual behaviors. In addition, the immune system and [redacted] were also influenced in adult male mice perinatally-exposed to cannabinoids. It is hypothesized that these effects may be mediated by cannabinoid-induced alterations in the fetal and/or neonatal hormonal milieu. In addition, the possibility that perinatal cannabinoid administration affects the subsequent ability of the exposed offspring to adapt to the environment is discussed. Finally, possible mechanisms of cannabinoid action in altering development are evaluated. It is concluded that the evidence to date indicates that cannabinoids can be embryocidal, affect gestational length and labor, induce maturational delays, and that these substances affect a myriad of physiological processes in the developing offspring, including effects on behavioral parameters, not only in laboratory animals, but also in the human neonate. Consequences of perinatal cannabinoid exposure on development are described and possible mechanisms of action of cannabinoids are discussed.

Cannabinoids Δ⁹-Tetrahydrocannabinol Cannabinol Cannabidiol Developmental effects
Perinatal exposure Mammary gland development Fetal androgens Adaptation to the environment
Follicle-stimulating hormone Hepatic function Immune system Testosterone
Luteinizing hormone Brain amines Fertility Sexual behavior Maternal variables Neonatal effects

IN the adult, administration of marihuana, or its purified components has been shown to affect a myriad of physiological processes (review in [7]). It is not, therefore, entirely surprising that exposure of the fetus or neonate results in long-term consequences for subsequent development.

In 1975 Fleischman *et al.* [32] reviewed the teratologic evidence from experiments in which various cannabis products were administered during gestation. Several variables, such as species or strain used, route, timing and dosage, and the type of cannabis preparation, influenced results. These studies evaluating possible cannabis-induced congenital anomalies employed high doses of cannabinoids, and it is possible that the route by which these substances were administered, and the vehicles in which these highly lipophylic agents are suspended, may have also influenced the results.

In a 1978 review, Block *et al.* [7] concluded that the existing data was consistent with evidence of teratogenic effects of cannabinoids in mice, with the most frequently reported defects being cleft palate and exencephaly. However, the high doses required to elicit these effects largely blunted the impact of these earlier reports. The accumulation of evidence regarding the effects of cannabinoids on fetal development did appear consistent with the contention that cannabinoids were embryocidal [7,73].

While earlier studies focused largely on the immediate effects of maternal cannabinoid administration on the fetus or neonate, there has been increasing interest in the long-term consequences of these substances on offspring.

ISSUES IN PERINATAL DRUG STUDIES

Maternal Factors

Several variables need to be considered in evaluating experiments involving pregnant and/or lactating animals. Certainly, stress may accompany any procedure involving handling and drug administration. Drug treatment may also affect maternal endocrine function, behavior, or nutritional status [3, 29, 73, 74]. There have been reports that THC treatment increases cannabalism of pups in mice [1], and also affects other maternal behaviors, such as pup retrieval [2]. In studies in this laboratory, maternal exposure to THC, or to the non-psychoactive, cannabinol (CBN), on the day prior to parturition and the first six days post-partum, did not affect such indices of maternal behavior as, time spent on nest, pup retrieval or lactational performance [16]. Other investigators also did not observe effects of maternal cannabis exposure on time spent on the nest or in pup retrieval [10]. Certainly, there have been several reports of decreased milk production in THC-treated females [8, 51, 70], probably since THC decreases prolactin levels in lactating females and interferes with the prolactin release in response to suckling stimulus [70]. It is possible that the early culling of litters to male pups

only in our experiments may have masked any lactational deficiency. In a recent study, in which the lactating females received a single oral administration on day 1 post-partum (within 12 hr of parturition), we observed milk bands which appeared normal in size in the neonates. Furthermore, postnatal mortality, and weight at weaning were quite normal by colony standards. However, the adult body weights from cannabinoid-exposed males were decreased [25]. In another report, increased mortality was observed after maternal administration of THC, but not after THC and cannabichromene (CBC), or after CBC alone [43]. However, in this study, litters were not culled until 10 days of age [43], while in our study the mice had been culled within 24 hr of parturition [16]. In a report by Charlebois and Fried [10], effects of administration of cannabis prior to, and during, gestation were found to interact with the level of protein in the diet, but these nutritional factors did not totally account for the effects of cannabis on the developing rat. These authors also suggest that the interactive effects of nutrition and cannabis exposure may be the result of diet-related changes in the hepatic drug-metabolizing enzyme systems, since it has been shown that nutritional deficiency impairs drug elimination [9].

It is conceivable that rearing practices or strain differences could influence the acute effects of maternal cannabinoid exposure. In our experiments, mice were obtained from a random-bred stock of animals which routinely produce 10–14 pups, and in which cannabalism is rare. Indeed, the only cannabinoid-related difficulties in our studies, as evidenced by increased neonatal mortality, occurred after administration of crude marihuana extract (CME) (Dalterio, unpublished).

Cross-fostering has been suggested as a method of dealing with the confounding effects of drugs on maternal functions, including food or water intake, which may affect development in their offspring [3]. While such an approach may be indicated for studies of other drugs, research on cannabinoids possesses some methodological problems that do not exist with water-soluble and/or shorter-acting substances. It has been well-documented that cannabinoids accumulate in the fetus and neonate as a result of maternal transfer via the placenta [6, 33, 49, 80], or milk [16, 46, 47]. Thus, uni-directional transfer of cannabinoids from mother to fetus or neonate has been demonstrated. However, the possibility of bi-directional transfer of cannabinoids has not been considered. The pups themselves should eventually excrete cannabinoids via the urine and feces, as does the adult [76]. Maternal grooming patterns in most mammalian species strongly indicate that surrogate mothers (assumed to be drug free), will ingest waste material from their suckled pups. Indeed, in earlier studies using adult animals, we observed behavioral alterations consistent with cannabinoid intoxication in the non-treated partner of a mating pair (Dalterio, unpublished). Thus, it became apparent that the fecal reingestion characteristic of the mouse insured that untreated animals, housed in contact with the treated mice, would receive some degree of drug exposure.

Route of Administration

In studies conducted over the past nine years, repeated administration of cannabinoids by oral feeding, i.e., 20–25 μl drop in sesame oil which the mice readily ingest, has not produced a single mortality in our cannabinoid-treated animals. Indeed, in studies involving repeated administration in adult male mice (3× week for seven weeks at 50 mg/kg) there were no final differences in body weight between THC-treated and control animals, which had been initially matched by litter and body weight [16].

It is possible that the route of administration and vehicle strongly influence cannabinoid-induced decreases in food or water intake. In some studies, oral administration has been used to designate per os, intragastric or intubation procedures. Certainly, the latter can be stressful, and, after repeated treatments, this could also affect the animal's food or water intake. In contrast, we have demonstrated the oral feeding, as employed in our laboratory, does not produce significant stress on the animals as indicated by levels of stress-labile hormones [20]. In our experience, the vast

TABLE 1
DEVELOPMENTAL EFFECTS OF PERINATAL CANNABINOID EXPOSURE

Treatment	Species	Effects
prenatal THC	rat	↓ protein, nucleic acids & lipids in brain [56]
prenatal THC	rat	delayed reflex development
prenatal cannabis	rat	↓ open-field activity, retarded wt. gain, eye opening & incisor eruption [10, 34]
prenatal THC	rat	fluctuating dental asymmetry [75]
prenatal THC	rat	↓ passive avoidance response [80]
perinatal hashish	mice	↓ body weight gain [36]
perinatal THC	monkey	altered visual attention [39]
prenatal cannabis	human	attention deficits [33]. ↓ birth wt., length & head circumference [44]; meconium staining [33]
prenatal	rat	↓ fertility & body wt. [34]
pregestational	male mice	↓ fertility & chromosomal anomalies in F_1 [22]
perinatal THC	mice	↓ adult sex behavior; ↑ plasma LH [16]
perinatal CBN	mice	↓ adult sex behavior; ↓ plasma LH and T at puberty [16]
prenatal THC	mice	↑ hepatic cytochrome P-450 [27]
prenatal CBN	mice	↑ *in vitro* T production, testes & seminal vesicles wt.; ↓ brain DA; ↑ hypothalamic 5-HT post-castration; ↑ hepatic cytochrome P-450 [24,27]
prenatal CBD	mice	↓ brain DA, ↑ hypothalamic 5-HT post-castration; ↑ hepatic cytochrome P-450 [24,27]
postnatal THC	mice	↓ body wt.; ↑ pituitary wt., & LH production *in vitro*; ↓ plasma LH and FSH; ↑ hypothalamic LHRH; ↓ hepatic cytochrome P-450; ↓ fertility [25–27]
postnatal CBN	mice	↓ body wt.; ↑ pituitary wt., & LH production *in vitro*; ↓ hepatic P-450; ↓ albumin & ↑ γ-globulin, ↓ fertility [25–27]
postnatal CBD	mice	↓ testes wt., plasma LH & hepatic cytochrome P-450; ↓ fertility [25,27]

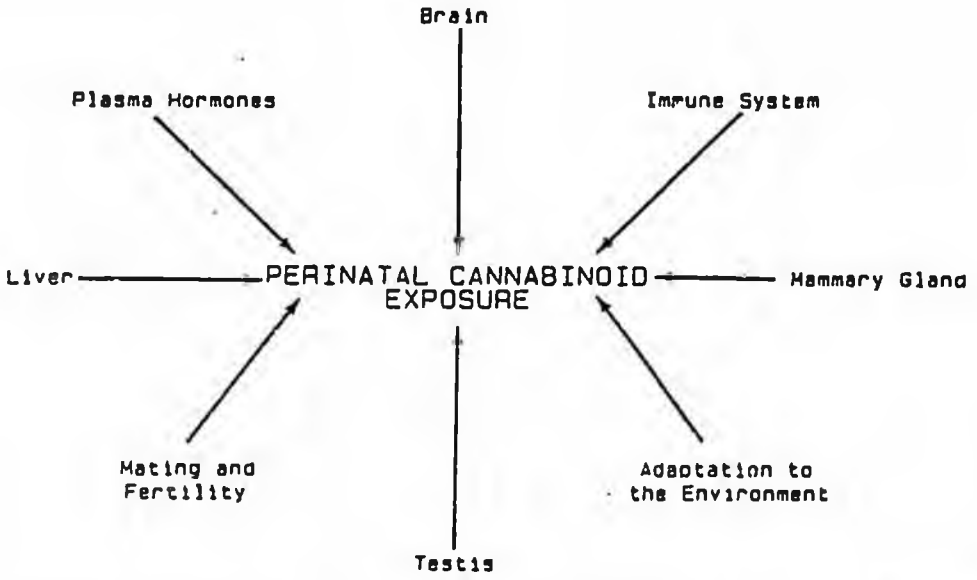

FIG. 1. Target areas whose functions may be altered as a result of perinatal cannabinoid exposure.

majority of mice receiving THC by the oral route show overt symptoms of behavioral intoxication within 15 min post-treatment (Dalterio, unpublished), and we have demonstrated that endocrine effects are already apparent at 5–10 min post-THC exposure in male mice [21].

MATURATIONAL EFFECTS

Delayed reflex development has been observed in rat pups exposed to THC on days 10–12 gestation [8]. Offspring also exhibited delayed incisor eruption and retarded development of cliff avoidance, and the visual placing reflex [8]. However, at 9 days post-partum, drug-exposed female offspring were more active in the open-field, but this effect was no longer apparent by weaning age [8]. Other investigators either found no effect [79], or decreased activity [35], after maternal cannabinoid treatment. In the Fried study [35] pups also presented evidence of retarded weight gain, eye opening and incisor eruption. Another study, which reported fluctuations in dental asymmetry in THC-exposed pups, suggested that this effect was related to THC "stressor" actions [75].

In another study in mice, Frischnecht *et al.* [36] reported that body weight gain was reduced in suckled mice during the entire lactation period, when mothers were given hashish. However, maternal weights and food intake were not affected [36].

Maternal cannabinoid exposure, therefore, affected dental development in different species, i.e., rats and mice, using PO, inhalation, or oral routes at different periods of gestation, with or without cross-fostering or pair-feeding, and in the absence of effects on maternal weights or food intake. It, thus, appears that maternal cannabinoid exposure affects at least this maturational index.

It is always difficult to explain differences between experimental results obtained in different laboratories. However, it is also difficult to ignore repeated evidence from several years experience in our own laboratory, indicating that effects on maternal behavior, general toxicity or stress effects do not appear to account for either cannabinoid-induced alterations in the reproductive system in the adult, or the long-term consequences on development in exposed offspring.

Perinatal cannabinoid exposure affects the development of a number of physiological systems (Fig. 1).

BRAIN BIOCHEMISTRY

Decreases in protein, nucleic acid and lipid synthesis have been observed in young rats exposed to maternal doses of 5–10 mg THC/kg [56]. In recent studies, we have reported that exposure on day 18 of gestation to CBN or CBD reduced the concentrations of norepinephrine (NE), and dopamine (DA) in hypothalamus, and in the remaining portion of the brain in adulthood [24]. In contrast, levels of serotonin (5-HT), and its metabolite, 5-HIAA, were elevated [25].

Adult mice exposed to THC on day 1 post-partum had significantly higher hypothalamic luteinizing hormone releasing hormone (LHRH) levels, and, in mice exposed postnatally to CBN, hypothalamic DA levels were significantly lower [25]. In addition, postnatal exposure to THC or CBN attenuated the depletion of catecholamines after α-methyl-p-tyrosine (α-MPT). Brain levels of 5-HT and 5-HIAA were also significantly higher in castrated, than in intact THC-exposed males. In CBN-exposed female offspring, hypothalamic levels of NE were lower, and the α-MPT-induced depletion of NE was attenuated in CBD-exposed females.

An interrelationship between gonadal steroids and the central nervous system biogenic amines has been reported [13, 28, 71]. It is, therefore, possible that cannabinoid-induced alterations in the biochemical function of these aminergic systems may be related to subsequent effects on endocrine functions.

BEHAVIORAL ALTERATIONS

It is difficult to determine whether any of the changes in brain biochemistry consequent to perinatal cannabinoid exposure is specifically related to long-term effects on behav-

ioral parameters. In our studies, we noted that perinatal cannabinoid exposure significantly affected adult male copulatory behavior [16]. In later studies, we observed an increase in brain 5-HT levels in adult males exposed postnatally to THC [25], and in mice exposed prenatally to CBN or CBD [25]. This latter group of males also had reduced levels of DA in brain [25]. It has been suggested that increased 5-HT may inhibit sexual behaviors, while the increased catecholamines appear to be facilatory [37]. Whether or not the alterations in visual attention observed in human infants [34], or in monkeys perinatally-exposed to cannabinoids has not been determined. In one study [39], administration of cannabis resin to pregnant rats affected subsequent learning behavior, body weight, brain weight and DNA ratio. At this point, any direct relationship between brain biochemical alterations induced by perinatal cannabinoid exposure, and the observed effects on open-field activity [8], reflex development [35], acquisition of the passive avoidance response [80], or any other cannabinoid-induced behavioral disruptions, remain to be established.

IMMUNE SYSTEM

Cannabinoid administration has been demonstrated to effect immune responses in laboratory animals [56, 63–65], and in man [14,67]. Recently, we have reported that postnatal exposure to CBN produces a concomitant decrease in plasma albumin, and an increase in γ-globulin concentrations in adult male mice [69]. At this point, it seems reasonable to suggest that cannabinoid-induced suppression of androgens could be related to this enhanced immunoglobulin level. Effects of the gonadal steroids on the development and function of the immune responses are well known [50, 55, 83]. Certainly, perinatal manipulation of the early steroid environment and/or administration of exogeneous androgens or estrogens during early development have been related to alterations in immunoresponsiveness [55,83].

NEONATAL EFFECTS

Rhesus monkey infants whose mothers received daily oral THC prior to, and during lactation, presented evidence of altered visual attention, which appeared to be characterized by sustained focus on a novel stimulus [39]. A significant increase in symptoms associated with nervous system abnormalities were also observed by Fried [34] in infants born to heavy regular marihuana users. Attention deficits, visual preference anomalities, tremors, and meconuim staining were also noted [34].

In a recent study by Hingson [44], women who smoked marihuana during pregnancy delivered infants with significantly reduced birth weights, length and head circumference. In addition, marihuana-exposed infants were 5 times more likely to exhibit features compatible with those of the fetal alcohol syndrome [44]. An association between maternal marihuana use and low Apgar scores in infants has also been observed [45].

ADAPTATION TO THE ENVIRONMENT

In our studies, we noted that, at puberty, male mice that had been perinatally-exposed to THC or CBN responded to individual housing with an immature female very differently than did the control males [16]. The THC- and CBN-exposed males housed with females, weighed significantly less than did animals which were housed in all male groups since weaning. In contrast, the control males gained weight as a result of female exposure [16]. In addition, in cannabinoid-exposed males, plasma corticosterone levels were increased one week after housing with an immature female (Dalterio, unpublished), suggesting that the housing arrangement was stressful for these males.

It is difficult to determine whether there is a common mechanism by which early cannabinoid exposure influenced the responses of these mice, or those of the human or nonhuman primates. It is conceivable that alterations in brain biochemistry may mediate these behavioral or perceptual alterations induced by perinatal cannabinoid exposure.

PLASMA HORMONES

Perinatal exposure to THC resulted in a marked elevation in plasma LH levels in pubertal and in adult mice [16]. In contrast, exposure to CBN during the same period resulted in a significant decrease in plasma LH concentrations at puberty, but with normal levels in adulthood [16]. Although plasma FSH levels tended to be reduced, they were not significantly different from those of the controls [16].

Prenatal CBN exposure significantly decreased plasma FSH levels [24], and tended to reduce LH, but this was not statistically significant. Prenatal THC exposure had no apparent effects on plasma gonadotropins in intact adult males [24].

In contrast, plasma LH concentrations were significantly lower in adult males exposed on day 1 post-partum, to THC, CBN, or CBD [25]. Although plasma FSH levels also tended to be lower, this was significant only in THC-exposed mice [25].

Plasma gonadotropin levels in response to castration were influenced by prior exposure to cannabinoids. Perinatal THC exposure resulted in a more marked elevation in plasma LH and FSH than those observed in the castrated controls [19]. In adult mice exposed to THC on day 18 of gestation, plasma LH and FSH levels were also higher than those observed post-castration in control males [24].

It is possible that cannabinoid exposure resulted in a differential sensitivity to the stress associated with castration. Or, perhaps, cannabinoid-induced alterations in neuroendocrine functions become more apparent when the neuroendocrine axis responded to the removal of steroid negative feedback. It does appear that cannabinoids affect the physiological reactions to events which disturb homeostatic conditions, or those that elicit endocrine responses.

MATING BEHAVIOR AND FERTILITY

In one study, the F_1 generation of rats exposed to cannabis smoke *in utero* took longer to mate and were less fertile than offspring of controls [35]. In addition, exposed females experienced more resorptions during pregnancy and offspring weighed significantly less at 1, 10, 11 and 30 days of age [35]. Recently, we observed that adult male mice exposed to cannabinoids on day 1 post-partum were less successful in mating, and produced fewer live offspring [26]. Pre-gestational exposure of the male parent also influences the subsequent fertility of the F_1 male offspring, and, indeed, results in congenital abnormalities in the F_2-generation [22].

Thus, maternal or paternal exposure to cannabinoids influences subsequent fertility in their offspring. This suggests that cannabinoids are either directly gametotoxic or mutagenic, or perhaps, that cannabinoid-induced endocrine alterations affect the subsequent production and/or integrity of gametes.

LIVER FUNCTION

Recently, we observed that prenatal exposure to THC, CBN or CBD significantly increased hepatic cytochrome P-450 concentrations, while levels of this enzyme are reduced in adult males exposed to these cannabinoids on day 1 post-partum [27]. These changes in hepatic enzyme activity may be related to the long-term effects of cannabinoids on plasma hormone concentrations, by affecting steroid metabolism or clearance. It is also possible that these long-term changes in enzymatic activity may be related to cannabinoid-induced alterations in perinatal androgen production. Certainly, the early hormonal milieu plays a critical organizational role in establishing sexual dimorphic hepatic functions [11, 30, 31]. This exerts an "imprinting" action on the liver, affecting subsequent sensitivity to the activational effects of steroids in adulthood [30,31]. However, in view of the effects of perinatal cannabinoid exposure on hepatic function in adulthood [5, 53, 54], it is possible that these substances may directly influence hepatic enzyme activity, possibly by interfering with macromolecular protein synthesis [65].

TESTES

Exposure to THC during the latter part of gestation and early post-partum resulted in a significant decrease in testicular weights at puberty [16], and also in adult male mice [16]. In one study, we observed that plasma T levels were significantly reduced [19], and, in another, in the low normal range [16].

Prenatal exposure to CBN did not affect testicular weights in adulthood, but did result in a reduction of testicular T concentration [24]. However, *in vitro* production of T was significantly increased after prenatal CBN exposure [24].

Testicular weights were increased in adult male mice exposed to CBD on day 18 of gestation [24], while these were significantly reduced in mice exposed to CBD on day 1 post-partum [25]. Interestingly, the *in vitro* responsiveness of testes obtained from these CBD-exposed mice to gonadotropic stimulation was enhanced [25].

These effects of early cannabinoid exposure on the testis may reflect long-term changes in the function of the hypothalamo-pituitary-gonadal (HPG) axis. In examining the diverse effects of perinatal cannabinoid exposure on hormone levels in adults, it is possible to conclude that cannabinoids disrupt the functional feedback regulation of the HPG system. Whether these disruptions reflect specific actions at a particular level of this system, or multiple actions, possibly by similar mechanisms, on HPG target sites, remains to be determined.

MAMMARY GLAND

We have demonstrated that exposure to THC or CBN during gestation suppresses androgen production in male fetuses [18]. Androgen exposure during gestation affects mammary gland development. In fetal male mice, within 36 hr of the initiation of fetal T production the mammary gland becomes sensitive to androgens, which results in separation of the epidermal bud from the mesenchyme, and ultimately, in necrosis [52]. This action of androgen occurs about day 13.5 of gestation, and androgen sensitivity of the mammary tissue is no longer apparent after day 15 [52]. It is, therefore, possible that the subsequent morphology and hormonal responsiveness of the mammary gland may be altered in the cannabinoid-exposed male. Since there have been reports of gynecomastia in human males who used marihuana [42], it is also conceivable that the cannabinoids can affect mammary development by direct actions on this tissue. Studies are presently underway to evaluate this possibility.

POSSIBLE MECHANISMS OF ACTION

It is possible that alterations in responsiveness to gonadotropins, either *in vivo* or *in vitro*, may reflect cannabinoid-induced alterations in gonadotropic action at the target tissue. It is also conceivable that cannabinoid exposure may have affected gonadal steroid feedback or pituitary gonadotropin release patterns. Cannabinoid-induced changes in the pulse frequencies, or duration [77,78], or perhaps, in the biological activity of LH, could have influenced the subsequent sensitivity of the testis to gonadotropic stimulation.

Cannabinoid influence on fetal and/or neonatal androgen production appears to be consistent with the observed effects of exposure to these substances. Certainly, it has been well-documented that the early hormonal milieu is critical for the establishment of sexual dimorphism in a number of physiological systems [41, 57, 58]. Hypothalamic nuclei regulating neuroendocrine and sexual functions are altered as a result of early gonadal steroid exposure [40, 41, 57, 58], and the reproductive structures are influenced, both in terms of morphology and function, by the fetal endocrine environment [12,84]. Androgen actions also affect the steroid and drug metabolizing enzymes in liver, and influence the development of immunoresponsiveness [11,50]. Obviously, if cannabinoids alter androgen production or actions during the masculinization of these systems, the long-term effects on hepatic and immune functions, such as those we have recently reported [26], are not surprising. Any long-term effects of cannabinoids on the pubertal and/or adult hormonal profile could also have an additional impact, by influencing the activational actions of the gonadal steroids on reproductive and non-reproductive systems [41, 57, 58].

The fact that estrous cyclicity (Dalterio, unpublished), and brain biogenic amines are also affected in female offspring perinatally-exposed to cannabinoids [25], does suggest that, either cannabinoids affect fetal or neonatal androgen production indirectly via interference with neuroendocrine functions, or, that these substances can directly affect several target areas independently, including the fetal and/or neonatal testis.

Certainly, there appears to be differences in the effects of cannabinoids, depending on the time of maternal exposure, and the particular cannabinoid administered. It may be that these differences represent cannabinoid-induced alterations in critical period phenomena during development, or perhaps, may be due to biphasic effects of these compounds on testicular steroidogenesis [17,23]. Thus, depending on the dose or timing of exposure, fetal and/or neonatal androgens may have been increased and/or decreased, as we have reported for adult mice [21].

In comparing these data from our laboratory with those of others investigating perinatal manipulations, certain similarities in the effects seem apparent. Protein malnutrition during prenatal periods reduced *in vitro* T production by neonatal rat testes [38], and maternal stress has been shown to reduce fetal T levels [82], as does THC and CBN [18], but did not affect subsequent testes weights [81]. In other studies, maternal stress has been associated with changes in

reproductive structures [15], and in brain catecholamines [62]. In addition, we reported that perinatal ethanol exposure decreased adult plasma T, as well as *in vitro* T production, and testicular weights [19].

CONCLUSIONS

Several lines of evidence suggest that the effects of perinatal cannabinoid exposure are most likely due to complex pharmacological actions, and not, simply, the result of stress, nutritional, toxic or behavioral factors. Differences between the long-term effects of the various cannabinoid products are apparent, and critical periods seem to exist for their developmental disruptions [24,25]. Strain differences in the behavioral responses to THC have been reported in adult mice [68], and pre-treatment with SKF-525A or phenobarbital, which influence THC metabolism, potentiated teratogenic effects in mice [59]. In another study, the long-term disruptions in reproductive functions in adult male mice perinatally exposed to THC could be prevented by concomitant CBC exposure [43]. These findings may indicate that CBC competitively interacts with an as yet unidentified receptor site or sites, or that CBC alters THC metabolism [43]. In our studies, the non-psychoactive CBN and CBD also produce long-term changes in reproductive functions in male and female offspring [16, 24, 25]. In addition, studies in adult male mice have suggested that there are differential effects among cannabinoids on testicular steroidogenesis [16,23]. It would be difficult to account for such findings without concluding that cannabinoids have specific effects on the development of biological systems.

Cannabinoid influences on maternal factors, including the uterine environment, nutritional intake, or maternal behaviors probably do interact with those directly attributable to the pharmacological effects of the cannabinoids themselves. Of course, it is important to determine, experimentally, the relative impact of such maternal factors in the overall actions of cannabinoids on development. However, it would seem that, if a drug affects maternal factors, that these must also be regarded as drug actions with possibly important consequences for fetal or later development. Thus, the relevance of maternal variables in the etiology of cannabinoid-induced teratogenesis, perhaps, need to be considered as possible mechanisms of cannabinoid action, not simply as extraneous variables, which need to be eliminated.

Cannabinoids represent a unique class of compounds. Their highly lipophylic property complicates drug administration procedures, as well as the determination of precise time courses or tissue concentrations at potential target sites. In addition, the insoluability of these substances in aqueous media has posed problems in the design and interpretation of data from *in vitro* experiments, the preparation of suspension vehicles, and in the determination of route of administration for *in vivo* studies. Cannabinoid effects can be biphasic, and dose effects are often absent. Nonetheless, the evidence to date strongly suggests that the cannabinoids, especially THC, are embryocidal, and that these substances affect the fetal endocrine environment. Maturational indices appear to be affected, and cannabinoid-induced alterations in brain biochemistry may mediate long-term effects on behavior, and possibly also neuroendocrine functions. While some of the consequences of perinatal cannabinoid exposure may be partly related to maternal effects, it seems probable that these substances also directly affect the developing fetus at a number of sites, and by several different mechanisms. Certainly, the review of the literature to date no longer confines effects of perinatal cannabinoid exposure to laboratory animals, but now also includes effects on the human neonate. Clearly, there are strong indications that perinatal cannabinoid exposure may also have long-term, perhaps subtle, effects on development in the human.

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angioedema, wheezing, laryngeal edema, or hypotension). Such patients do seem to be at increased risk of a similar reaction to cephalosporin. Most patients with penicillin allergy, however, have a rather vague history of rash, usually of the delayed variety. They are no more at risk of severe, IgE-mediated reactions than patients without such a history. Alternative antibiotics, such as vancomycin or erythromycin, should be used if there is any possibility of a history of an immediate-type allergic reaction to a penicillin.

Dr. Saxon has focused on our data on the teichoic acid antibody, which must indeed, although strongly suggestive, be viewed as preliminary evidence that a positive test is associated with metastatic seeding during bacteremic staphylococcal infections. Like all other tests, the teichoic acid–antibody assay needs to be used with its benefits and limitations kept clearly in mind. A prospective study of whether patients whose treatment is managed with the benefit of information yielded by the assay do better than those cared for without such information is definitely needed and is now feasible, since sufficient quantities of standardized antigen are commercially available.

Dr. Rahal's points are similarly cogent, and I would agree that there is no method by which a metastatic abscess secondary to *S. aureus* bacteremia can be absolutely excluded after two weeks of intravenous therapy. However, since some authorities suggest that a two-week course of therapy is enough for a clinically uncomplicated episode of staphylococcal bacteremia, a test that helps to distinguish between patients with and without metastatic complications should be considered an extremely useful adjunct to clinical decision making, unless proved otherwise. Again, a prospective study of the usefulness of the teichoic acid–antibody test in these patients is needed to assess the expense of the assays and outcome data and the expense (in this age of skyrocketing health costs) of arbitrarily treating all patients with bacteremia parenterally for four weeks. The suggestion that a course of oral therapy be continued in all patients who seem to have no complications at two weeks also needs study, but such a course may be a prudent approach until more data are available on these controversial questions.

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HUMAN PLACENTAL TRANSFER OF CANNABINOIDS

To the Editor: Cannabis and its derivatives have been shown to cross the placenta in pharmacologic studies of animals, but concentrations were found to be lower in fetal than in maternal tissues.[1-4] No comparable information has been available regarding fetal blood or tissue levels of cannabinoids associated with marijuana smoking by pregnant women. We studied women who reported heavy marijuana consumption at the end of pregnancy, in order to determine the relative levels of delta-9-tetrahydrocannabinol (Δ9-THC) and its principal metabolite, 11-nor-delta-9-carboxylic acid (9-carboxy-THC), in the mother and fetus.

Ten women who reported that they smoked marijuana daily in the third trimester of their pregnancy were identified by personal screening interviews in two Denver public hospitals. The highest consumption reported was five marijuana cigarettes per day.

At delivery, blood samples were drawn from the mother's arm, and cord-blood specimens were taken from the umbilical remnant before delivery of the placenta. The two specimens were collected within 10 to 20 minutes of one another and analyzed at the University of Utah for Δ9-THC and 9-carboxy-THC by gas chromatography–mass spectrometry according to the Foltz method.[5]

Six of the 10 women and 3 of their infants had detectable levels of Δ9-THC (Table 1). The level of Δ9-THC in maternal blood was 2½ to 6 times greater than in cord blood. All maternal and cord-blood samples had detectable levels of the metabolite 9-carboxy-THC. Maternal levels of the metabolite were from four to seven times higher than cord levels. The observation that levels of 9-carboxy-THC were higher than those of Δ9-THC was consistent with reports that concentrations of the metabolite were higher several hours after smoking.[6]

The findings indicate that cannabinoids are detectable in fetal cord blood at delivery when there are appreciable levels in the mother's plasma. The data from this study are limited to the difference in marijuana components in the infant at term and may not be applicable to other periods of gestation. Furthermore, they do not provide information about the maternal/fetal ratios that are present closer to the time of peak exposure (seven to eight minutes after beginning to smoke a marijuana cigarette[6]).

Table 1. Serum Levels of Tetrahydrocannabinol (Δ9-THC) and Its Metabolite (9-carboxy-THC) in Maternal Blood and Fetal Cord Blood.*

Case No.	Δ9-THC (ng/ml)		9-carboxy-THC (ng/ml)		Hours since Smoking
	Maternal	Fetal	Maternal	Fetal	
1	6	1.0	125	18	5
2	1.2	0.3	39	5.2	10
3	1.0	<0.2	31	7.2	12
4	0.8	0.3	19	3.5	19
5	0.4	<0.2	3.8	2.3	
6	<0.3	<0.2	14	1.8	12
7	<0.2	<0.2	18	7.1	17
8	<0.2	0.4 †	3.9	0.9	24
9	<0.2	<0.2	8.1	1.5	26
10	<0.2	<0.2	2.3	0.4	12

*The lower limit of sensitivity on gas chromatography–mass spectrometry was 0.2 ng per milliliter for Δ9-THC and 0.1 ng per milliliter for 9-carboxy-THC.

†The laboratory had reservations regarding the accuracy of this value.

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VITAMIN A TERATOGENICITY

To the Editor: I was pleased by the excellent review of vitamin A and retinoids by Goodman in the April 19 issue.[1] However, I was greatly distressed that the article did not mention the teratogenic nature of vitamin A or retinoids taken in therapeutic doses. Almost half the persons who take such doses are women of childbearing age.[2] Vitamin A in the form of isotretinoin (e.g., Accutane, or 13-*cis*-retinoic acid) has been clearly shown to be teratogenic in human beings.[2-4] The risk of spontaneous abortion or congenital malformations may be as high as 100 per cent if the drug is taken in therapeutic doses into the second month of gestation. Absence or hypoplasia of the external ears, central-nervous-system anomalies (including microcephaly and hydrocephaly), cortical blindness, and severe congenital heart disease have been reported singly and in combination.[2,3] These anomalies were predictable from animal studies,[3] and use of the drug during pregnancy is clearly contraindicated in the information for patients and prescribing information for physicians. I was surprised that this potentially devastating complication of vitamin A therapy was not brought to the attention of practitioners in such an excellent review article.

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Induction of sister-chromatid exchanges in heroin-cannabis, heroin and cannabis addicts

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Summary

The aim of this study was to determine the frequency of sister-chromatid exchanges (SCEs) in heroin-cannabis, heroin and cannabis addicts. The group of 84 subjects consisted of 42 controls, 16 heroin-cannabis addicts, 12 heroin addicts and 14 cannabis addicts.

The mean number of SCEs/cell was 12.95 in heroin-cannabis addicts, 12.05 in heroin addicts and 11.99 in cannabis addicts. These values are significantly ($P < 0.002$) higher than the mean values found in controls. This increase in SCEs may be related to reduced DNA repair in chronic drug addicts, which would allow the fixation or retention of a greater fraction of the DNA lesions caused by normal environmental exposure.

The cellular site of mutagens and carcinogens is thought to be nuclear DNA. It has been well established that many compounds which damage DNA induce SCEs (Faed and Mourelatos, 1978). Because of its sensitivity and ease of performance, the SCE assay is commonly used to assess the DNA-damaging potential of suspected mutagens. The purpose of this study is to demonstrate how the SCE analysis in human lymphocytes can serve as a rapid and sensitive genetic screening method in cases of chronic drug addiction.

This study refers to a group of 84 volunteers. Some of the subjects had received medically prescribed drugs and the addicted subjects had taken no drugs (of abuse), other than those indicated. The group consisted of 42 controls with a mean age of 26.5 years, 12 heroin addicts (8 males, 4 females) with a mean age of 28.33 years and a mean period of heroin addiction of 6.29 years, 14 cannabis addicts (11 males, 3 females) with a mean age of 28.91 years and a mean period of addiction to cannabis of 6.32 years and 16 heroin-cannabis addicts (15 males, 1 female) with a mean age of 27.68 years and a mean period of addiction to heroin and cannabis of 9.06 years.

The control subjects were divided into 3 groups, the numbers of males and females equalling those in the drug addict group to which they were being compared. Both controls and drug addicts groups include members with similar habits of tobacco, alcohol and coffee consumption.

The daily heroin dose varies from addict to

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dict within the range 30 mg (minimum) to 2 g aximum), while the daily cannabis dose ranges om 450 mg (minimum) to 6 g (maximum). We nnot be sure about the purity of heroin and nnabis taken by some participants during their ng period of addiction.

Lymphocyte cultures were prepared by adding drops of whole blood from each participant to 4 l of chromosome medium 1A (Gibco).

Air-dried preparations were made and stained y the FPG procedure (Perry and Wolff, 1974). he cultures were incubated for 72 h at 37°C and ietaphases collected during the last 2 h with olchicine at a concentration of 0.3 μg/ml. To emonstrate SCEs, 4 μg/ml 5-bromodeoxyuridine BrdUrd) was added during the last 48 h of culure. Throughout the experiment, all cultures were naintained in the dark to avoid photolysis of 3rdUrd. The chromosome analyses were performed blind.

For the statistical evaluation of the experimental data, the chi-square test was used for the cell-kinetic comparisons, whereas for the SCE-frequencies, Student's *t*-test was performed to determine whether any values deviated significantly ($P < 0.01$) from the appropriate controls.

Heroin addicts were found to have a mean of 12.05 SCEs/cell, cannabis addicts had a mean of 11.99 SCEs/cell, while heroin-cannabis addicts had a mean of 12.95 SCEs/cell. These values are significantly ($P < 0.002$) higher than the mean values of corresponding controls (Table 1). In spite of the significant ($P < 0.001$) increase in SCEs in cannabis addicts, compared with controls, the range of 3–24 SCEs per metaphase is considered to be very close to normal (Table 1). Ranges of 1–21 SCEs/cell are considered to be normal for human lymphocytes at BrdUrd concentrations of up to 10 μg/ml (Deknudt and Kamra, 1983). However, the findings concerning cannabis addicts may also seem to be biologically relevant, since a cell division delay, although non-significant ($P > 0.05$), was observed in cultures from heroin-cannabis, heroin and cannabis addicts compared with cultures from the corresponding controls (Table 1). Chemically induced cytotoxicity is clearly manifested as a change in the relative proportions of cells in their first, second and subsequent divisions (Morimoto and Wolff, 1980). Studies in search of a relationship between SCE induction and other expressions of genotoxicity have found a positive relationship between SCEs and alterations in cell

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TABLE 1

INDUCTION OF SISTER-CHROMATID EXCHANGES[a] IN HEROIN ADDICTS, CANNABIS ADDICTS AND HEROIN CANNABIS ADDICTS

	Subjects (*n*)	Mean age	Mean period of addiction (years ± S.E.M.)	Mean SCEs/cell ± S.E.M. (range)	*t*	*P*	PRI[b]
Heroin addicts	12	28.33	6.29 ± 1.92	12.05 ± 0.70 (3–30)	3.73	< 0.002	1.98
Controls	12	26.7		9.22 ± 0.28 (0–19)			2.13
Cannabis addicts	14	28.91	6.32 ± 1.43	11.99 ± 0.42 (3–24)	4.18	< 0.001	2.01
Controls	14	27.1		9.31 ± 0.47 (0–21)			2.12
Heroin and cannabis addicts	16	27.68	9.06 ± 1.50	12.95 ± 0.76 (3–38)	4.14	< 0.001	1.95
Controls	16	25.7		9.51 ± 0.32 (1–22)			2.11

[a] Each subject's SCE value was established as the mean of 30 counted metaphases (*n*).

[b] For proliferation Rate Index (PRI) 100 cells, at least, were scored. PRI was calculated as $(1M_1 + 2M_2 + 3M_{3-})/100$, where M_1 the percentage value of cells in the 1st, M_2 in the 2nd and M_{3-} in the 3rd and higher divisions.

cycle kinetics. These findings suggested that a common element, possibly a type of DNA damage, produced by certain agents was responsible for inducing SCEs and reducing cell growth (Morimoto and Wolff, 1980; Morris and Heflich, 1984).

To date, the available literature does not report any clastogenic effect produced by cannabis, with the exception of the report by Chiesara et al. (1983) who found increased chromosome aberrations in marijuana addicts. A clastogenic effect of heroin has been described in pregnant monkeys and their offspring by Fischman et al. (1983).

Since there is already some evidence that chronic opiate addicts have a reduced capacity for DNA repair (Shafer et al., 1983), and marijuana addicts an increased chance of chromosome damage (Chiesara et al., 1983), we propose that the increase in SCEs observed in this study may be related to the reduced DNA-repair capacity which such chronic drug addicts may have acquired. The genetic material is constantly attacked by various environmental factors and these premutation defects have to be continuously corrected by the natural repair system. Reduced DNA-repair capacity in chronic drug addicts, as in those currently studied, would allow the fixation or retention of a greater fraction of DNA lesions caused by normal environmental exposure. It has been proposed that the induction of SCEs may be related to the repairability of DNA lesions prior to or during the replication process (Shafer et al., 1983; Dozi-Vassiliades and Mourelatos, 1985).

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THE EFFECTS OF MARIJUANA SMOKE ON GAS EXCHANGE IN OVINE PREGNANCY

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Summary

The effects of marijuana smoke on maternal respiratory rate and gas exchange were examined in nine chronically instrumented, late gestation ewes carrying singletons. The magnitude of exposure was randomly varied producing peak plasma levels of delta-9-tetrahydrocannabinol (Δ-9-THC) ranging from 0 to 161 ng/ml. Δ-9-THC levels, respiratory rate and arterial blood gas tensions were monitored before and for two hours after inhalational exposure. When compared to placebo, marijuana smoke produced a dose dependent and sustained decrease in maternal respiratory rate and arterial oxygen tension without evidence of either systemic acidosis or carbon dioxide retention. A logarithmic relationship was observed between the blood level of Δ-9-THC and the change in respiratory rate. The change plateaued at 30% of control at levels above 80 ng/ml. However, the relationship between the blood level of Δ-9-THC and the change in arterial oxygen tension had a linear fit with a maximum decrease of 45% at a blood level of 160 ng/ml. No change was detected in minute ventilation. Fetal oxygen tension fell significantly and remained depressed after maternal values had returned to control levels. We conclude that, in this species, inhalational exposure to marijuana smoke induces a prolonged maternal ventilation/perfusion imbalance and limits fetal oxygen availability by one or more mechanisms.

The physiological changes which accompany marijuana smoking during pregnancy are of societal concern as little is known about the effects of repetitive exposure on fetal well-being (1, 12). The recent development of a simple system for reproducible inhalational exposure in large animals (2, 3) has allowed us to begin to assess the effects of both acute and chronic exposure on the maternal fetal unit using the chronically instrumented pregnant ewe animal model (2, 8). During our initial dose ranging studies, we monitored respiratory rate and arterial blood gas tensions in the mother and fetus, as initial studies using nonpregnant animals suggested that substantial effects on pulmonary gas exchange should be present. This communication reports our findings in nine late gestation animals randomly exposed to varying doses of marijuana smoke. The data indicate that maternal respiratory rate and arterial oxygen tension are valuable indicies of the intensity of exposure and that marijuana smoke exposure in late gestation impairs pulmonary gas exchange in this species.

Materials and Methods

Nine singleton pregnancies were surgically prepared for chronic study between the 105th and 130th day of gestation (term is 147 days). Details of the preparation appear elsewhere (2, 8). Briefly, polyvinyl sampling catheters were placed in the maternal and fetal inferior vena cava and distal aorta and a silastic T tube was implanted in the maternal trachea for smoke exposure. In addition, extradural stainless steel electrodes for monitoring electrocortical activity were placed over the fetal parietal cortex and either the umbilical or uterine circulation was instrumented to estimate flow. For this purpose a Dienco electromagnetic flow transducer was placed on the main uterine artery supplying the pregnant horn or alternately on the fetal common internal iliac artery. It is unlikely that the additional instrumentation had any systematic effect on the changes observed in either arterial blood gas tensions or maternal respiratory rate following maternal exposure to marijuana smoke.

After a 3 to 5 day recovery period, the animals were exposed every third day in random order to variable amounts of smoke from either a marijuana placebo cigarette or a marijuana cigarette containing 2.64% Δ-9-THC. The magnitude of exposure was controlled by varying the exposure time between 5 and 13 minutes. The cigarettes were prehumidified and burned in a small, hand-held cylinder which delivered fresh smoke through the tracheal T tube with each inspiration. This system produces an appearance and decay curve of Δ-9-THC in arterial plasma similar to that observed with human smoking while minimizing both irritative disturbances in respiratory pattern (coughing and/or breath holding) and the production of side stream (2, 3, 13). On each day of exposure, the animal's respiratory rate was monitored continuously with a pneumotachometer for at least 90 minutes before and 120 minutes after smoking with blood sampling at specified intervals. Samples for Δ-9-THC levels were obtained prior to, immediately after, and 2 hours post-smoke from the mother and prior to and 2 hours post-smoke from the fetus as earlier kinetic studies indicated peak and trough levels occurred in the two compartments at these times (3). Arterial samples for measurement of pH and gas tensions were obtained anaerobically from the mother 60, 30 and 2 minutes prior to smoking, immediately post-smoke, and at 15, 20, 25, 30, 40, 60 and 120 minutes after the initiation of smoking. Fetal samples were drawn 30 minutes before and 15 and 120 minutes after the initiation of smoking to assess the relative effect on fetal oxygenation of changes in maternal gas tension versus those of placental perfusion imbalance. Plasma levels of Δ-9-THC were measured by radioimmunoassay (9). Whole blood pH, pO_2, pCO_2 were measured immediately with a precalibrated Radiometer microblood gas analyzer at 38°C using Clark and Severinghaus electrodes. Regression, using the least squares method, was employed to assess dose-response relationships while the unpaired t test and repeated measures were used to detect between and within group differences over time. A significant difference was defined as a p value of < 0.01.

On six separate occasions three additional animals plus a single animal from the above experimental group were studied to assess the effects of exposure on minute ventilation which was estimated intermittently before and after smoking by measuring expiratory minute volume. This was accomplished using a low resistance, one-way valve and a 50 L Tissot spirometer which was attached to the side arm of the tracheal T tube after balloon occlusion of the proximal tracheal arm.

Results

The nine animals weighed between 50 and 61.4 kg (mean = 55.5±1.4 kg) at

the onset of study and maintained or increased their weight over time. Thirty-one studies were conducted between the 110th and 136th day of gestation (mean = 125±2 days). Based on magnitude of exposure they were divided into high (entire 2.64% cigarette), low (0.25-0.5 of a 2.64% cigarette), and placebo (0.25 to entire placebo cigarette) dose groups with 11, 11 and 9 studies in each of the three groups respectively. In the high exposure group, peak maternal blood levels of Δ-9-THC ranged between 62 and 161 ng/ml (mean = 100±11 ng/ml) while the range was 9 to 55 ng/ml (mean = 28±4 ng/ml) in the low exposure group. Values were consistently below the detection threshold after exposure to placebo smoke. There were no significant between group differences in either gestational age or maternal weight and the number of smoke exposures ranged between two and six per animal. The variability in the number of exposures was due in large part to an unanticipated high incidence of premature labor.

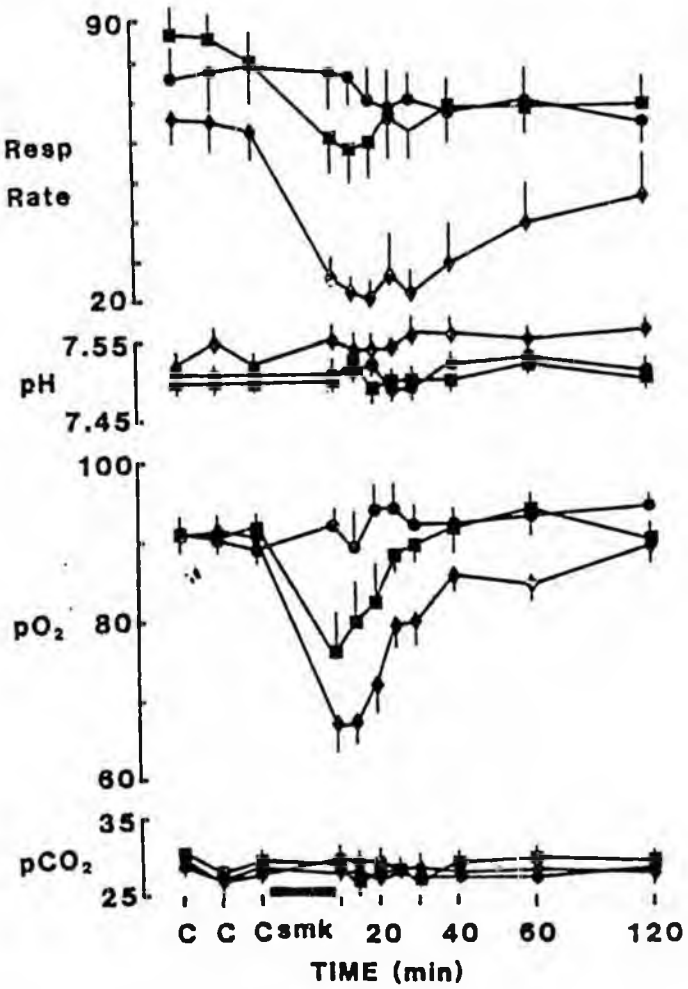

FIG. 1

The longitudinal changes observed in maternal respiratory rate, pH, pO_2 and pCO_2 with exposure to placebo (●), low dose (■), or high dose (◆) marijuana smoke. Data shown as mean ± s.e.m.

affects of cannabis extracts and constituents (bronchodilation and changes in respiratory rate) have been described in anesthetized experimental animals (6, 7, 10, 15), the specific issue of gas exchange has not been previously examined in detail and there are no data other than the preliminary report of Niederreither et al. (13) that deals with the effects of inhalational exposure on blood gases in an unanesthetized chronic model. In the human marijuana smoking has been reported to have either no effect or to increase minute ventilation without evidence of CO_2 retention and to decrease airway resistance (4, 5, 14, 16). However, its impact on ventilation/perfusion balance and oxygenation has not been assessed. Support for the possibility that marijuana smoking disrupts ventilation/perfusion balance in the human as well as the sheep is found in the pharmacokinetic studies of Perez-Reyes and associates (14). They noted that plasma levels of Δ-9-THC peaked in their volunteers before they finished smoking. While they felt that this probably was due to subtle changes in smoking technique for the latter half of a cigarette, they could not detect any differences in smoking technique. Although they did not consider the possibility, a disruption in ventilation/perfusion balance during the smoke would explain their findings as it would impair drug uptake during the remainder of the smoke. Therefore, peak levels would be reached during rather than at the end of the smoke. It is also of note that in the initial pharmacokinetic studies of Abrams et al. (3) Δ-9-THC levels peaked in at least three of their ewes before the end of smoke exposure. Thus, the ovine data coupled with evidence from human pharamacokinetic studies suggests that the issue of ventilation/perfusion imbalance following marijuana smoking deserves further evaluation in the human.

The data from the present study demonstrates a clear relationship between the magnitude of exposure, as measured by the plasma Δ-9-THC level at the end of smoking, and changes in the physiological parameters of maternal respiratory rate and arterial oxygen tension. Both relationships have high r values and appear to hold true both within and between animals. As one might anticipate, maternal weight did not affect the relationships and, with exposure every third day, there was no evidence of tolerance. Thus, if our initial experience is confirmed, the impact of intermittent inhalational exposure on one or both of these parameters can be used during experiments to assess the intensity of exposure and perhaps to standardize it both within and between animals. The same may be true for the induced inspiratory pause which has also been noted by others (11).

These dose ranging experiments also confirm that placental transfer of Δ-9-THC occurs in this species and that, despite its highly lipophilic nature, fetal levels only reached 0.3 of maternal levels at 2 hours. Despite the wide range in the magnitude of exposure in the present study, this value for the feto-maternal ratio is quite similar to the mean value of 0.298 achieved with standardized dosing in an earlier kinetic study (3).

Finally, these data indicate that, in this species, maternal inhalational exposure to marijuana smoke in late gestation limits fetal oxygen availability by at least one mechanism. Namely, by producing a significant and prolonged decrease in maternal arterial oxygen tension that is dose dependent and often lasts for more than 30 minutes. Although this decrease in maternal oxygen tension results in an average, dose dependent decrease of only 2-5 mmHg in fetal arterial oxygen tension, it is important to remember that at normal fetal oxygen tensions of 20-25 mmHg and with the high oxygen affinity of fetal hemoglobin, this decrease in fetal oxygen tension represents a decrease in oxygen contents of between 2 and 4 ml of oxygen per 100 ml of blood. Also of interest was the finding that fetal arterial oxygen tension remained depressed long after maternal arterial oxygen tensions had returned

to control levels. This cannot be explained by the data available and suggests that additional direct or indirect effects may also exist.

Acknowledgements

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EFFECT OF MARIJUANA USE IN PREGNANCY ON FETAL GROWTH

ELIZABETH E. HATCH AND MICHAEL B. BRACKEN

Hatch, E. E., and M. B. Bracken (Yale U. School of Medicine, New Haven, CT 06510). Effect of marijuana use in pregnancy on fetal growth. *Am J Epidemiol* 1986;124:986–93.

In a prospective study of 3,857 pregnancies ending in singleton live births at Yale-New Haven Hospital, New Haven, Connecticut, in 1980–1982, 9.5% of mothers reported using marijuana (4.1% occasionally and 5.4% at least 2–3 times monthly). Among white women, regular use was associated with an increased risk of delivering a low birth weight (<2,500 gm) infant (odds ratio (OR) = 2.6, 95% confidence interval (CI) = 1.1–6.2) and small for gestational age infant (OR = 2.3, 95% CI = 1.3–4.1) after adjustment for other risk factors. Nonwhite marijuana users were not at further increased risk for delivering a low birth weight or small for gestational age infant beyond the elevated rates of these conditions already experienced by nonwhites in general. Marijuana use was also related to preterm delivery (gestational age <37 weeks from last menstrual period) in white women (OR = 1.9, 95% CI = 1.0–3.9) but not nonwhite women. Occasional use was unrelated to the risk of low birth weight, small for gestational age, or preterm delivery.

birth weight; delivery, preterm; infant, small for gestational age; marijuana; pregnancy

Studies of pregnant women (1–5) have found that at least 10 per cent report some marijuana use during pregnancy, however, the effects on pregnancy outcome are still uncertain. Delta-9-tetrahydro-cannabinol; a major component of marijuana, has been shown (6, 7) to cross the placenta in rats, mice, and dogs. Less of the drug is absorbed by the fetus than by the mother, but clearance is also slower. The cannabinoids from marijuana tend to be stored in fat and may be detected in body tissues for up to 30 days following administration of a single dose (8), indicating the potential for prolonged fetal exposure in regular marijuana users.

Reported developmental effects in animals include increases in fetal and embryonic mortality, fetal resorption, reduction in birth weight, growth retardation, and neurobehavioral abnormalities (6).

There have been a few case reports in humans which implicate marijuana as a teratogen (9–11), however, in each case the mothers had used multiple drugs during pregnancy. Several cases of a "fetal alcohol-like" syndrome were recently described (12, 13) in infants whose mothers used marijuana but denied alcohol use during pregnancy.

Results of epidemiologic studies are in-

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Abbreviations: CI, confidence interval; OR, odds ratio; RR, risk ratio.

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way by which it could affect fetal growth. Cannabinoids are also metabolized more slowly than components of cigarette smoke (7), which might explain why the effects on the fetus were found at lower levels of the drug than those seen for tobacco smoking.

It is of concern that nearly 10 per cent of the women in our study reported some marijuana use. Because the drug is not legal, this may be an underestimate of the true extent of marijuana use during pregnancy, although it is in close agreement with the 10–14 per cent marijuana use reported during pregnancy in similar populations (4, 5). Definitive conclusions about the effect of marijuana on pregnancy outcome cannot yet be reached. Further research should attempt to collect detailed information on marijuana use at several times during pregnancy, and, if possible, should verify self-reports with biochemical screens. The possibility that marijuana use may result in features similar to those seen in the fetal alcohol syndrome (4, 12) should also be explored.

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study (5), while another study (4) did find a reduction in mean birth weight, and yet another study (15) found an increased rate of preterm delivery but not low birth weight among marijuana users. There are several possible explanations for these inconsistent results. In the negative study by Linn et al. (5), marijuana use was treated as a dichotomous variable which may have obscured any effect in the regular users. The data from the present study were collected prospectively, shortly after the first prenatal visit, whereas the data in the study by Linn et al. (5) were collected after delivery. Animal studies have indicated that marijuana use during early pregnancy may have a greater effect on the developing fetus than later on (6). If this is true in humans, collection of data early in pregnancy may result in a more valid estimate of effect. Finally, an interaction between race and marijuana use was not considered in the study by Linn et al. (5).

Gibson et al. (15) found that heavy marijuana use increased the risk of preterm delivery but had no effect on birth weight after preterm infants were excluded from the analysis. Our analysis controlled for gestational age, instead of excluding preterm infants, which may account for the different results.

In summary, our study found an increased risk of delivering low birth weight, small for gestational age and preterm infants among white women who reported regular marijuana use during pregnancy. Certain limitations of our study should be noted in interpreting this finding. Of foremost concern is that the result may be due to unidentified confounding variables such as unreported psychoactive drug use, poor maternal health, an inadequate diet, or some other correlate of lower socioeconomic status. Other potential problems with the study include possible misclassification of both marijuana use and confounding variables such as cigarette smoking, and assessment of marijuana use at only one point in pregnancy. The overall rate of low birth weight in our sample is somewhat lower than the rates for the United States as a whole (21). This is presumably because our study is based upon women who seek prenatal care, whereas the US rates are based on all deliveries. However, this difference is unlikely to bias our assessment of the effect of marijuana use. It should also be noted that the outcomes of low birth weight, small for gestational age, and preterm births are not entirely independent. Low birth weight infants are a heterogeneous group, consisting of some who are low birth weight solely because of a premature delivery, and some who are delivered at term, but whose growth has been retarded in utero. In our study, among white infants classified as low birth weight (n = 88), 53.4 per cent were preterm, 35.2 per cent were small for gestational age, 10.2 per cent were both, and 1.1 per cent (n = 1) were neither. There were an additional 115 infants who fell above the 2,500 gm cutoff point but who were classified as small for gestational age. Among infants delivered prematurely (n = 126), 43.1 per cent fell into the low birth weight category, and 7.1 per cent were also classified as small for gestational age. Because these outcomes are not mutually exclusive, we attempted to determine if the effects that were found were due primarily to one of the outcomes. We saw no evidence for this in our data.

It is worth noting that in our study, the risk of having a small for gestational age and/or low birth weight infant was more strongly associated with regular marijuana use than with smoking 20 or more cigarettes daily, and that the marijuana effect was in addition to the effect of cigarette smoking, which is an established risk factor for those conditions. Since the effect of marijuana on fetal growth is occurring at much lower levels of use than the corresponding effects due to tobacco, it is probably not due to the carbon monoxide contained in smoke, which is often implicated as the causal agent in fetal growth retardation due to tobacco smoking (7). Marijuana use has been shown to alter hormonal levels (7), which may be an indirect path-

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TABLE 4

Odds ratios for variables significantly related to delivery of low birth weight and small for gestational age infants to white women at Yale-New Haven Hospital, 1980–1982*

Variable	Odds ratio	95% confidence interval
Low birth weight		
Frequency of marijuana use		
Occasional†	0.3	-2.8
Regular‡	2.6	1.1-6.2
20+ cigarettes/day vs. none	1.5	0.9–2.4
Nulliparity	1.8	1.1–3.1
Small for gestational age		
Frequency of marijuana use		
Occasional	1.3	0.6–2.9
Regular	2.3	1.3–4.1
20+ cigarettes/day	1.9	1.4–2.4

* Adjusted for other variables in the model.
† Occasional use = once per month or less.
‡ Regular use = 2–3 times per month or more.

ally variables which significantly predicted the occurrence of a preterm birth were race (for nonwhites vs. whites, OR = 1.8; 95 per cent CI = 1.3–2.5) and education, which was inversely related to the risk of preterm delivery (OR = 1.3 for a reduction of four years of education). The adjusted odds ratio for regular marijuana users from the final model was 1.5 (95 per cent CI = 0.9–2.5). The model was fitted separately for white women in further analyses, and the association of regular marijuana use and preterm delivery was of borderline significance (OR = 1.9, 95 per cent CI = 1.0–3.9).

Multiple linear regression was used to estimate the effect of marijuana use on mean birth weight, using all variables listed above in the full model. The interactions between marijuana use and tobacco and alcohol were not significant ($p > 0.50$) and were dropped from the model. The interaction with race was also not significant ($p = 0.10$) and was dropped. Other variables not significantly related to birthweight were history of induced abortion, alcohol consumption, education, and maternal age, whereas caffeine use was significantly related to a reduction in mean birth weight. Neither category of marijuana use was significantly related to mean birth weight in the final model (F ratio = 0.91, $p = 0.40$; for occasional users, $\beta = +1$ gm, and for regular users, $\beta = -44$ gm). However, when models were fitted separately for white women in exploratory analyses, regular marijuana use was related, although not quite significantly, to a reduction in mean birth weight (F ratio = 2.7, $p = 0.07$; for occasional users, $\beta = -24$ gm; for regular users, $\beta = -97$ gm).

DISCUSSION

The results of this study indicate that white women who reported regular marijuana use during pregnancy had a significantly higher risk of delivering a low birth weight or small for gestational age infant. The risk of delivering prematurely was also elevated in white marijuana users, although this relationship was of borderline statistical significance. Equivalent effects were not observed among nonwhite marijuana users. It is not known whether these differential effects by race could be due to innate biologic characteristics. It seems more likely that the reporting of marijuana use was less accurate in nonwhites than in whites, resulting in a greater degree of misclassification which could explain the lack of an effect in nonwhites. If underreporting in nonwhites had been associated with other risk factors for the outcomes which were analyzed, this would have led to a more dramatic reduction in the odds ratios than if the underreporting had been entirely random. Alternatively, nonwhites have a much higher risk of these adverse pregnancy outcomes, and perhaps the effect of marijuana use is difficult to detect in the presence of other strong risk factors.

These results conflict with those of one

TABLE 3

Mean birth weights and per cent of infants classified as low birth weight, small for gestational age, and preterm, by frequency of marijuana use during pregnancy and by race: infants delivered at Yale-New Haven Hospital, 1980–1982

	Frequency of marijuana use		
	None	Occasional*	Regular†
Whites	(n = 2,778)	(n = 105)	(n = 122)
Birth weight (gm)			
Mean	3,455.1	3,424.2	3,268.0
SD‡	495.9	548.6	589.2
% <2,500 gm	2.7	1.9	8.2
% Small for gestational age§	4.9 (n = 2,733)	7.1 (n = 99)	12.5 (n = 120)
% <37 weeks‖	4.0	3.8	8.2
Nonwhites	(n = 706)	(n = 53)	(n = 86)
Birth weight (gm)			
Mean	3,147.9	3,136.1	3,108.6
SD	563.9	483.4	535.4
% <2,500 gm	9.2	5.7	9.3
% Small for gestational age§	8.2 (n = 685)	7.6 (n = 53)	6.0 (n = 84)
% <37 weeks‖	8.8	11.3	10.5

* Occasional use = once per month or less.
† Regular use = 2–3 times per month or more.
‡ SD, standard deviation.
§ The number of infants considered in the analysis of small for gestational age is lower due to the exclusion of 76 infants with a recorded gestational age greater than 44 weeks.
‖ Calculated from first day of last menstrual period.

race and marijuana use was of borderline significance (p = 0.06), therefore separate logistic models were fit for whites and nonwhites, as well as for both races combined. Variables not significantly related to the risk of low birth weight in any of the models were history of induced abortion, alcohol and caffeine use, education, and maternal age. Maternal age was also entered into the model as trichotomous variable (<20, 20–34, 35+ years), and as a continuous variable with both first and second order terms but it still did not contribute significantly to the models. When whites and nonwhites were considered together, the adjusted odds ratio for low birth weight in regular marijuana users relative to nonusers was 1.5 (95 per cent confidence interval = 0.8–2.8).

The odds ratios and 95 per cent confidence intervals from the final model for whites are shown in table 4. The risk of delivering a low birth weight infant in regular marijuana users relative to nonusers was significantly elevated, an odds ratio of 2.6, after adjustment for parity, cigarette smoking, and gestational age. Occasional use was not associated with low birth weight. In nonwhites, no effect of either category of marijuana use was found (for occasional users, odds ratio (OR) = 0.4, 95 per cent CI = 0.1–1.5; for regular users, OR = 0.7, 95 per cent CI = 0.6–1.8). The final models were also run excluding eight women with a known history of drug abuse, but this did not change the results.

For analyzing the proportion of infants who were small for gestational age, the same variables listed above were included in the initial models, with the exception of parity because adjustments for parity were made in classifying an infant as small for gestational age. Again, the alcohol-marijuana and cigarette-marijuana interactions were not significant and were dropped from the model, whereas the race-marijuana interaction was significant (p = 0.01). The results of the final model for whites are shown in table 4. Regular marijuana users had a significantly increased risk (OR = 2.3) of delivering an infant who was small for gestational age. The only other variable significantly associated with this outcome was cigarette smoking. In nonwhites, regular marijuana use was not associated with adverse fetal growth, the odds ratio for regular marijuana users being 0.6 (95 per cent CI = 0.2–1.6).

Race did not appear to modify the effect of marijuana use on preterm delivery. The

TABLE 4

Odds ratios for variables significantly rel delivery of low birth weight and small for ge age infants to white women at Yale-New Hospital, 1980–1982*

Variable	Odds ratio	95 confidence
Low birth weight		
Frequency of marijuana use		
Occasional†	0.3	0.0-
Regular‡	2.6	1.1-
10+ cigarettes/day vs. none	1.5	0.9-
Nulliparity	1.8	1.1-
Small for gestational age		
Frequency of marijuana use		
Occasional	1.3	0.6-
Regular	2.3	1.3-
10+ cigarettes/day	1.9	1.4-

* Adjusted for other variables in the mod
† Occasional use = once per month or le
‡ Regular use = 2–3 times per month or

only variables which significantly p the occurrence of a preterm birth w for nonwhites vs. whites, OR = 1. first CI = 1.3–2.5) and educatio was inversely related to the risk of delivery (OR = 1.3 for a reductio years of education). The adjusted o for regular marijuana users from model was 1.5 (95 per cent CI = The model was fitted separately f women in further analyses, and th tion of regular marijuana use and delivery was of borderline significa 1.9, 95 per cent CI = 1.0–3.9).

Multiple linear regression was mate the effect of marijuana birth weight, using all variab were in the full model. The int between marijuana use and tob alcohol were not significant ($p >$ (were dropped from the model. T

marijuana and tobacco and marijuana interactions were also tested initially.

Logistic regression models were fit to the data to estimate the effect of marijuana use on the proportion of low birth weight, small for gestational age, and preterm infants, controlling for potential confounding variables. Variables included in the initial models of low birth weight were maternal age (<20 years versus 20+ years), race (white versus nonwhite), parity (0, 1+ births, completed years of education, marital status (currently married versus not), history of induced abortion, alcohol consumption (none, <0.25 oz (<7.1 ml), ≥0.25 oz (≥7.1 ml) of absolute alcohol/day), number of cigarettes smoked per day in the first month of pregnancy, caffeine intake in mg per day, gestational age of the infant, and two-way interactions between alcohol, cigarette smoking, and race and the categories of marijuana use. The interaction between

TABLE 1

Associations between frequency of marijuana use during pregnancy and other maternal characteristics: infants delivered at Yale-New Haven Hospital, 1980–1982

Maternal characteristic	Total	Frequency of marijuana use (%)*		
		None	Occasional†	Regular‡
Age (years)				
<20	380	80.5	6.8	12.6
20–34	3,273	91.1	4.0	4.9
35+	204	98.5	1.0	0.5
Parity				
Nulliparous	1,770	87.9	5.4	6.8
One or more	2,087	92.7	3.0	4.3
Race				
White	3,005	92.5	3.5	4.1
Nonwhite	845	83.6	6.3	10.2
Education				
Less than high school	523	83.4	5.2	11.5
High school graduate or more	3,334	91.6	3.9	4.5
Marital status				
Married	3,014	93.8	3.0	3.2
Not married	840	78.7	8.0	13.3
Cigarette smoking				
None	2,658	94.2	3.0	2.8
1–10/day	623	82.8	6.5	10.8
11+/day	566	81.6	6.7	11.7
Alcohol (oz/ml)/day)				
None	1,190	94.7	2.4	2.9
<0.25 (<7.1)	2,352	90.1	4.7	5.2
≥0.25 (≥7.1)	315	77.8	5.7	16.5
Caffeine (mg/day)				
None	895	90.8	3.8	5.4
1–150	1,896	91.6	3.7	4.7
151–300	737	88.6	5.8	5.6
301+	329	87.2	3.3	9.4
Previous induced abortion				
Yes	819	82.3	7.1	10.6
No	3,038	92.7	3.3	4.0

* All differences between subgroups are statistically significant, $p < 0.0001$.
† Occasional use = once per month or less.
‡ Regular use = 2–3 times per month or more.

TABLE 2

Mean birth weights, gestational ages, and the per cent of infants classified as low birth weight, small for gestational age, and preterm by frequency of marijuana use during pregnancy: infants delivered at Yale-New Haven Hospital, 1980–1982

	Frequency of marijuana use		
	None (n = 3,490)	Occasional* (n = 158)	Regular† (n = 209)
Birth weight (gm)			
Mean	3,392.8	3,327.6	3,206.4
SD‡	524.7	530.7	573.7
Gestational age (weeks)			
Mean	40.0	40.2	39.8
SD	2.3	2.6	2.5
% <2,500 gm	4.0	3.2	8.6
% Small for gestational age§	5.6 (n = 3,424)	7.2 (n = 152)	9.8 (n = 205)
% <37 weeks‖	5.0	6.3	9.4

* Occasional use = once per month or less.
† Regular use = 2–3 times per month or more.
‡ SD, standard deviation.
§ The number of infants considered in the analysis of small for gestational age is lower due to the exclusion of 76 infants with a recorded gestational age of greater than 44 weeks.
‖ Calculated from first day of last menstrual period.

occasional users (once per month or less), and 3) regular users (2–3 times per month or more). We hypothesized that occasional users would not be at greater risk for adverse outcomes than nonusers, because the majority of these had used marijuana only once since conception. The remaining women who reported regular marijuana use were considered together in order to provide adequate statistical power for the multivariable analyses.

Crude mean birth weights and gestational ages, and the per cent of infants who were low-birth weight, small for gestational age, or preterm were computed within the categories of marijuana usage. Potential confounding variables were identified by assessing their association with both outcome variables and the categories of marijuana usage by means of chi-square tests (18). Three-way stratified analyses between marijuana use, covariates, and the outcome variables were performed to identify potential interactions. Multivariable analyses were conducted using linear regression (19) and logistic regression (20). Other covariates which were assessed include maternal age, race, parity, education, marital status, history of stillbirth, spontaneous abortion, or induced abortion, cigarette smoking, and average daily alcohol and caffeine intake. Race was treated as a dichotomous variable (white vs. nonwhite), since the majority (84 per cent) of nonwhites were black, and since the numbers of Hispanics and other races were too small to allow meaningful analysis. To identify the final models in both linear and logistic regression analyses, backwards stepwise variable selection (19, 20) was used and, at each step, the parameter estimates were analyzed to ensure that deletion of the variable did not change the estimates of marijuana use.

Results

The majority of the sample (n = 3,490 or 90.5 per cent) reported no marijuana use between the estimated date of conception and the date of interview. There were 158 women (4.1 per cent) who reported occasional use of marijuana and 209 women (5.4 per cent) who reported that they used marijuana 2–3 times per month or more, of whom 43 reported daily use that ranged from 1–5 times per day.

The association of marijuana use with other maternal characteristics is shown in table 1. Women who use marijuana during pregnancy were more likely to be young, nonwhite, nulliparous, and have less than high school education. They were also significantly more likely to report cigarette smoking, alcohol, and high caffeine use. A history of induced abortion was more common in marijuana users, whereas a history of previous stillbirth or spontaneous abortion was unrelated to marijuana use.

Mean birth weights, gestational ages, and the per cent of low birth weight, small for gestational age, and preterm infants according to frequency of marijuana use are shown in table 2. Women who report occasional use of marijuana have a reduced but not statistically significant, risk of low birth weight infants relative to nonusers. Regular users have an elevated risk of delivering a low birth weight infant (risk ratio (RR) = 2.1, 95 per cent confidence interval (CI) = 1.3–3.4) and/or a small for gestational age infant (RR = 1.7, 95 per cent CI = 1.1–2.6) relative to nonusers. The risk of a preterm delivery is also elevated in regular marijuana users (RR = 1.8, 95 per cent CI = 1.2–2.9). Mean birth weights decreased across the categories of marijuana usage, whereas there are no major differences in mean gestational age.

Preliminary stratified analyses suggested a possible interaction between race and marijuana use on the outcomes of mean birth weight, low birth weight, preterm delivery, and small for gestational age. Although nonwhites were both more likely to use marijuana and to deliver an infant with these adverse outcomes, the risk was not further increased in nonwhite marijuana users (table 3). Therefore, an interaction term between race and marijuana use was included in all initial models. Alcohol and

marijuana and tobacco an
teractions were also tested
Logistic regression mode

TABLE 1

Associations between frequency during pregnancy and other mat infants delivered at Yale-New 1980–1982

Maternal characteristic	Total	Freq Non
Age (years)		
<20	380	80.5
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35+	204	98.5
Parity		
Nulliparous	1,770	87.8
One or more	2,087	92.7
Race		
White	3,005	92.5
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Education		
Less than high school	523	83.4
High school graduate or more	3,334	91.7
Marital status		
Married	3,014	93.4
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Cigarette smoking		
None	2,658	94.1
1–10/day	623	82.2
11+/day	566	81.1
Alcohol (oz(ml)/day)		
None	1,190	94.1
<0.25 (<7.1)	2,352	90.2
≥0.25 (≥7.1)	315	77.8
Caffeine (mg/day)		
None	895	90.4
1–150	1,896	91.1
151–300	737	88.2
301+	329	87.2
Previous induced abortion		
Yes	819	82.2
No	3,038	92.1

* All differences between sub
nificant, $p < 0.0001$.
† Occasional use = once per
‡ Regular use = 2–3 times p

conclusive. The majority have reported some adverse effects of marijuana use including precipitate labor and meconium passage (3, 14), altered visual, tremor, and startle responses in neonates (1, 2), lower birth weight (4), increased frequency of preterm delivery (15), and shorter infant length at eight months of age (16). However, other studies have found no effect on birth weight (5, 15) or preterm delivery (5).

The present study is part of a series of analyses on various exposures during pregnancy and pregnancy outcomes. The association between reported marijuana use and the outcomes of low birth weight, small for gestational age, preterm delivery, and mean birth weight and gestational age are analyzed.

Materials and Methods

The study population consisted of all women who made a first prenatal visit to a private obstetric or midwifery practice, health maintenance organization, or hospital clinic in the greater New Haven, Connecticut area between May 12, 1980 and March 12, 1982 and who intended to deliver at Yale-New Haven Hospital. A total of 4,219 women had the study introduced to them by their health care provider, and 3,331 (85.7 per cent) agreed to be contacted by a member of our research staff. Of this number, 405 women did not meet the eligibility criteria for the study because: 1) they planned to deliver somewhere other than Yale-New Haven Hospital; 2) they demonstrated poor English language comprehension; 3) they were not pregnant at the time that the study interview was to be conducted; or 4) they were familiar with the study. In all, 4,926 eligible subjects were contacted regarding the research, and valid interviews were completed on 4,186 (85 per cent) of those contacted. The majority of women (76 per cent) were interviewed before the 20th completed week of gestation. Of the original 4,186 women who were interviewed, 76 had moved or were lost to follow-up, 59 did not deliver at Yale-New Haven Hospital, 116 had spontaneous abortions or stillbirths (including three women who had an induced abortion, two with hydatidiform mole, and one who was not pregnant), 44 had multiple births, and 34 had missing information on birth weight and/or gestational age of the infant. This left a total of 3,857 singleton live births for analysis.

Women were interviewed within a few weeks of their first prenatal visit. The majority of interviews were conducted in the women's homes and consisted of questions on history of prior pregnancies, demographic characteristics, contraceptive practices, medical history, and exposure to possible risk factors, such as alcohol and tobacco. Women were asked whether they had used marijuana or hashish since they had become pregnant. If they responded positively, they were asked how frequently they had used the drug since pregnancy, and were shown a response card with answers which ranged from "less than once per month but once since pregnant" to "five or more times daily".

Information on outcome of each pregnancy was obtained from the medical records of the mother and infant. Low birth weight was defined as less than 2,500 gm. Gestational age was calculated from the first day of the last menstrual period, and preterm delivery was defined as a birth which occurred before 37 completed weeks of gestation. Birth weight standards developed by Brenner et al. (17), from a sample of 30,772 deliveries in Cleveland, Ohio, were used to define a population of infants who were small for their gestational age. Any infant whose birth weight was less than the tenth percentile for race, sex, mother's parity, and gestational age according to the standards of Brenner et al. was defined as small for gestational age. These standards were used in addition to low birth weight in order to separate out infants who were small for gestational age from those who were low birth weight because of shortened gestations.

Three categories of marijuana use during pregnancy were defined: 1) nonusers, 2)

Maternal Marijuana Use and Neonatal Outcome: Uncertainty Posed by Self-Reports

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Abstract: To assess the validity of self-reported marijuana use during pregnancy, this study randomly allocated pregnant women into a group who were told their urine would be tested for marijuana, alcohol, and other drugs and another group not so tested. Women told they would be tested reported more marijuana use during pregnancy than did untested women. Moreover, urine assays identified more women who used marijuana during pregnancy than were willing to admit it in the interview even after being told their urine would be tested. No differences in reported drinking or cigarette smoking during pregnancy were found between tested and untested women. (*Am J Public Health* 1986;76:667–669.)

Introduction

Research on maternal smoking and drinking during pregnancy has consistently revealed that women who smoke cigarettes during pregnancy on average deliver infants whose birthweight is 150–250 grams lower and experience a one to two day lower mean duration of gestation than nonsmoking women.[1] This association has held up through social classes, and over different age groups, ethnic groups, and geographic locations. In contrast, the relation of maternal drinking during pregnancy and low birthweight or pre-term delivery has been less consistently observed.[1]

Only four published studies of the effects of maternal marijuana use on fetal development have examined samples of at least 500 mother-child pairs and analytically controlled for potential confounding. Two studies in Boston interviewed mothers after delivery about their habits during pregnancy. One study of 12,718 mother-child pairs[2] found a suggestive association between maternal marijuana use during pregnancy and congenital malformations, but no association between maternal marijuana use and shorter gestation or lower infant birthweight. Another Boston study of 1,690 mother-child pairs[3] found an independent association between maternal marijuana use during pregnancy and lower infant birthweight. The mean reduction was 105 grams. Mothers who smoked marijuana during pregnancy delivered infants who were also more likely to have features compatible with the fetal alcohol syndrome. Both findings were observed after the effects of maternal cigarette smoking, drinking, weight gain, and illnesses were analytically controlled. An association with shorter duration of gestation, however, was not observed.

Prospective studies of 7,301 births[4] in Australia and 583 infants in Canada[5] both found independent associations between maternal marijuana intake during pregnancy and shorter gestation after cigarette use, alcohol use, and several other variables were controlled analytically. Only the Australian study noted an independent association with low birthweight, and neither identified an association with congenital malformation. Mothers in these two studies were interviewed prior to delivery about their habits during pregnancy.

A possible reason for the inconsistency in study results is the reliance by these studies on maternal self-report of marijuana use, smoking, and drinking with disproportionate underreporting by different study populations. Maternal marijuana use during pregnancy in particular may be underreported relative to cigarette and alcohol use because marijuana is illegal.[6]

This study explores whether self-reported maternal marijuana use is underreported relative to self-reported cigarette and alcohol use during pregnancy.

Methods

We undertook a study of pregnant women who spoke English or Spanish and who received prenatal care at Boston City Hospital between June and December 1984. Women were asked if they would be interviewed for 20 minutes about their nutrition, work, illnesses, and habits such as marijuana use, drinking, and cigarette smoking during pregnancy. The mothers were told these factors were being explored to assess what effects, if any, they might have on the development of the child they were carrying. Prior to the interview, these women were randomly divided into two groups. One group of women was told, "Urine samples are requested as part of standard prenatal care from you to examine sugar, protein, nutritional problems, and infections. As part of this study we would also like to recheck the sample for kidney function and presence of alcohol, marijuana, prescription, and non-prescription drugs." The other group of women was not told about urine testing and their urine was not tested for marijuana or other drugs. Approval to conduct this study was granted by the Boston City Hospital Human Subjects Committee in May 1984. A member of the study team other than the interviewer explained the urine testing to respondents.

Interviewers did not know which women were told their urines would be tested. In the interview women were asked if they had ever used marijuana and those responding affirmatively were asked if they had used it during the three months prior to pregnancy and if they used it since they became pregnant. The bogus pipeline paradigm[6,7] offers reason to expect higher self-reported marijuana use in the group given urine assays. Of 276 women asked to participate

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266 (96 per cent) agreed to be enrolled in the study. Of the ten refusals, four were originally assigned to the urine tested group, three to the nontested group, and three initial assignments were not recorded.

After the interview, the urine specimen provided by each subject in the first group of women was immediately labeled with subject identification number and refrigerated in the clinic. Within 24 hours, the urine samples were received in the Massachusetts State Laboratory and frozen at −20°C in plastic containers until analyses were performed. Use of cannibinoids was determined by a positive result from the EMIT d.a.u. Urine Cannabinoid Assay (EMIT) which is designed to detect 11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid (THC-C●●H).[8] THC-COOH is the major urinary metabolite of delta-9-tetrahydrocannabinol (delta-9-THC). The assay also detects other delta-9-THC metabolites. When sufficient urine was available, samples that tested positive by EMIT assay were tested by High Pressure Liquid Chromatography (HPLC) to confirm the presence of THC-COOH.[9]

Levels of urinary metabolites are detectable within a few hours after exposure of marijuana[10] and can remain detectable seven to ten days after smoking.[11] Frequent users often have continually detectable baseline levels. Only as much as 50 per cent of an initial dose may be excreted within 72 hours.

One hundred twenty-nine samples were tested for cannabinoid use by EMIT. Eight women were unable to provide samples because of an inability to urinate during their clinic visit. Nineteen samples yielded a positive result. Sixteen of those samples were confirmed by HPLC. The remaining three samples were not tested because there was an insufficient amount of urine.

Results

Forty-five per cent of women in the urine assay group reported ever smoking marijuana, compared to 51 per cent in the non-assayed group (Table 1). There were no important differences between groups in race, religion, marital status, and trimester of pregnancy at the time of interview. No differences were observed in the proportions of respondents who had ever drank or smoked cigarettes, who drank or smoked cigarettes during pregnancy, or during the three months prior to pregnancy.

Subjects within the group that had ever smoked marijuana did not differ appreciably in age, race, marital status, education, religion, or trimester of pregnancy, nor did they differ in their reported use of cigarettes prior to pregnancy or during pregnancy, drinking either during the three months prior to pregnancy or the first three months during pregnancy. As shown in Table 2, women in the group that knew their urine would be assayed were more likely to report using marijuana during the three months prior to pregnancy (63 per cent vs 41 per cent) and more likely to report marijuana use during pregnancy (37 per cent vs 24 per cent). During pregnancy, women in the group told their urine would be assayed reported greater frequency (Table 3) and greater amounts of marijuana use during pregnancy (Table 4) than women in the non-assayed group. No differences in reported frequency or amount of either cigarette smoking or drinking were observed between the groups. This was also true when the two total groups (137 and 129) were compared.

In the urine assay group, 23 women acknowledged smoking marijuana during pregnancy. The urine test further identified five subjects whose urine was positive for marijuana but who did not report such use in the interview. By combining urine and self-report results, overall use during pregnancy was identified among 20 per cent in the assay group, compared to a reported level of 12 per cent in the group that were not told about urine testing (95 per cent confidence interval of difference: 1, 15).

TABLE 1—Characteristics of Pregnant Mothers in Urine Assay and No Urine Assay Groups

	Urine Assay	No Urine Assay
Ever Smoked Marijuana	45% (62/137)	51% (66/129)
	Of Respondents Who Ever Smoked Marijuana	
Characteristics	Assay (N = 62) %	No Assay (N = 66) %
Race		
White	18	20
Black	71	61
Other	11	20
Religion		
No Religion	13	8
Catholic	32	44
Protestant	34	36
Other	21	12
Education		
Elementary	8	6
Some High School	39	33
High School	37	42
College	16	18
Marital Status		
Single	60	57
Single, Living w/Father of child	23	12
Married	11	19
Separated, Divorced, Widowed	7	12
Mean Age	22.2	22.8
Trimester of Pregnancy at time of Interview		
1st	16	20
2nd	39	33
3rd	45	47

TABLE 2—Self-Reported Marijuana Use, Cigarette Smoking, and Drinking Prior to and during Pregnancy of Respondents in the Two Groups Who Ever Smoked Marijuana

Self-reported Use	Urine Assay (N = 62) %	No Urine Assay (N = 66) %	Difference (95% C.I.; one-tailed)
Smoked Cigarettes			
Prior to Pregnancy	65	59	6 (−9, 21)
During Pregnancy	50	53	−3 (−18, 12)
Drank			
Prior to Pregnancy	66	68	−2 (−16, 12)
During Pregnancy	55	49	6 (−8, 20)
Smoked Marijuana			
Prior to Pregnancy	63	41	22 (7, 37)
During Pregnancy	37	24	13 (0, 27)

Discussion

All of the epidemiologic studies of maternal marijuana use during pregnancy and fetal development have recognized that marijuana users also tend to smoke cigarettes, drink, and take more illicit psychoactive drugs. When the independent variables are so highly interrelated, measurement becomes a major concern. None of the published studies with large samples have attempted to verify maternal self-report with urine or blood testing. This comparison of interviews with

TABLE 3—Reported Frequency of Marijuana Use (%) in the Two Groups Prior to and during Pregnancy

Reported Frequency of Marijuana Use	Urine Assay (N = 62) %	No Urine Assay (N = 68) %
Prior to Pregnancy		
None	37	59
Monthly	21	20
Weekly	31	11
Daily	11	11
During Pregnancy		
None	63	76
Monthly	23	11
Weekly	10	14
Daily	5	0

TABLE 4—Usual Number of Marijuana Joints Reported Consumed on Days Respondents in the Two Groups Smoked Marijuana

Reported Joints Smoked	Urine Assay (N = 62) %	No Urine Assay (N = 68) %
Prior to Pregnancy		
None	37	59
1	21	19
2	19	6
3+	23	15
During Pregnancy		
None	63	76
1	24	11
2+	13	14

pregnant women told and not told that their urine would be tested for marijuana, alcohol, and other drugs indicates that women told their urine would be tested report more marijuana use during pregnancy than untested women. (We obtained similar results in our pilot study [12] conducted in our own clinic.) Little difference between groups in reported cigarette smoking or alcohol use during pregnancy was observed. Further, the urine test results revealed even more women who smoked marijuana during pregnancy than those willing to admit to it in an interview. Because this study was conducted at an inner-city hospital with a high proportion of unmarried subjects and of ethnic and racial minority groups, the study will need to be replicated with a sample more representative of the US population.

Nevertheless, these findings raise concern about conclusions that have been reached in studies on fetal outcome that rely entirely on maternal self-report of marijuana, alcohol, and cigarette use during pregnancy. If marijuana use is underreported relative to alcohol and cigarettes as this study suggests, it is possible the potentially adverse effects of marijuana may be inadvertently misattributed to alcohol or nicotine. It is also possible that potentially interactive effects of marijuana with alcohol, tobacco, or other drugs have not been adequately examined.

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Perinatal Cannabinoid Exposure: Effects on Hepatic Cytochrome P-450 and Plasma Protein Levels in Male Mice

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ABSTRACT Maternal exposure to the major psychoactive Δ^9-tetrahydrocannabinol (THC), or to the nonpsychoactive cannabinol (CBN) or cannabidiol (CBD) on day 12 of gestation, or on day 1 postpartum, affected the concentrations of hepatic cytochromes P-450 in adult male offspring. Levels of P-450 were significantly increased in adult males prenatally exposed to cannabinoids, but were reduced after postnatal exposure. The response to exogenous testosterone was also differentially affected by perinatal cannabinoid exposure, with reduced plasma androgen in males prenatally exposed to THC, but increased levels of hormone in mice exposed postnatally to THC or CBN. There was a concomitant decrease in plasma albumin and increased γ-globulin in adult males postnatally exposed to CBN. Beta-globulin levels were also significantly increased in adult males exposed to cannabichromine (CBC) on day 1 postpartum. Cannabinoid exposure during perinatal periods of development exert effects on hepatic function, plasma androgen levels, and on the immune system. These effects may reflect the ability of perinatal cannabinoid exposure to interfere with androgen-mediated processes of differentiation.

Perinatal cannabinoid exposure influences androgen-dependent sexual differentiation in male mice (Dalterio and Bartke, '79; Dalterio et al., '80; Dalterio et al., '84a,b). It is well documented that the early hormonal environment affects the subsequent development of nonreproductive functions, such as hepatic enzyme activity (Einarrsson et al., '73; Chung et al., '75) and immune responsiveness (Kenny and Gray, '71; Kalland, '80). Sex differences in hepatic enzyme activity have been demonstrated in laboratory rodents and in man (Vessel, '68; El Defrawy and Mannering, '74; Gustafsson and Stenberg, '76), and the mammalian liver has receptors for the gonadal steroids (Eisenfeld et al., '75). While hepatic enzymes appear to be androgen-regulated to maintain the male metabolic pattern, another group of enzymes is partially dependent on androgen, but castration does not induce a female pattern (Quinn et al., '58; Brown et al., '76; Al-Turk et al., '80). Androgens induce liver production of secretory proteins and are known to affect the rates of hepatic metabolism of certain drugs and steroids through effects on cytochrome-P-450-dependent monooxygenases (Rumbaugh et al., '84). It is also known that these sex differences in hepatic enzyme activity are a function of the neonatal and/or adult gonadal-steroid environment and are also influenced by factors of hypothalamic and pituitary origin (Denef '74; Gustafson et al., '76). Administration of cannabinoids has been reported to exert immunosuppressive effects in adult animals (Cushman et al., '76; Munson et al., '76; Zimmerman et al., '77). In mice, Δ^9-tetrahydrocannabinol (THC), the

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TABLE 2. Effect of postnatal cannabinoid exposure on plasma protein levels in male mice (values expressed as % for albumin and globulins; means ± SE)

	Sesame oil	CBD	THC	CBC
n	10	19	11	19
Albumin	31.50 ± 1.20	27.70 ± 0.80*	30.70 ± 1.00	27.30 ± 1.10
Globulins				
α-1	18.70 ± 1.20	17.20 ± 1.10	20.60 ± 1.00	18.10 ± 1.00
α-2	21.00 ± 1.20	21.60 ± 0.30	21.40 ± 1.60	20.80 ± 1.80
β	11.60 ± 0.60	12.80 ± 1.00	10.30 ± 0.40	19.00 ± 1.90
γ	7.50 ± 1.30	9.10 ± 0.90*	7.50 ± 1.30	8.60 ± 0.50
A/G ratio	0.46 ± 0.03	0.40 ± 0.02*	0.45 ± 0.02	0.38 ± 0.02*

*Significantly different from controls, ($P < .05$).

to CBD also exhibited polyclonal gammapathy.

Beta-globulin or heme-binding globulin was also significantly elevated in animals exposed to CBC during early postnatal life (Table 2).

DISCUSSION

Prenatal exposure to cannabinoids increased hepatic cytochrome P-450 levels and liver weights. In contrast, postnatal exposure decreased the concentrations of this enzyme in liver, but did not affect liver weights. Body weights were also increased in adult males exposed prenatally to CBN, or postnatally to THC. A concomitant decrease in plasma albumin and increased γ-globulin levels were also observed in adult males postnatally exposed to CBD. Exposure on day 1 postpartum to the nonpsychoactive CBC also increased the levels of β- or heme-binding globulin. Plasma testosterone concentrations after a measured dose of exogenous androgen were lower in adult males prenatally exposed to THC, but were increased in animals exposed on day 1 postpartum to THC or CBN.

The increased body weights observed in males postnatally exposed to THC was consistent with, but not as marked, as the increases observed with combined pre- and postnatal exposure (Dalterio and Bartke, '79). Certainly the fact that the liver weights were quite similar in control and postnatally exposed animals, together with the findings that body weights were either not affected, or were increased, would suggest that perinatal cannabinoid exposure was not producing general toxicity.

It has been shown that THC accumulates in the liver (Bloch et al., '78) and alters hepatic enzyme activity after administration in adult animals (Benowitz and Jones, '77). It has also been shown that THC competitively inhibits the 5-α reduction, as well as the hydroxylation of testosterone (Chan '78). In addition, THC and CBN I spectral changes, indicating the of an enzyme-substrate complex chrome P-450 (Kupfer et al., '72; '79).

In the present study the plasma one concentrations after exogenous administration were differentially prenatal and postnatal cannabi sure. In fact, the reduced levels of one in peripheral plasma in males THC on day 12 of gestation were with the increased levels of hepa chrome P-450s. Indeed, the increas androgen in animals exposed to THC postnatally also correlated with the hepatic cytochrome P-450 levels obs this group. Although the effects CBN, or CBD on hepatic cytochrom levels were more consistent than plasma androgen concentrations, factors may have influenced the pla netics of the injected testosterone. The natal CBD exposure also reduced albumin, which may have affected ity of these animals to transport low lar weight substances, including the steroids. It is also possible that the albumin levels may reflect the ac early cannabinoid exposure of the site of albumin production.

It is interesting to note that the cytochrome P-450 levels in the pren trol animals whose mothers received oil on day 12 of gestation were consi different that those whose mothers oil on day 1 postpartum. It is possi the difference between exposure thro centae or milk, even to small amo sesame oil, could have altered fetal natal hepatic functions, either dur possibly via changes in the endocrin ronment. Hepatic cytochrome P-450 le

trols were inversely correlated with sma androgen levels after exogenous T inistration, as was observed for canna-oid-exposed offspring. Thus, it appears t hepatic cytochrome P-450s are vulnera- to manipulations of the perinatal envi- ment; that such effects persist into ulthood; and t .at they are correlated with e fu.ctional ability of the liver to metabo- gonadol steroids.

It is possible that perinatal cannabinoid posure affects androgen metabolism. In a vious study, we reported that, in intact strous females injected with testosterone opionate (TP), concomitant exposure to C did not affect plasma testosterone, but ncentrations of the 5-α-reduced metabolite, hydrotestosterone, were markedly higher animals receiving TP and THC (Dalterio al., '83b). Although the metabolic clear- ce rate was not actually measured, these sults are compatible with the hypothesis t cannabinoids induce changes in adult patic function, with resultant effects on drogen metabolism or distribution (Con- et al., '65; MasKarinec, '78).

In adult rats, chronic administration of HC or CBD decreased levels of cytochrome 450s, and selectively stimulated the con- sion of gonadal steroids in hepatic micro- omes (List et al., '77). We have previously monstrated that, in adult, TP-treated cas- ated male mice, concomitant administra- n of THC increased plasma testosterone, while in intact TP-treated males, THC re- uced plasma testosterone levels (Dalterio et al., '81a). In fact, in this study, we also noted t THC modified the response of the pitui- ary to negative feedback inhibition, possibly ggesting THC-induced alterations in the tabolism of the exogenous androgen. Ef- cts of cannabinoids on hepatocytes could o be responsible for the increased produc- n of β-globulin. Indeed, certain drugs, in- ding some carcinogens, have been shown increase levels of this plasma protein ith et al., '84).

It is interesting that in the present studies male mice exposed perinatally to cannabi- oids appear to have hyperactive immune stems, at least as indicated by increased munoglobulin levels. We have previously monstrated that these male mice present ficiencies in androgen production or ac- n (Dalterio et al., '84a,b). Since it has n demonstrated that androgens suppress mune function (Sitteri et al., '80), it is pos- ible that the effects of perinatal cannabinoid exposure on the immune system are a result of decreased fetal and/or neonatal androgen production. Females, in general, have higher immune responses, but are more prone to autoimmune diseases (Siterii et al., '80). Therefore, the immune system, which is still developing during the perinatal period (Owen, '72), may be influenced by cannabinoid effects on the fetal and/or neonatal hormonal milieu. Thus, it is possible that cannabinoid exposure may have "feminized" the immune system in the male mice in the present study.

Maternal exposure to synthetic estrogen alters cell-mediated and humoral immune function (Luster et al., '78, '79; Steven and Snook, '75). Neonatal exposure to estradiol, progesterone, testosterone, cortisol, or to diethylstilbestrol (DES) produces an initial hyperstimulation in spleen cell response, followed by a decline in immune responsiveness as animals age (Ways et al., '80). It has also been suggested that the diminished antibody response induced by neonatal DES is due to a defect in the T lymphocyte populations (Kalland, '80). It has been shown that there is increased antibody responses in estrogen-treated male mice immunized with testosterone-independent antigens (Luster et al., '78), and administration of estrogens decreases thymic weights in mice (Greenman et al., '77).

Although the proposal that THC is estrogenic is highly controversial (Solomon et al., '77; Virgo, '79), certain similarities between the effects of estrogens and those of cannabinoids do exist. Cannabinoid exposure has also been reported to affect T lymphocytes and immune responses in humans and in laboratory animals (Nahas et al., '74; Luthra et al., '80; Peterson et al., '76; Baczynsky and Zimmerman, '83). Early cannabinoid exposure may represent a situation, like that with DES, in which exposed fetuses and newborns exhibit no apparent immediate effects. Indeed, early exposure to methyl-mercury has been demonstrated to have delayed teratogenic effects on hepatic cytochrome P-450s (Robbins et al., '78). Certainly, cannabinoid-induced alterations in the subsequent function of hepatic microsomal enzymes and immunoglobulins may affect susceptibility to environmental toxins, including carcinogens, and may therefore, represent a serious potential risk to the exposed individual.

It is clear from the present studies, as well as from previous reports from this laboratory, that a single maternal exposure to can-

nabinoids has long-term consequences for subsequent development of neuroendocrine and reproductive as well as hepatic and immune functions. It is evident from these studies that differences exist in the effects of cannabinoids, depending upon the time during development in which the animal is exposed. However, the effects of either psychoactive or nonpsychoactive cannabinoids appear to be long-lasting, with effects on reproductive and nonreproductive systems. While the mechanism(s) of action of perinatal cannabinoid exposure remains to be determined, there is mounting evidence that cannabinoid exposure is capable of affecting those processes of differentiation which are dependent on the fetal hormonal milieu, particularly those of the gonadal steroids. Certainly it is clear that the consequences of perinatal cannabinoid exposure are complex, involve several complementary processes, and may also compromise the ability of the exposed animal to develop normal physiological response mechanisms.

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Journal of Studies on Alcohol, Vol. 44, No. 3, [illegible]

The Effects of Alcohol, Marihuana and Their Combination on Driving Ability[1]

Lawrence R. Sutton, Ph.D.

SUMMARY. *The combination of marihuana and alcohol yielded significant impairment during a driving test but neither drug alone did.*

DESPITE data (2) which indicate that many teenagers of driving age report use of marihuana and laboratory studies using driving simulators (3–7) which show significant impairment of skills essential for driving under the influence of marihuana, law-enforcement officials acknowledge the lack of attention to problems of youth who combine drinking, drugs and driving. The Director of the Allegheny County Bureau of Public Protection wrote: "Somehow, I think it was believed that if the problem were ignored, it would go away."[2] A possible reason for the lack of attention to this problem is the absence of definitive guidelines regarding the effects of different levels of marihuana and of alcohol–marihuana combinations on driving ability.

[1] From the Institute for Driver Research and Substance Abuse, Inc., 237 Magnolia Place, Pittsburgh, Pennsylvania 15228. This article is based on a dissertation [illegible] in partial fulfillment of the requirements of the doctoral degree from the University of Pittsburgh. The Human Use Committee of the School of Medicine and the School of Education of the University of Pittsburgh gave approval for human subjects to participate in this study. Positive review and permission to conduct this study were granted by the following agencies: the National Institute on Drug Abuse, the Drug Enforcement Administration, the Food and Drug Administration, the Allegheny District Attorney's Office, and the Pennsylvania Department of Justice.

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[2] DANZILLI, J. [Personal communication. 1 June 1979.]

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...Motor Club A.A.A.,
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Prior to this study, there have been only a few on-road studies which examined the effect of marihuana on driving. One of those driving studies (8) compared marihuana intoxication with alcohol intoxication, but none examined the joint consumption of marihuana and alcohol.

This study was undertaken to examine the effects of varying levels of alcohol and marihuana consumption and their combined effect on driving performance. Driving performance was measured in a controlled obstacle course which closely paralleled actual driving situations.

Method

Subjects

Nine male volunteer subjects, all graduate students at the University of Pittsburgh, were selected on the basis of self-reports of at least weekly use of alcohol and marihuana, and of having driven under the influence of both drugs. Subjects were matched in terms of driving ability (mean, seven years' experience), age (mean, 25.1), weight (mean, 164.7 lb) and health (blood pressure and pulse within normal range, absence of allergic reaction to medication and normal electrocardiogram).

Measures

Drug Levels. Blood alcohol concentration (BAC) and serum tetrahydrocannabinol (THC) level were drawn to verify levels of the drugs. Serum samples were drawn approximately 45 min after alcohol consumption and 15 min after marihuana consumption based on prior research experience showing that these time periods coincide with peak blood concentration of the two drugs.

Driving Performance. Driving performance was measured in two ways. The first was an evaluation of driving performance using Pennsylvania motor vehicle code Title 67, Chapter 153—Driver Examination Statutes. This evaluation was made independently by a safety manager from the American Automobile Association and by a high-school driver-education instructor. The second performance measure was an evaluation made by an off-duty patrol officer who followed each driver on the obstacle course in an unmarked automobile. The officer attempted to determine whether the driver was impaired enough to warrant his being stopped for further investigation. His evaluation criteria included: traffic violations, speed (used to show cautiousness or aggressiveness), slow or quick starting or stopping, weaving over the yellow center line, hugging the yellow center line, and leaving the driving course (Figure 1).

Self-Reports of Feeling "High." Self-reports of feeling "high," using a scale from 1 (not being high,) to 10 (being the highest they had ever been), were collected from the subjects prior to their driving under the influence of the drugs.

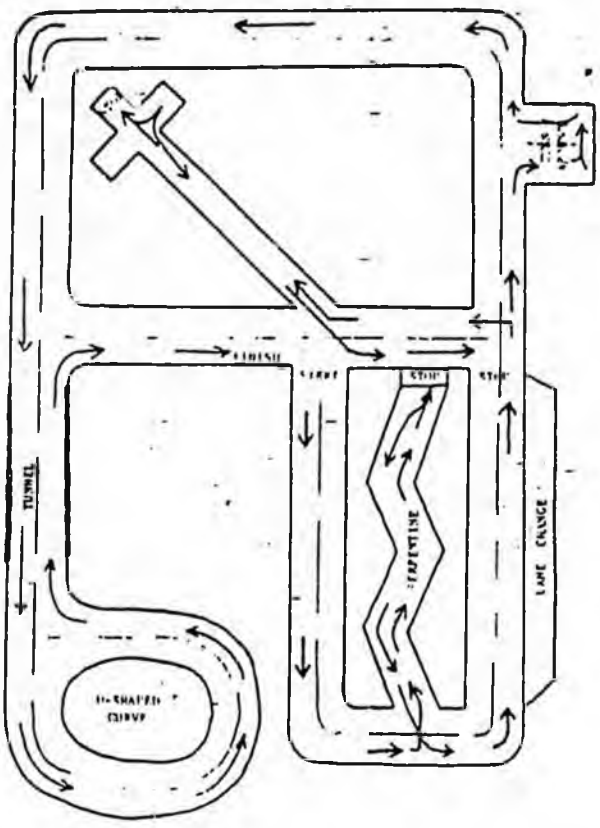


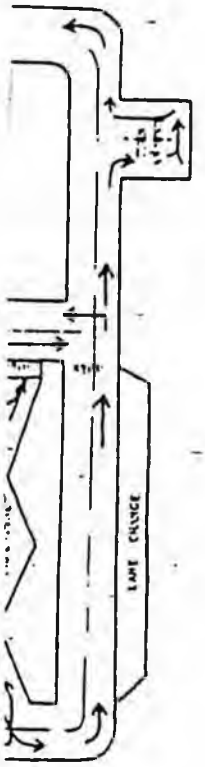
FIGURE 1.—*Experimental Driving Course Used by Subjects*

Procedure

Subjects were randomly assigned to one of four experimental groups. A repeated-measures design was used so that all subjects participated in each experimental condition.

Urine samples were taken from each subject at the beginning of each session to rule out the possibility that a drug other than those introduced during the study was responsible for driving impairment. Pulse rates were monitored before drugs were given and again after each experimental condition was completed.

Driving trials were conducted over a four-day period. During the first day, subjects were trained on the obstacle course through the use of a dual-controlled automobile. Subjects practiced until they were able to complete each maneuver in the course without error (mean, three trials). On each of the three following days, subjects completed the course one time as a reorientation measure prior to receiving any drug. Following practice trials each day, pulse rates were taken and subjects were then



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given alcohol (either a placebo or enough vodka to approximate a .06% BAC) and marihuana (either a placebo or 2% D-9-THC). To ensure that they were not aware of their conditions, all subjects received an equal amount of beverage (three glasses), and the placebo drinks were "misted" with a small quantity of vodka to create an odor of alcohol. The marihuana placebo consisted of a marihuana cigarette detoxified of all THC.[3] To achieve peak intoxication for both drugs simultaneously, subjects were given the marihuana-like cigarette 25 min after ingesting the desired alcohol dosage. The subjects were required to smoke the entire cigarette with cycles of inhaling, holding the smoke in the lungs for 15 sec and then exhaling (9). Two blood samples were drawn approximately 45 min after the subjects stopped drinking. It was at this time that the subjects were asked to rate how high they thought they were. Subjects then entered the dual-controlled automobiles with a driving instructor. The driving instructor answered any questions posed by the subject and then instructed the subject to drive through the obstacle course.

RESULTS

A one-way analysis of variance (ANOVA) to evaluate the effects of alcohol and marihuana on driving performance, as rated by the driving instructors, yielded a significant effect under the combination condition ($F = 4.00$, 3 df, $p < .05$). Neither alcohol alone nor marihuana alone resulted in significantly poorer driving performance when compared with the same subjects' performance under the placebo state.

A one-way ANOVA to compare the patrol officers' evaluation of driving impairment across the four conditions yielded a significant effect for the combination condition ($F = 11.70$, 3 df, $p < .01$). Using Scheffé post-hoc comparison, significant impairment was noted for the combination condition but not for the alcohol or marihuana conditions. The patrol officer indicated that he would have stopped drivers in a total of 15 trials, including all those in the combination condition. According to this measure, therefore, neither marihuana alone nor alcohol alone at the levels used in this study impaired driving performance to a significant degree, but use of both drugs simultaneously resulted in significant driving impairment.

Pulse rates taken before drug use and at the conclusion of driving were compared with a one-way ANOVA; significant differences were noted ($F = 34.62$, $p < .01$). A Scheffé post-hoc comparison showed the marihuana and combination conditions to be associated with

[3] Supplied by the National Institute on Drug Abuse.

significant increases in pulse rates ($p < .01$). The alcohol and placebo conditions were not significantly different from each other, nor were the combination and marihuana conditions. Mean increases in beats per minute were as follows: placebo, 6.89; alcohol, 9.22; marihuana, 35.67; combination, 38.78.

Subjects' ratings of feeling "high" were compared by a one-way ANOVA, yielding a significant overall effect ($F = 59.61$, $p < .01$). A post-hoc Scheffé comparison showed that subjects rated themselves as significantly more "high" in the combination and marihuana conditions than when under the placebo or alcohol conditions ($p < .01$). The alcohol condition resulted in a significantly greater "high" feeling than the placebo condition ($p < .05$). Mean ratings for each condition were as follows: placebo, 1.44; alcohol, 3.78; marihuana, 7.56; combination, 8.89.

Discussion

The combination of marihuana and alcohol, even at low levels of the drugs, proved to have a potentially dangerous effect on the driving task. The impairment created by the combination of the two drugs was much greater than that created by either drug separately.

The most practical dependent variable was the blinded evaluation of the patrol officer. It was most practical because this type of evaluation is used every day in the apprehension of alcohol-intoxicated drivers by patrol officers. The patrol officer stopped every driver under the combination condition. This is an important result with rather serious implications. The most serious implication is that, at the present time, Pennsylvania and almost every other state have no way of detecting or prosecuting drivers under this condition, because there is no simple or practical way to detect or measure marihuana intoxication. Under the conditions in this study, all drivers in the state of Pennsylvania, barring a traffic accident or fatality, would be cited with only a minor charge because their BACs would be significantly lower than the legal criterion for intoxication (.10%).

Marihuana alone did not significantly impair driving performance as measured in this study. This result is puzzling because of the elaborate efforts made in this study to maximize marihuana intoxication (9). Klonoff (10) and Le Dain (8) found serious impairment when marihuana was given at a dosage similar to that used in this study. Driving-simulator studies (3–7) found impair-

ment on numerous skills essential for driving at this level of intoxication. It is imperative to include maneuvers testing perception and attention in any study examining the effects of marihuana intoxication on driving performance. Unfortunately, the course used in the current study had very few such maneuvers and subjects consequently showed very little driving impairment under the influence of marihuana. Another reason that so little impairment was visible on the course may have been the experience of the subjects in the use of marihuana. Each subject smoked marihuana at least once a week and had driven an automobile on at least one occasion under the influence of marihuana. The results of the study would most likely have been different if subjects naive to marihuana use had been used.

The subjects used in this study were good representatives of the population that consumes marihuana and alcohol socially—they were relatively young and were often in situations where smoking marihuana and consuming alcohol are socially acceptable, e.g., at parties. As reported by Small and Rush (2), the age range of 20–34 reports the highest use of both marihuana and alcohol.

Because of the high potency of the drugs used, most subjects indicated that they could tell when they were smoking marihuana after only a few "hits" from the cigarettes. In other words, the usefulness of the placebo cigarettes was greatly limited and all future experiments must consider this. Effective ways of eliminating this problem in the future would be to use different subjects in each condition rather than repeating the same subjects through all conditions, or to have two marihuana conditions in addition to the placebo condition. For the most part, subjects indicated that the alcohol placebo was an adequate disguise.

The subjects also made several useful comments about the off-road course. Many of the subjects stated that they were too intoxicated to drive (in fact, some had difficulty walking to the automobiles), but once in the automobiles they stated that they "crawled" through the course at a much slower speed than in the training exercises in order to compensate for their intoxication. The subjects indicated that the most difficult parts of the course were the U-shaped curve, the tunnels and the "T" exercise. A few stated that they had to force themselves to keep their attention on the course. Many of the subjects stated that they had made a great effort to drive the best they could, apparently in an effort to show that the drug had no effect on their driving.

Of particular interest was the impairment demonstrated under the combination condition, which suggested a synergistic reaction between the two drugs. This would make the task of operating a motor vehicle much more difficult and dangerous, particularly for youth. In a recent survey[4] which examined marihuana and alcohol use and attitudes toward driving, high-school-aged students showed a high use of both drugs combined. Some even stated that, contrary to existing literature, the drugs acted in an antagonistic manner, thereby making the driving task easier. It is imperative that educators and psychologists properly educate this more vulnerable segment of our society.

The current research demonstrated a serious interaction effect between alcohol and marihuana and driving performance. With the growing combined use of alcohol and marihuana,[2,4] future research must be designed to examine the role of this combination on the operation of motor vehicles. Future research must (*1*) investigate further the effects of marihuana intoxication on driving performance using actual road studies, (*2*) investigate the combined effect of marihuana and alcohol on driving performance using actual road studies and driving simulators, and (*3*) develop legislation concerning marihuana intoxication while driving.

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The Effects of Marijuana and Alcohol on Actual Driving Performance

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OVERVIEW

Approximately 80 volunteer male marijuana and alcohol users received one of four experimental treatments: (1) marijuana, (2) alcohol, (3) marijuana and alcohol, or (4) double placebo. After consumption, each subject drove a vehicle over a test course which simulated a number of real-world driving conditions. Four post-drug runs were involved, separated by one-hour intervals. The subject's performance was rated by an in-car examiner, outside observers, and computerized vehicle measurements. Blood and urine specimens were extracted after each run to establish levels of tetrahydrocannabinol (THC), serum carboxy, and alcohol. A variety of multivariate statistical techniques were applied in evaluating treatment effects. Both marijuana and alcohol had significant effects on driving performance, and the effects were particularly detrimental under the both-drugs treatment. The effects of marijuana were more rapid than those of alcohol and somewhat less severe for most tasks.

INTRODUCTION

This paper summarizes Phase II of an effort to characterize and quantify the effects of marijuana use, alone and in combination with alcohol, on driving performance. An earlier study (Department of Justice [DOJ] Incidence Study) funded by the Office of Traffic Safety indicated that Δ^9-THC was present in a significant proportion of the submitted blood samples drawn from California drivers detained by Highway Patrol officers because of ostensibly impaired driving performance (Zimmerman et al., 1983). Phase I of this grant suggested that volunteers given ad lib doses of marijuana by inhalation were subsequently considered impaired when required to perform the standard field sobriety tests (Reeve et al., 1983). These impairment ratings persisted for up to three hours after smoking and were

Acknowledgement. This paper is a condensation of a technical monograph titled *Marijuana and Alcohol Performance Study* (Biasotti, Boland, Mallory, Peck and Reeve, California Department of Justice and California Department of Motor Vehicles, 1986). The research was supported by funding from the National Highway Traffic Safety Administration through a grant administered by the Office of Traffic Safety (#087902). The opinions, findings and conclusions expressed in this publication are those of the authors and not necessarily those of the State of California or the National Highway Traffic Safety Administration. The authors wish to acknowledge the contribution of Fe Arconado-Hignight, Seresa Hartwell, Debbie Difuntorum and Karri Yee in typing this manuscript under the pressures of a very tight time deadline.

associated with mean hemolyzed blood concentrations of Δ^9-THC measured from the subjects. One limitation of the Phase I study was the absence of experimental controls for placebo bias. Phase II is designed to extend this research to include actual driving performance within the confines of a rigorously controlled experimental design. Subjects received a standard dose of marijuana by inhalation, and a double blind control condition was included to minimize experimenter and subject bias. In addition, since alcohol was observed in a large number of cases in association with Δ^9-THC during the DOJ Incidence Study, the present study included alcohol and marijuana plus alcohol as additional experimental conditions.

The specific objectives of the study are listed below:

1. To determine the singular and combined effects of marijuana and alcohol on driving performance on a closed-course driving range.

2. To determine if there is a relationship between the ranges of Δ^9-THC in blood and/or alcohol in breath and measures of driving performance.

3. To determine if the various driving performance measures are differently affected by marijuana and alcohol ingestion.

4. To determine the relationship between the time following marijuana and/or alcohol ingestion and driving performance.

5. To determine the interrelationship among the performance factors affected by the marijuana and alcohol ingestion.

6. To determine whether marijuana, alone or in combination with alcohol, results in impairment that can be reliably detected through external observation of the driving and standard field sobriety tests.

It was beyond the scope of this study to establish a definitive relationship between performance decrements on the various driving range maneuvers and impaired driving ability on public streets. Instead, the study measured performance of various driving range maneuvers related to "real world" driving. One limitation of using a closed-course driving range is that some behavioral domains that are known to be critical to accident avoidance, such as risk taking and response to other vehicles, are not tapped. In spite of these limitations, the impairment of any skill component of a driving task has potential safety implications and is therefore deserving of serious scrutiny. In addition, some driver-behavior investigators, such as McPherson and McKnight (1981), suggest that deficiencies on the skill and motor components of the driving task may indirectly degrade accident avoidance components. Such an effect would be mediated by a reduction in the "spare capacity" for handling emergency situations that could occur in drivers whose low skill level requires use of large portions of their perceptual and attentional capacity to maneuver a vehicle through traffic.

The following results and methods sections present only a brief overview of the major findings and methodology, followed by a detailed discussion of the complete findings contained in the technical monograph (Biasotti et al., 1986). Readers interested in the complete results should refer to the latter report.

METHODS

Research Design

Subjects were randomly assigned to the four treatment combinations created by the following 2 x 2 factorial design:

(1) alcohol plus marijuana placebo;
(2) marijuana plus alcohol placebo;
(3) marijuana and alcohol; and
(4) double placebo.

BITE and CTT. The mean BITE and CTT scores by treatment groups and run are presented in Table 3. On each measure, higher scores indicate better performance.

TABLE 3

Treatment Means for BITE and CTT Measures

BITE

Run Number	Placebo	Marijuana	Alcohol	Both
Run 3	60.63	53.82	56.16	52.55
Run 4	62.52	56.47	58.95	53.43
Run 5	58.32	57.58	62.30	49.90
Run 6	57.45	53.93	52.33	57.40
Total	59.89	55.20	57.55	52.89

CTT

Run Number	Placebo	Marijuana	Alcohol	Both
Run 3	5.03	4.93	4.34	4.47
Run 4	4.89	4.94	4.21	4.16
Run 5	4.93	5.17	4.48	4.45
Run 6	5.04	5.20	4.63	4.67
Total	4.98	5.01	4.49	4.45

Although there was a definite trend on the BITE task for the placebo group to perform best, and the both-drugs group to perform most poorly, none of the analysis of variance tests produced a significant difference at $p<.05$. The results are nevertheless suggestive of impaired time estimation, particularly when both drugs are combined.

The results on the CTT measure show that the alcohol and both-drugs groups did significantly worse (lower means) than did the placebo and marijuana groups, indicating a clear-cut alcohol effect. The differences reached statistical significance ($p \leq .05$) at runs 4 and 5 and on the total composite (runs 3-6 combined). Somewhat surprisingly, there is not even a directional trend toward marijuana impairment on the CTT. The scores for the placebo do not change materially from run to run, whereas all three drug groups tended to improve. Thus, there is no evidence of residual practice effects but there is clear indication of reductions in impairment on the CTT over time.

DISCUSSION AND CONCLUSIONS

The Main and Interactive Effects of Alcohol and Marijuana—General Characteristics

The results of the univariate and multivariate analyses indicate that both substances affected driving performance. The MDF analyses resulted in two significant linear composites (functions) of the 12 performance measures which

were most consistently and uniquely impacted by the treatments. These two functions explained between 65% to 70% of the between-group variance on the 12 measures across the four posttreatment trials. Approximately 60% of the explained variance was attributed to the first function compared to 20% for the second function. The first function produced maximum discrimination between the placebo and the both-drugs groups, with marijuana alone and alcohol alone occupying intermediate positions between these two performance extremes. Inspection of the group means on the 12 variables which defined the function indicated the both-drug polarity was generally indicative of impaired performance.

The second function tended to separate the marijuana and alcohol groups from the placebo group, with the both-drugs group occupying an intermediate position.

An attempt was made to interpret the "meaning" of the two functions by inspection of the standardized discriminant function coefficients and structure loadings. Persons scoring higher (better) on the first function produced higher estimates of the speed at which they could drive the chicane and drove more quickly through it; drove at lower and more appropriate speeds when the speedometer was covered, as well as on most other parts of the course; drove more cautiously; made more accelerator reversals on the extended drive; performed better on the detour task; performed better on the field sobriety tests; were judged to be less impaired by the officer; rated their driving and field sobriety performance higher (less impaired); received higher overall ratings from the driver's license examiner (LRE); and made fewer driving errors on the drive course. This function clearly reflects between-group variations and performance decrements on a wide variety of measures: (1) subjective self ratings; (2) LRE ratings of speed control, overall performance, cautiousness and number of driving errors; (3) officer field sobriety and vehicle control ratings; (4) objective measures of performance (number of stanchions knocked down, accelerator reversal, urban driving speed; and (5) number of attempts on the risks task. Since this function produced maximum separation between the both-drugs and placebo groups with the latter falling at the positive end of the first function, higher scores on most of the preceding variables were associated with not being drugged, and lower scores with being exposed to alcohol and marijuana combined. The nature and range of variables affected indicate that exposure to the combined marijuana/alcohol condition resulted in impaired vehicular control and an accurate subjective awareness of the impaired performance.

Inspection of the second function indicated that higher scores on the function were associated with the marijuana and alcohol condition, and the structure loadings indicated that it is primarily a measure of impaired stopping. By far the highest loading on the function was on the variable POSTOP, which correlated +.69 with the function. This variable represents the LRE's rating of proper stopping position on all stopping maneuvers throughout the driving range. Since the variable was scaled so that low scores indicate proper stopping position (1=smooth stop, 2=abrupt or misjudged stop, and 3=rolling or no stop), the high positive correlation between the function and variable is indicative of a higher proportion of improper stop ratings among marijuana and alcohol subjects. Unfortunately, the method of scaling did not distinguish between stopping too soon or too late relative to the sign.

Four other stopping measures also had significant positive loadings on the second function: (1) SStop (stopping errors on the speedometer-covered segment of the course, (2) EStop (stopping errors on the extended drive), (3) Stops (total number of stopping errors on all segments of the course), and (4) BIPOST (bipolar rating of stop position cautiousness). A fifth stopping measure, BIStop, yielded a negative loading (-.31), indicating that stopping position caution on the speedometer-covered portion of the course was negatively associated with the function.

Taken together, the above results indicate that marijuana and alcohol affected stopping behavior but that the negative effects were reduced when both drugs were combined. The mechanism underlying what appears to be a suppressive interaction is not clear, and interpretation is further complicated by the above-mentioned scaling problems. One possibility is that the separate drugs produced different types of stopping errors (e.g., delayed vs. early stops) which cancelled out when both were combined.

The main and interactive multivariate effects of marijuana and alcohol on the 12 variable discriminant functions were evaluated through a series of canonical analyses, and an analysis of variance procedure was used to evaluate univariate effects. The canonical analyses indicated that both substances had highly significant multivariate main effects on all four posttreatment runs. The marijuana condition explained between 23.1% to 29.2% of the variance on the 12 most discriminating performance measures, averaging 25.1% for all four trials. The alcohol condition produced a somewhat larger effect, accounting for 29.9% to 32.3% of the performance variance, and yielding an average effect of 31.4% for all four trials. The multivariate effects were largely additive, although small but

significant interactions did occur on runs 3 and 6 where the respective explained-variance totals for the marijuana by alcohol interactions were 12.0% and 12.9%, respectively.

Factorial analyses of variance of univariate effects on each of the 12 discriminating variables (not shown) provided additional confirmation on the locus of treatment effects and on their interactions with variables that were considered to be the potential moderators of treatment effects (baseline performance on the 12 discriminating variables and five background characteristics representing prior alcohol/drug use and driving experience). These analyses indicated that marijuana had significant main effects on three measures: (1) COGNIT, (2) SMPH, and (3) ESTCHIC. A suggestive main effect also occurred on attempts (risk task). Inspection of the means indicated that the marijuana negatively affected performance on the cognitive factor of the field sobriety test; produced higher speed while the speedometer was covered; resulted in a lower self assessment of the fastest speed the subject could drive through the chicane; and required more attempts to complete the risk task. The alcohol condition produced a significant main effect on four measures: (1) BSPEED, (2) STOUCH, (3) CTT, and (4) SMPH. Suggestive main effects were also noted on attempts (risk task), COGNIT, and BISKILLS. Inspection of the means for these variables indicated that all of the effects were suggestive of impairment. No consistent evidence for a marijuana/alcohol interaction emerged from these analyses, or of an interaction with any of the baseline and background factors. Thus, these analyses support the conclusion that the effects of marijuana and alcohol are largely additive with each other and with the background and baseline performance characteristics of the subject sample.

The above conclusion of general additivity requires some qualification and further discussion. The detailed interaction analysis was limited to the 12 variables identified from the discriminant function analysis and was further limited to the total runs-composite (runs 3-6 combined). Since the effects of marijuana were most acute at run 3 and declined thereafter, the use of the composite measure could have masked some of the effects. In addition, interaction effects on variables other than "the best 12" were not evaluated.

There was, in fact, evidence of a small, but statistically significant, interaction between marijuana and alcohol at run 3, cited above in connection with canonical analyses of treatment effects. Further evidence of non-additivity also emerged in connection with the homogeneity of slopes test for the regression of baseline (run 2) performance on posttreatment performance (runs 3-6 combined). The slope differences were particularly dramatic for the CTT and ESTCHIC variables, suggesting that response to treatment varied as a function of subject's baseline level on these measures. The structure and substantive meaning of these interactions are not clear and seem in conflict with the failure to find significant treatment x baseline interactions in the analyses of variance. Two reasons can be advanced to explain the above paradox. First, the baseline measures were collapsed into dichotomous categorical factors for the analysis of variance test, whereas the slopes test treated each variable as a continuous measure. If relationships and interactions among the measures were approximately linear, the categorical approach would significantly reduce the sensitivity for detecting interactions. Second, the slopes test was based on a slightly smaller sample size (n=63) due to the deletion of cases with missing values on some of the measures.

The Main and Interactive Effects of Marijuana—Detailed Characteristics of Effects within Trials

The above discussion has primarily focused on the effects on all posttreatment trials combined into single composite measures. It has also been limited to the 12-variable core selected through the multiple discriminant function analysis (MDF).

A complete understanding of the results of the experiment requires interpretation of effects within and across trials and consideration of the many variables not included in the final MDF analyses.

The evaluation of treatment x trial interaction was achieved through a test of slope differences on the trial factor. Since the trials occurred at fixed points in time from a single drug ingestion, the trial slopes represent the effects of time, and the slope differences reflect temporal differences in each treatment group's performance gradient. These tests indicated significant slope differences on each of the 12 measures selected from the MDF analysis. A major source of the difference was marijuana's tendency to result in maximum impairment in the first posttreatment trial while alcohol's effect maximized at run 4 and did not decline as rapidly as the marijuana effect. The both-drugs group tended to show the impairment gradient that would be expected from the component drugs, evidencing maximum impairment at both runs 3 and 4 and consistently showing greater impairment than either marijuana or alcohol alone.

In addition, the combination of the two substances significantly lengthened the duration of effects, resulting in a rather remarkable increase in impairment from runs 5 to 6. The emergence of a synergistic marijuana-alcohol interaction at run 6 suggests an effect mediated by some residual mechanism occurring when the two substances are combined. An obvious intuitive explanation would be that marijuana and alcohol interact to produce greater fatigue and "hang over" effects.

Other results of interest are the findings on various peripheral measures, such as FALLCAR, field sobriety tests, self-rating and the CTT. In general, the subject self-rating of impairment was among the more sensitive indicators of treatment and tended to parallel the objective measures. The fact that the self-rating impairment indices closely mirror both the objective indicators and the overall LRE and officer rating provides confirmation for the reliability and validity of the results.

That the officers in the following-car (FALLCAR) were able to detect driving impairment with a significant degree of accuracy is notable. The FALLCAR results also clearly reveal the different time gradients for marijuana and alcohol. The marijuana subjects were detectable only at run 3, whereas alcohol peaked at run 4, and the both-drugs group was detected as impaired on all runs except 6.

The results on the CTT variable are surprising in that marijuana alone did not produce evidence of impairment, which is in conflict with prior research findings. This complex psychomotor task was originally devised to detect alcohol impairment. The fact that alcohol and marijuana plus alcohol combined did produce impairment would seem sufficient to dispel the hypothesis that the marijuana finding can be attributed to some type of error or procedural artifact. Some possible reasons for the findings are discussed below in connection with the review of relevant literature. Surprisingly, the marijuana-only condition resulted in fewer stanchions being knocked down at run 3—where the level of intoxication was actually greatest. However, it is important to note that persons receiving marijuana or marijuana and alcohol tended to drive more slowly through the chicane than did the placebo and alcohol-alone subjects. Speed through the chicane was measured by the vehicle line sensor, which produced the following elapsed times for the placebo, alcohol, marijuana, and both-drugs treatments, respectively: 16.7, 16.3, 17.3, and 18.4. Although the differences were not statistically significant (p=.22), it is instructive to note that other researchers have found that marijuana tends to cause persons to compensate for subjective impairment by reducing task difficulty through reduced vehicle speed.

Blood Levels

One of the objectives of the study was to assess the feasibility of developing an objective chemical index of marijuana impairment. Although the results did show that the quantitative levels of THC and carboxy combined resulted in some increase in the ability to explain performance variations, the practical and theoretical implications of the finding are not entirely clear. Experimental replication of the study and use of a wider range of marijuana-dose levels is needed before the feasibility of establishing a quantitative threshold can be fully evaluated. We are not optimistic about the prospects for development of quantitative thresholds for marijuana impairment.

Relationship to Prior Studies

There is a vast amount of empirical evidence documenting the effects of marijuana on a wide array of human performance measures—cognitive, psychomotor and affective. Although the literature has clearly established that marijuana affects all three domains and results in detriments in the ability to perform many psychomotor and cognitive tasks, the evidence is somewhat more equivocal on the question of actual driving skill and even more equivocal on the question of those aspects of driving skill that are *related to safety and accident avoidance*. Any attempts at formulating a comprehensive and coherent theory on the effects of cannabis on driving performance, or reconciling the various empirical outcomes of different studies are complicated by the differing circumstances unique to each investigation. Among the variables to be considered are: (1) the specific performance task; (2) the frequency of prior marijuana usage and the strength of the typical THC concentration of the marijuana; (3) previous experience driving after consuming marijuana; (4) the amount and strength of the experimental dosage; (5) mode of ingestion (oral or smoke); and (6) the type of research design employed in each study. The demonstration of behavioral change following ingestion, and the magnitude of the performance change, can obviously be affected by each of the above variables. Finally, there is the problem of equating change with detriment and then generalizing the inferred

detriment to real world accident avoidance behavior. With the above cautions in mind, we will attempt to show some tentative conclusions as to how the present findings articulate with the conclusions of other investigators.

Studies of marijuana's impact on driving performance can be grouped into five general categories:

(1) Laboratory studies.
(2) Simulator studies.
(3) Closed-course driving range studies.
(4) On-street driving studies.
(5) Epidemiological studies of accident-involved drivers and victims.

With the few exceptions discussed below, we believe that the measurement domains and research design of the present study are too dissimilar to warrant detailed comparison with the results of studies from areas 1 and 2. (The implications of study area 5 are discussed later in connection with traffic safety ramifications of marijuana and driving.) One area of conflict between the present and prior studies is the failure of marijuana alone to exhibit even a suggestive detrimental impact on the CTT measure. The critical tracking task was originally designed to detect alcohol impairment, and has been shown to be sensitive to relatively moderate levels of alcohol. Sharma and Moskowitz (1975) reported that a dose of 200 µg/kg THC resulted in significant impairment lasting throughout the four hours of a repeated measures test session. Remarkably, the impairment was almost as great in the fourth hour as in the first hour after ingestion. More recently, Barnett et al. (1985), using data from the above Sharma and Moskowitz (1975) study, reanalyzed the effects of the three dose levels of marijuana (100, 200, and 250 µg/kg) on divided attention, visual search and CTT performance. All three measures exhibited dose-related marijuana effects which, in the case of the CTT, lasted roughly 7.1 hours.

Given this evidence, the present authors would be inclined to dismiss the present result as an artifact were it not for the fact that both the alcohol and both-drugs groups did show the expected decrement. Any error or procedural artifact would be expected to have affected all groups, since assignment to the experimental conditions was random and was rigorously monitored.

Two explanations are proposed here for consideration. The first is the differences in experimental design between this and the above two studies. The present study utilized an independent-group design and also treated the trials condition as a collapsed factor for most of the analyses. In contrast, the studies by Sharma and Moskowitz, and Barnett et al. used repeated-measures designs in which each subject received all experimental conditions and were compared to their own baseline scores. Repeated-measures designs have greater sensitivity than do independent-group designs when the very strong mathematical assumptions on which the designs are based are satisfied. (These assumptions are often *not* satisfied in experiments on human subjects.) Although it is doubtful from the inspection of pre- and posttreatment means that creation of pre- vs. postdifference scores or use of analysis of covariance would have materially altered the results, one can always posit that the randomization did not completely control for idiosyncratic differences in drug response. There was also a slight trend in the data for marijuana subjects to achieve lower (worse) scores than the placebo at run 3, which is also the trial where marijuana intoxication was most intense. Any use of analysis of covariance or repeated measures differencing to increase the sensitivity of the run 3 contrast are complicated by the significant treatment by baseline CTT score interaction encountered in comparing regression slopes.

A more reasonable hypothesis is that the studies were not equivalent in terms of subjects' prior marijuana use (frequency and potency). There is reason to believe that persons accommodate, at least partially, to the effects of marijuana through acquired tolerance and/or experience in performing tasks while intoxicated. Even though learning new tasks is generally impeded by marijuana use, there is evidence to show that recall of material originally learned while intoxicated is greatest during subsequent periods of intoxication, i.e., "state dependent learning" (Darley et al., 1974). If one accepts the preceding evidence and line of reasoning, it seems clear that investigations of marijuana-induced performance decrement can produce conflicting results if based on subjects with different levels of tolerance and experience.

It appears that subjects in the present study were, in fact, heavier users than subjects in the Sharma and Moskowitz, and Barnett et al. data sets. The latter data were based on subjects whose current use frequency did not exceed three cigarettes per week and a minimum lifetime use of only ten episodes. The present study required subjects to be current users of 1-7 "joints" per week, to have been users for at least two years, and to have experience with marijuana that was "at least" as potent as that used in the study.

The average impairment/intoxication rating given at run 3 by the subjects in the marijuana-alone group was only 3.41 on a scale of 1-9. This, combined with the extremely high serum carboxy level of some of the subjects at baseline, suggests a chronic use of high potency marijuana that in many cases exceeded the self-reported use frequency. In any event it seems clear that the subjects of this study were heavier users than those used in the Sharma and Moskowitz, and Barnett et al. studies and many of the other studies cited in the literature. This speculation is also consistent with the prevalent availability and use of the high potency "sinsemilla" variety of marijuana grown in northern California.

Variations in acquired tolerance and accommodation could also explain conflicting results of other investigators. For example, most studies, including the present, have not produced psychomotor decrements approaching the magnitude, consistency and duration of those reported by Belgrave et al. (1979). These investigators used orally ingested THC on subjects whose use history appeared quite moderate. In addition, the oral ingestion of THC—a mode not normally encountered and which produces slower but more enduring effects—further confounds interpretation and any generalization as to what would be expected from smoking normative dose levels.

Several of the results obtained in the present study articulate quite well with those reported by other investigators. The ability of the police observers in the following car to detect impairment, particularly in subjects who received both marijuana and alcohol, is consistent with the results of Sutton (1983). However, neither alcohol nor marijuana alone could be detected in Sutton's study, which is in conflict with the present results.

The fact that marijuana and alcohol exerted a relatively additive effect on many driving behaviors is also consistent with prior research findings. The consistency of this effect and the range of the affected behaviors is notable. The emergence of a significant synergistic interaction between marijuana and alcohol in the fourth hour after ingestion is a novel finding. The mechanism underlying such an effect requires further study.

One limitation of the study was the lack of emergency response and accident avoidance tasks. A forced lane change (FLC) maneuver was included to tap the ability to respond to a choice reaction task, involving some of the same psychomotor components required to avoid accidents; it was not consistently affected by any of the drug conditions (other than a tendency for the drugged subjects to more often drive below the minimum speed threshold). Although across-study comparisons are tenuous, the failure to find a marijuana main effect on this task is consistent with the Stein et al. (1983) finding that even a substantial dosage of marijuana (200 µg/kg) had no effect on the ability to avoid accidents on a simulated driving task. However, Stein did find evidence of a marijuana-alcohol interaction on accident avoidance, with lower doses (100 µg/kg) of marijuana decreasing the negative effect of alcohol and larger doses (200 µg/kg) accentuating alcohol's negative effects.

An important limitation of the forced lane change task as a proxy for accident avoidance is that it was introduced as a discrete "off-line" task rather than integrated into the driving course. It, therefore, does not really measure vigilance and divided attention which are critical components of accident behavior and attributes which are more likely to be affected by marijuana (Sharma & Moskowitz, 1973; Moskowitz, 1976).

Since this study utilized a closed-course driving range, a detailed comparison with prior research using similar task modes is in order (one such study by Sutton was already alluded to above). Several other such studies have been reported in the literature (Klonoff, 1974; Attwood et al., 1981; Smiley, 1974; Casswell, 1979; and Hansteen et al., 1976).

Hansteen et al. found that marijuana (88 µg/kg THC) resulted in a significant increase in the number of cones overturned on the slalom portion of the course but did not lead to increased erratic vehicle handling as judged by raters, whereas alcohol impaired both measures. In contrast, the present study found that marijuana significantly reduced the number of cones knocked over in the chicane task but that the marijuana subjects tended to drive more slowly through the chicane. The both-drugs group also reduced their speed compared to the placebo but hit the same number of cones as the placebo. The alcohol-alone group tended to drive the fastest and also tended to hit the most cones.

Casswell found that marijuana alone decreased vehicle speed and course steering corrections. In contrast, alcohol, and marijuana plus alcohol, decreased fine steering reversals and increased variation in lateral placement of the vehicle. Casswell concluded that marijuana subjects tended to compensate for their perceived impairment by reducing vehicle speed, thereby reducing task difficulty and information processing demands. This conclusion is consistent with our finding, cited above, concerning marijuana's effect on the chicane task. However, marijuana did

not result in reduced speed on most parts of the course and was associated with increased speed when the speedometer was covered. This can easily be attributed to the fact that most parts of the course were of minimal difficulty and did not require compensation. Although there was little evidence from the present study to show impact on steering reversals, marijuana and alcohol did impair steering control as rated by the in-car observer. The failure of the vehicle steering reversal sensor to detect change in the present study could be due to the sensor defects and signal loss caused by equipment malfunction, and to the fact that the scores were limited to mean values of nondifference parameters (Biasotti et al., 1986).

The study by Smiley (1974) is one of the few examples of a marijuana-alcohol interaction in which marijuana appeared to reduce the negative effects of alcohol. Such an interaction occurred on stopping accuracy. In contrast, the present research showed that marijuana was associated with more stopping errors than alcohol but did show evidence of significant negative interaction (interference) in which the combination of alcohol and marijuana resulted in better stopping position than marijuana alone. Attwood et al. (1981) found no persuasive evidence of any univariate effects of marijuana and alcohol on driving range performance as measured by an instrumented vehicle. However, they did find significant multivariate effects. The strong tendency of multivariate methods to capitalize on chance relationships in small samples requires that the results of Attwood et al. be interpreted with caution until replicated.

The driving range portion of the study by Klonoff (1974) most resembles the present study in method and scope with respect to the driving course tasks. Klonoff found that the higher marijuana dose (one cigarette of 1.2% THC) resulted in an increase in the number of cones hit on a slalom task, risk task, a funnel task, two tunnel maneuvers, and total composite score. No effects occurred on the back-up and corner tasks. The low dose condition resulted in detriment on one of the tunnel tasks, the cornering task, and on the total composite score. Effects on braking distance were suggestive but equivocal. Klonoff also found evidence of marijuana-induced improvement on various in-car observer ratings of on-street performance. The largest effects occurred on ratings of judgment, care, and concentration (since these are highly subjective ratings, the possibility of some observer halo bias should be noted, particularly if the raters were able to accurately guess the treatment condition).

While the majority of Klonoff's subjects showed impairment due to marijuana, a substantial minority actually improved. Several variables were analyzed as potential moderators of treatment response, including prior experience driving while under the influence of marijuana, and none produced evidence of interaction. (The present study also found no evidence of interaction on similar background variables.)

The present study was not analyzed in a way which would permit direct comparison with Klonoff's conclusion that some subjects improved following marijuana ingestion. However, we do know from the discriminant function classification matrices (which were not presented) that a small number (n=2) of marijuana subjects could not be differentiated from placebo subjects at run 3 based on their discriminant function scores. This, of course, does *not* necessarily mean that the misclassified subjects were not impaired, because these analyses did not take into account performance at baseline. It is therefore possible that the misclassified marijuana subjects represent persons who possess an extraordinarily high degree of skill, which was reduced to an average level by the marijuana treatment. This hypothesis and its articulation with Klonoff's findings will require a more in-depth analysis of the present data.

Traffic Safety Implications

Authorities are not in agreement on the traffic safety threat posed by marijuana use (Warren & Simpson, 1980). In a recent series of papers, McBay and Owens (1980) and Mason and McBay (1984, 1985) concluded that marijuana is a relatively minor factor in traffic accidents and they questioned the feasibility of relating impairment to specific levels of THC. Although many of their criticisms of past studies are both astute and pertinent, we believe these same limitations prevent forming unqualified opinions in any direction about the role of marijuana in traffic accidents. Many of the conclusions formed by McBay and his associates are based on the failure to find a substantial incidence of THC in the blood or plasma levels of drivers killed in single vehicle accidents in North Carolina. Considerable caution is necessary in generalizing incidence data from North Carolina to a state like California. Not only are there likely to be large differences in marijuana usage, there may also be large differences in driving task complexity between such states and in the use of cannabis in conjunction with vehicle travel.

In addition, Moskowitz (1985) has recently pointed out that behavioral impairment and subjective intoxication are still manifest after THC has dissipated from the blood. This factor results in an unknown proportion of false

negative findings from analyses of accident victim blood specimens. Nevertheless, the point remains that the traffic safety implications of marijuana use must ultimately be based on direct evidence of its *causal* role in increasing accident risk. This necessitates establishing accurate "population-of-risk" baselines for: (1) the incidence at which persons drive under various levels of THC alone; (2) the same incidence in combination with alcohol; and (3) the same incidence in combination with other drugs. The fact that marijuana is so often detected in conjunction with alcohol makes it difficult to establish a case against marijuana since any increase in relative risk could be due to alcohol alone. Establishing incident rates for the above risk groups would facilitate interpretation of the respective incident rates among accident-involved drivers.

Probably the most consistent and important finding of this study was the demonstration of an additive marijuana/alcohol effect on a wide array of performance measures. If one accepts the thesis that marijuana in conjunction with alcohol makes people "drunker," then it follows that marijuana in this context increases accident risk. A public policy implication of such a thesis might be to reduce the illegal, *per se*, BAC level for persons detected with both substances in their blood.

The question of the traffic safety risk posed by marijuana alone is not as clear cut as the risk presented by marijuana and alcohol in combination. Although evidence of impairment was identified in both the present and numerous past studies, the translation of this evidence into inferences about *accident causation* presents numerous difficulties. Before explaining why, we offer a dissenting opinion from a recent comprehensive review of the literature by Moskowitz (1985):

> It should be clear from the above review that there is more than sufficient experimental evidence to conclude that marijuana seriously impairs psychomotor performance required for driving. Among the areas which exhibited overwhelming evidence for impairment were: A. coordination...; B. tracking; C. perception; D. vigilance; E. driving and flying performance measured by simulators; F. driving performance on the road....
>
> Clearly, marijuana is a substance which produces serious behavioral toxicological effects. Any situation in which safety both for self and others depends upon alertness and capability of control of man-machine interaction precludes the use of marijuana.

Based on the present study and past evidence, we agree that marijuana undoubtedly impairs psychomotor abilities that are functionally related to skillful driving and that driving skill itself may be impaired, particularly at high dose levels or among naive subjects. Given these facts alone, Moskowitz' implicit recommendation that people not drive after consuming marijuana should obviously be heeded. However, the extent to which marijuana-impaired driving causes accidents cannot be deduced from the present study, or from any of the studies cited by Moskowitz. Our more conservative posture in regard to this question is based on the following rationale:

(1) In their multidisciplinary investigation of traffic accidents, Treat et al. (1979) identified "improper lookout" and excessive speed as the two most frequent human factor causes of accidents. Harano, Peck and McBride (1975) evaluated a large array of psychomotor measures including divided attention, and concluded that none were important predictors of a driver's accident propensity.

Although improper lookout may involve some of the perceptual and information-processing components affected by marijuana, it is more closely related to the search and scan strategies utilized by drivers in anticipating and detecting potential conflicts. In the only study of marijuana's impact on traffic visual search behavior, Moskowitz et al. (1976) found no evidence of a negative effect on search and scan behavior. Excessive speed can be best viewed as a reflection of attitude toward risk, risk assessment and aggressiveness. Several investigators have reported that marijuana reduces risk-taking propensity and driving speed. Because of these compensating tendencies, it is presently not possible to assess the *net impact* of marijuana as a causal agent in traffic accidents. Although some increased accident risk appears likely, the magnitude of the risk remains obscure.

(2) Many of the laboratory marijuana studies which have shown the greatest psychomotor impairment have utilized tasks that are only abstractly related to driving. Although divided attention and tracking are required for driving, it does not necessarily follow that performance on a highly novel and complex laboratory task designed to magnify performance decrements is correlated with actual "real world" performance in a vehicle. The fact that attempts to measure response to simulated accident situations

have not consistently detected a marijuana-induced decrement, even at high dose levels, underscores the need for more research (Stein et al., 1983).

Future Research Needs

In addition to the need for improved epidemiological studies mentioned earlier, the relationship between marijuana consumption and driving behavior can be clarified by a research design possessing the following characteristics:

(1) A multi-method/multi-criterion approach in which subjects perform relevant psychomotor, driving simulator, and actual driving tasks. The utilization of different measurement domains will permit an assessment of the multivariate effects across domains, leading to more generalizable characterizations of the extent and locus of marijuana-induced impairment.

(2) At least three dose levels of marijuana should be used (none, moderate, and high) in order to obtain a greater range of THC variation for investigating dose-response relationships.

(3) Frequency of prior marijuana usage should be treated as an experimental factor by selecting subjects who vary substantially on use rate. At least three levels should be employed—light users, moderate users, and heavy users. Such a design would permit an evaluation of treatment x use frequency interaction, resulting in a better understanding of whether acquired tolerance and accommodation are important factors in influencing impairment.

(4) An independent-groups design with repeated measurement trials should be employed in preference to latin square designs in which each subject receives all treatments. Individual differences in drug response and experimental error could be reduced through matching and analysis of covariance procedures.

(5) The design should include some tasks under reduced illumination to simulate night-driving conditions. Serious accidents more often occur at night, and there is reason to suspect that marijuana-induced impairment would be greater under simulated night-driving conditions.

Further research is also needed to validate the relationship between tasks (or simulators) designed to detect drug impairment and actual driving behavior, as measured by driving performance tests and accident involvement rates.

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Epidemiology of Road Accidents Involving Marijuana

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INTRODUCTION

Overview

The point of departure for this paper is captured in the contrast afforded by two quotations that summarize the state of knowledge concerning marijuana and traffic safety in 1977:

> All these studies indicate that cannabis is, as should have been anticipated, a hazardous drug for the road user.... Judgement, perception, mood, coordination and attentiveness are all affected.... At this point in time marijuana and other cannabis intoxication effects would seem to be a very real hazard in our community, especially in terms of the road toll. (Milner, 1977, p. 2)

> At the present time there is no evidence that marijuana is a significant public safety problem or is about to become one. The effects of marijuana reported in these studies are such that it is unlikely that a person driving erratically and recklessly would do so because of the influence of the drug. (McBay, 1977, p. 97)

These disparate views illustrate that unanimity of opinion regarding the issue of marijuana and traffic safety had certainly not been achieved less than a decade ago. The present paper, which focuses principally on epidemiological research since that time, is intended to determine whether the burden of evidence now weighs more heavily in one or the other direction. The purpose of this review is, therefore, to identify what is known about the magnitude of the problem of marijuana in road crashes and the level of risk it poses for traffic safety, insofar as can be determined from epidemiological research.

Background

It is widely accepted that many drugs can have serious impairing effects that could contribute to traffic accidents. The purpose of experimental research is to determine the nature and extent of those effects; the purpose of epidemiology is to determine whether those effects are translated into real problems on the highway. For example, if a drug like marijuana is shown to increase distractability in controlled settings, it would still be necessary to demonstrate not only that people actually drove under the influence of the substance, but were in fact involved in

As in the previous investigations, results from the Williams et al. (1985) study showed that drinking drivers were more likely to be responsible for their crashes than were the drug-free drivers (92% vs. 71%). However, in contrast to the previous studies, Williams et al. (1985) found that drivers in whom only marijuana was detected were *less likely* to be responsible for the crashes (53% vs. 71%). Those who had used both alcohol and marijuana were slightly more likely to be seen as responsible than those with alcohol alone. These disparities within and between the studies cannot easily be reconciled. In summary, three studies suggest that marijuana contributed to the risk of collision, one study suggests it was unimportant (may have contributed to one out of 600 fatalities) and in one study marijuana-users were actually less likely to be judged responsible for the crash than drug-free drivers. To say the least, the results are mixed and inconclusive.

CONCLUSIONS

The epidemiological literature relevant to marijuana and driving is fragmented and relatively sparse. What does exist shows that people do drive after or during marijuana-use, not infrequently, and people involved in crashes (both injury producing and fatal) show evidence of marijuana use, often quite frequent use. But, the significance of those findings remains disputed and certainly is rendered no less equivocal to date by attempts to establish the contributory role of marijuana to collisions by culpability or responsibility analysis. Closure has not yet been attained. While this may appear distressing, progress in the past decade should be judged against that made in understanding the role of alcohol in road crashes. The indictment of this relatively simple substance has required decades of research and even given such research, fundamental questions about *how* alcohol-induced impairment contributes to road crashes and the extent of this contribution remain unanswered today. In this context, there is no need to apologize for the current, relatively pathetic state of knowledge regarding marijuana and traffic safety.

As a closing note, to illustrate the complexities in the field and to amplify the diversity of opinion that exists, it is interesting to trace an issue that has recently come full circle. Early work on the involvement of marijuana in road crashes was based on toxicologic tests performed on urine specimens. Such studies were soundly criticized, since cannabinoids in urine could be present for many days after use, so the significance of the findings for road safety were indeterminate. As a result, researchers began to rely on the incidence of THC in blood, which indicated more recent use and, therefore, could potentially have more relevance to the collision. But, detections in blood, *per se*, were also judged inadequate, since low concentrations were regarded a unlikely to affect driving performance. Even this was disputed because the dose-response data needed to state what levels result in impairment were unavailable. More recently, it has been suggested that preoccupation with findings in blood are unfortunate, since there is evidence that the behavioural effects of marijuana can be detected even when there is no longer evidence of the substance in blood. Accordingly, it has been argued that what is needed in addition to blood, is urine. And, the issue has come full circle.

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The Clinical Syndrome of Marijuana Dependence

By FOREST S. TENNANT, Jr. MD. DrPH

Dependence upon cannabis sativa was initially described in the United States about 40 years ago.[1] In 1944, 55 "confirmed marijuana addicts" were admitted to a military hospital and developed withdrawal symptoms. In the same decade, Fraser in India reported on soldiers who had been ganja smokers for some years and, after joining the army, exhibited severe withdrawal symptoms due to difficulty in obtaining cannabis products.[2] Since these initial reports, a number of studies clearly document that tolerance, dependence, and withdrawal symptoms may occur after chronic administration of cannabis.[1-7] Supporting data comes from clinical observations, animal studies, and a carefully controlled trial where humans were given known quantities of tetrahydrocannabinol (THC) and then observed for tolerance and withdrawal symptoms.[3-7]

There is little question that the need for clinical treatment of marijuana dependence will escalate. Many persons who have used marijuana for several years are now beginning to realize that they are dependent and will not be able to cease use without medical intervention.

Until very recently, cannabis dependence had not been a significant clinical concern in the United States. This is accounted for by two factors. First of all, the form of cannabis usually consumed in America is marijuana, and its THC content throughout the 1970s generally ranged from about 1% to 3%. This contrasts with other countries where the more potent forms of cannabis, including hashish, ganja, and dagga have been traditionally used, and where observation on cannabis withdrawal symptoms have frequently been made.[1] In the decade of the 1980s, however, potent forms of marijuana with a THC content of 5% to 15%, as well as hashish, have emerged as the usual forms for self-administration. This high THC content makes it relatively easy to consume over 180 mg per day, which was the daily dose given to human volunteers for 11 to 21 days by Jones and co-workers, and which showed an opioid-like withdrawal syndrome when it was abruptly discontinued under controlled conditions.[7] A second factor that has helped make cannabis dependence an increasingly common clinical entity in the United States is the recent development of low-cost, urine screening technology that can detect marijuana metabolites.[8] Wide-spread urine screening in the workplace, criminal justice system, and clinical settings are now identifying persons dependent upon marijuana. This practice has resulted in routine referrals for treatment in my ambulatory clinics located in West Covina, California (East Los Angeles County). This article reviews pertinent literature and summarizes some of my clinical experiences.

EVIDENCE OF DEPENDENCE

In 1971, Deneau and Kaymakcalan succeeded in producing self-administration of THC in monkeys.[5] When THC was abruptly discontinued,

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TABLE 1
Commonly Observed Cannabis Withdrawal Symptoms*

Insomnia	Anorexia
Nausea	Photophobia
Myalgia	Cannabis craving
Anxiety	Depression
Restlessness	Mental confusion
Irritability	Yawning
Chills	Anergy

* *These symptoms have been reported in animal and human studies*

the monkeys exhibited a withdrawal syndrome that was not dissimilar to the opioid abstinence syndrome. Other investigators were able to repeat these experiments and make similar observations.[1] Self-administration has also been induced in rats following a forced injection period.[1] In early studies, rats given THC chronically also appeared to develop an opioid-type withdrawal syndrome when THC was abruptly discontinued.[1] These observations were confirmed when, in 1974, Hirschhorn and Rosecrans gave naloxone to rats treated with THC for five weeks and precipitated an opioid-like withdrawal syndrome.[5] Kaymakcalan duplicated this study and also found that naloxone produced withdrawal symptoms in THC-treated rats.[6] The most common withdrawal signs observed in both studies were diarrhea, teeth-chattering, wet-dog shakes, salivation, ptosis, piloerection, yawning, and increased activity.[1]

After the human observations of withdrawal in the 1940s, there were no reports of cannabis dependence and withdrawal symptoms in humans until the 1970s.[1] In a research project sponsored by the World Health Organization (WHO) in 1976, 50 long term cannabis users in India were compared with 25 non-user controls.[1] It was found that the majority of users (98%) felt uncomfortable if they were unable to obtain their daily supply or dose of cannabis, and in addition to a strong craving for the drugs (86%), the majority also showed mental irritability and feelings of anxiety (74%) as well as profound lethargy and physical weakness (60%). About 70% of the users reported some kind of physical discomfort in the absence of the drug. There are reports from other countries, including Greece and Egypt, where there is a relatively high hashish consumption. Tennant and Grossbeck observed dependence in American soldiers in West Germany who were able to obtain large amounts of hashish.[9] Bensusan described five young South Africans who had marijuana withdrawal symptoms for one to three days and who were able to relieve them by re-administering marijuana.[10] Teitel reported three cases of manic-depressive illness that followed withdrawal after prolonged use.[11] Other clinicians have reported that heavy marijuana users may develop tolerance rapidly, become dependent, and experience flu-like withdrawal symptoms following cessation of use.[1]

To substantiate whether withdrawal symptoms exist with chronic marijuana use in humans, controlled human studies have been done. Volunteers have been given bedtime dosages of THC and monitored in sleep laboratories. When THC is administered nightly for only four to 15 nights and then abruptly discontinued, there is insomnia and increase in REM sleep and eye movements that last for up to 12 days.[12] In addition to controlled sleep studies, Jones and co-workers gave oral THC to volunteers for 11 to 21 days and then substituted placebo. They observed a variety of withdrawal symptoms similar to those described in clinical reports and animal studies.[7]

Based on numerous reports and studies, it is clear that there is a cannabis withdrawal syndrome. I have frequently observed marijuana-dependent patients in withdrawal, and my observations support previous reports. In particular, my patients have reported insomnia, nausea, myalgia, restlessness, and irritability. Table 1 summarizes the common withdrawal symptoms that have been reported in human and animal studies. A major question is whether this syndrome is identical to the opioid withdrawal syndrome. To date there are no reports of naloxone challenges in cannabis-dependent humans. A recent animal study, however, shows that THC will deplete endogenous opioid peptides, so marijuana dependence and withdrawal may be at least partially mediated through the endogenous opioid system.[13] THC administration also has effects on the catecholamine system.[14] Another study suggests that marijuana withdrawal may be mediated through the serotonergic system.[15] Rats made dependent on THC were given chlorimipramine, which is a potent inhibitor of serotonin re-uptake. Following this challenge, they developed a clear and quantifiable withdrawal syndrome similar to that observed when naloxone was given.[3,6]

CLINICAL TYPES OF DEPENDENCE

Two types of marijuana dependence will con-

TABLE 2
Two Clinical Forms of Marijuana Dependence

	Frequency of Self-Administration	Likely Dependence Metabolite(s)	Usual Referral Route	Patient's Perceived Dependence	Usual Severity of Withdrawal Symptoms	Relapse Rate
Type One	Multiple times each day	THC 11 OH-THC	Voluntary: self referred	Significant	Moderate	High
Type Two	Every 24 to 48 hours	THC-C	Involuntary: Detected by mandatory screening	Minor to moderate	Mild	High

ront today's clinician (Table 2). Type One is an ndividual who will self-administer marijuana sev- ral times per day, usually at an interval of about vo to four hours unless asleep. This individual iay voluntarily present to the clinician with the omplaint that their daily dosage has escalated and iat they are unable to cease use without medical sistance. The patient may or may not relate men- l impairment primarily related to memory, otivation, time-keeping, abnormal thoughts, and ork or school performance. In addition, they may 'ate a number of withdrawal symptoms that :ur when they attempt abrupt cessation. The 'iety of symptoms generally resemble those :cribed in the controlled animal and human stud- (Table 1), although they may report others. The 'cise relapse rate following withdrawal is :nown, but it occurs.

SE REPORTS

Case 1: Marijuana Dependence: Voluntary Admission to Treatment

MV was a 25-year-old male who presented with ie complaint that he could not "stop marijuana by iyself." He was a 12-year user having begun mari- iana smoking at 13 years of age. He had used arijuana daily for about five years and was using :o to three joints per day at the time of admission outpatient treatment. The patient was married d held a regular job as a warehouse superinten- nt. He claimed he was having considerable con- :ts with his wife and employer. In addition, he d noticed in the two months just prior to admis- n that he occasionally heard voices that were t real, did not always have total "control over his id," and had some thoughts of suicide. He ied use of any other drug or excessive alcohol ike. His treatment admission breath alcohol negative, and his urine contained marijuana metabolite but no other abusable drug. The patient was administered desipramine, 25 mg, three times per day and was given weekly psychotherapy for approximately six months. During the first ten days of treatment, he reported insomnia, abdominal cramps, diaphoresis, tachycardia, and anxiety. These symptoms subsided, and he submitted a urine void of marijuana approximately 30 days after admission. Most of the thought disturbances noted above disappeared after about two to six weeks of treatment. He denied any marijuana use during the six months after entering treatment, and he submitted monthly urine tests that showed no marijuana.

Case 2: Volunteer with Unsuccessful Treatment

JS was an 18-year-old male who voluntarily presented because he "wanted to stop." Consumption of drugs consisted of about 3.5 grams of marijuana and hashish per day for one year prior to seeking treatment. He self-administered every one to four hours while awake and complained of chronic cough, anorexia, depression, and weight loss. When he had tried abruptly to cease marijuana by himself, he had hallucinations, depression, and anergy. Urinalysis testing revealed the presence of marijuana, but no other drugs. The patient entered a counseling program, but received no medications. Only one return appointment was kept, and he was lost to followup.

Type Two form of marijuana dependence is primarily being identified as a result of mandatory urine screening and treatment referral in the workplace. Seldom does a Type Two voluntarily present for treatment, although it may occur. In this form, the patient is usually self-administering marijuana every 24 to 36 hours and may give a history of carrying on this habit for several years. As in Type One, reported impairment relative to memory, motivation, time-keeping, and job performance is

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variable. In contrast to Type One, however, the patient may report few if any symptoms of withdrawal upon abrupt cessation. Relapse, however, is common.

Case 3: Mandatory Work-Site Detection and Referral

HS was a 37-year-old male salesperson. He was reported to the management of his company to be a marijuana user who also sold it to other employees while on company premises. A mandatory urine test revealed the presence of marijuana metabolite, and in order to retain employment he was required to undergo withdrawal and enter a periodic urine-testing program. Upon interview, he stated that he had used marijuana every evening for approximately 22 years. He believed this habit had not been injurious to himself until approximately three months prior to treatment when he began to notice some defects in his short term memory. Physical examination was normal. Plasma analysis showed there to be 148 ng/ml of 11-OH THC and 80 ng/ml of THC-C. He was administered desipramine, 25 mg, three times per day and tyrosine. During the first three weeks following cessation of marijuana, he reported mild insomnia, depression, anergy, and craving. Urine analysis showed no marijuana metabolite after about 30 days. After six weeks of abstinence, he reported improvement of short term memory and improved job performance.

METABOLIC BASIS FOR TWO FORMS OF DEPENDENCE

New data on the metabolism and pharmacokinetics of marijuana provide a sound rationale as to why two basic clinical forms of dependence appear to exist. When a marijuana cigarette is smoked, THC is converted to two major metabolites, 11-Hydroxy-THC (11-OH-THC) and 11-Nor-THC-9-Carboxylic Acid (THC-C). THC and 11-OH-THC both have psychoactive effects, and they remain in the plasma at concentrations above about 5 ng/ml to 10 ng/ml for only about two to six hours.[16-18] During this period they appear to produce a short-term characteristic "high" or euphoria. This time period correlates well with the self-administration frequency of Type One marijuana dependence. The THC-C metabolite remains in plasma at concentrations above 5 ng/ml to 10 ng/ml for at least 48 to 72 hours. Although this metabolite may produce little or no euphoria, it is likely the compound that sustains Type Two dependence. A similar phenomenon also exists with some benzodiazepines, such as diazepam, and with the opioid methadone. For example, methadone will provide analgesia and euphoria for about four to six hours, but it and its metabolites will remain in plasma for 24 hours and sustain dependence. A similar time course may be observed with

A number of studies clearly document that tolerance, dependence, and withdrawal symptoms may occur after chronic administration of cannabis.

diazepam, which also has long-lasting metabolites. For example, some withdrawal symptoms and even seizures may not appear for several days following cessation of diazepam dependence.[19] I have recently observed that withdrawal symptoms following abrupt cessation of marijuana dependence may not appear for several days.

The following is an illustrative case in which plasma concentration of THC-C was assessed at three intervals during the first week following abrupt cessation of Type Two marijuana dependence. Withdrawal symptoms did not occur until the eighth post-drug day at which time plasma concentration of THC-C was undetectable. The delay in withdrawal symptoms is undoubtedly related to slow clearance of plasma and tissues of marijuana metabolites, particularly THC-C.

Case 4: Delayed Withdrawal Symptoms

A 27-year-old male was admitted to a day-treatment program for marijuana dependence. He had been identified at work for being "under the influence" on more than one occasion and was, therefore, referred for treatment. Drug consumption consisted of intermittent cocaine use and daily use of about one marijuana joint. He perceived that he had been "addicted" to marijuana for about 15 years, and that he had skipped marijuana use on very few days during this time. A physical examination was normal except for mild nasal-septum inflammation and a swollen uvula. Urine analysis showed the presence of marijuana metabolite and marijuana plasma analysis by high performance liquid chromatography (HPLC) showed no 11-OH-THC and THC-C to be 8 ng/ml. A 24-hour urine specimen showed secretion of 2-methoxy-4-hydroxy-phenyglycol (MHPG) to be 143.0 MCG/24 hours (normal is 1164 to 2216). Since his continued employment was dependent upon attending the day-care program until his urine was void of all drugs, compliance with treatment and testing procedures was good. Withdrawal medication consisted of desipramine, 25 mg, administered three times per day, and the amino acid, tyrosine. On the third treatment day, his urine still contained metabolite, and his plasma contained 5 ng/ml of THC-C. On the eighth day of attendance, he complained of a flu-like illness consisting of nausea, vomiting, diaphoresis, chills, myalgia,

TABLE 3
Clinical Patients to Screen for Covert Marijuana Dependence

Psychiatric patients under age 35
Adolescents and young adults with recurrent respiratory ailments
Adolescents and young adults with recurrent accidents and unexplained somatic complaints
Patients under age 35 who abuse alcohol, cocaine, phencyclidine, hallucinogens, and amphetamines

anorexia, and insomnia. The patient did not relate these symptoms temporally to his marijuana use, since he had ceased use eight days previous. Plasma analysis showed no detectable presence of 11-OH-THC or THC-C, but marijuana metabolite was still present in urine at this time. The apparent withdrawal symptoms resolved within 48 hours. Marijuana metabolite remained in his urine until the 34th day of treatment.

SCREENING

There are some clear clinical indications to screen for marijuana dependence. Proper screening requires urine testing, physical examination, and history-taking relative to frequency of use (Table 3). Once detected, a treatment program can be developed. Patients who should particularly be screened by urine test are those who are under age 35 and who exhibit psychiatric symptoms, deviant behaviors, use cocaine, phencyclidine, or amphetamines, abuse alcohol, or have recurrent respiratory ailments. The association of various psychiatric symptoms and chronic cannabis use has often been described.[9] Although it is difficult, if not impossible, to always determine whether psychiatric symptoms pre-date or post-date the cannabis dependence, the association is so high that it is prudent to screen for it. In particular, chronic cannabis use has been associated with chronic thought disorders that are characterized by delusions, hallucinations, depersonalization, poor ability to perform at work or school, and inappropriate interpersonal relationships. Physical examination can often give clues to marijuana dependence. In particular, chronic marijuana smoking produces a swollen uvula and signs of chronic bronchitis. A generally unappreciated clinical candidate to screen for marijuana dependence is the adolescent or young adult who presents with apparent abuse of another drug or alcohol. For example, the underlying marijuana dependence may pharmacologically potentiate another drug, but remain unrecognized if a urine screen is not done.

Case 5: Marijuana Dependence Underlying Alcohol Abuse

A 17-year-old girl was arrested for being "drunk in public" on more than one occasion, and was referred for treatment. As part of a routine urine drug screen done for all persons under age 35 with substance abuse or psychiatric problems, she was found to have marijuana metabolite in her urine. Upon questioning, she stated that she drank alcohol only once or twice per week, but smoked marijuana daily. In addition, she questioned whether she could cease all marijuana use. Physical examination on admission to treatment revealed strabismus on the right and non-reactive pupils. She was administered desipramine, 25 mg, three times per day and tyrosine. She participated in outpatient counseling weekly. After approximately one week, the strabismus disappeared and pupils began to react. Marijuana metabolite could not be detected in urine after approximately two weeks of treatment. After three months of treatment, no known episodes of drunkenness occurred.

TREATMENT

At present there is no recognized medical withdrawal regimen for marijuana dependence. Outside of this review, the author cannot identify any reported use of a medical regimen for this purpose. Additionally, the use of the tricyclic antidepressant, desipramine, and tyrosine, a precursor of norepinephrine, as reported here, is not necessarily the optimal treatment. Recent studies of cannabis administration given to animals and humans indicate that it reduces noradrenergic activity and endogenous opioids.[13,14] For this reason desipramine, which is a potent blocker of the reuptake of norepinephrine, may be an effective withdrawal agent. For example, a case described here showed extremely low urinary excretion of MHPG, which is a metabolite of norepinephrine. Although this regimen appeared clinically effective in the cases reported here, plus others treated by me, only a double-blind, placebo-controlled study can prove true effectiveness. Regardless of pharmacologic effectiveness, I have observed that patients who present for treatment and who do not receive withdrawal medication for at least a few days tend to drop out of treatment just as did one of the illustrative cases described above. This appears to apply to both Type One and Type Two dependency.

Although there has been a scarcity of attempts at medical withdrawal, there are recent reports of hospitalization and withdrawal attempts.[20,21] Swatek found that many patients would drop out or fail to reduce marijuana use enough to ever clear

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their urine of marijuana metabolite.[20] This study points out the necessity to regularly monitor urine for marijuana metabolite as an indicator of successful treatment. I have found that assessment of the plasma concentration of 11-OH-THC and THC-C to be useful in determining whether the patient is ceasing self-administration of marijuana.

Regular psychotherapy to accompany urine monitoring and possible medication appears essential in most cases. Patients dependent upon marijuana tend to have a plethora of psychiatric symptoms and considerable problems with interpersonal relationships, motivation, and reality functioning.[9,11]

TRENDS AND RESEARCH NEEDS

There is little question that the need for clinical treatment of marijuana dependence will escalate. Many persons who have used marijuana for several years are now beginning to realize that they are dependent and will not be able to cease use without medical intervention. This realization is enhanced by the availability of more potent forms of cannabis that were not available just a few years ago. Some persons are probably becoming dependent as a result of these potent forms, where they might not have done so if their only consumption was the low potency forms that were formerly available. Perhaps the biggest impetus for dependency treatment will be the identification of dependent persons in mandatory urine screening programs operated by industry.

Research is needed to develop a medical withdrawal treatment for marijuana dependence. From a prevention perspective, we need information as to how frequently and for what length marijuana must be used to develop dependence. For example, I have clinically observed that withdrawal symptoms will occur in persons who use marijuana on a daily basis, but I am not clear as to whether they will occur in persons who use marijuana every second or third day. Since THC has long-acting metabolites whose pharmacologic activity is uncertain, our concepts of dependence must be refined. Lastly, there is almost no available data on relapse rates with marijuana dependence.

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Effects of Long Term Marijuana Use

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INTRODUCTION

While one or a few exposures to cannabis may occasionally result in untoward reactions (anxiety or panic states or accidents in connection with the intoxication), it is the consistent, heavy usage of the drug that concerns the public, the clinician and the researcher. A brief review of the impact of chronic cannabis use will be attempted here. Only selected organ systems will be mentioned since information on others remains incomplete or inconclusive.

Pulmonary Function

A few clinical studies have addressed the question of whether habitual marijuana smoking significantly increases the risk of developing lung disease. Although there have been reports of bronchitis after heavy or chronic smoking of marijuana, these are either anecdotal or based on uncontrolled clinical observations. For example, in India, Chopra (1973) observed an apparently high prevalence of asthma, bronchitis and nose and throat irritation among 124 selected cannabis users. In Jamaica, Hall (1975) noted that an emphysematous configuration of the chest was particularly common among frequent, heavy users of cannabis. However, neither of these authors systematically compared their observations in marijuana smokers with findings in a control group of subjects and both failed to take into account the variable of tobacco smoking since most Indians and Jamaicans who smoke marijuana also smoke tobacco.

In the study of Tashkin et al. (1980) in which the results of lung function tests in 74 young habitual marijuana smokers were compared with those in a control group, comparison was also made of responses to a detailed respiratory questionnaire incorporating questions relating to cough, phlegm production, shortness of breath and other respiratory symptoms. No differences were noted on comparing the symptoms reported by the marijuana smokers with those reported by the control subjects. However, in this study, the marijuana-smoking participants were carefully screened to exclude individuals with obvious respiratory disease, thereby tending to minimize the presence of respiratory symptoms in the marijuana-smoking group.

A more damaging case against cannabis was made by Tennant (1971) and Henderson (1972) and their colleagues from their observations in young U.S. servicemen in West Germany who smoked more than 50 grams of hashish per month and sought medical attention because of respiratory symptoms. Among these hashish smokers the authors found frequent, severe nose and throat inflammation, as well as X-ray findings of sinusitis and clinical and functional evidence of significant lower airway disease (bronchitis and asthma). Several of these patients with chronic cough underwent bronchoscopy and biopsy of the epithelial lining of the posterior wall of the trachea. On microscopic examination of these biopsy specimens, extensive cellular abnormalities were noted, including loss of cilia, basal epithelial cell proliferation and atypical cells, findings which have been associated with the later development of lung cancer and COPD (chronic obstructive pulmonary disease). Although most of these men also smoked tobacco along with hashish, they were in an age group in which such extensive microscopic abnormalities involving the larger airways are not generally noted among smokers of tobacco alone. In a follow-up study by the

same investigators (Tennant et al., 1980), bronchoscopy was performed in an additional group of 30 heavy hashish smokers (25-150 grams/month for 3–24 months) of whom seven did not smoke tobacco. In addition, three non-smoking control subjects and three tobacco smokers (average of 1.6 packs per day for 11.3 years) who did not smoke hashish, also underwent bronchoscopy. All of the smokers of both hashish and tobacco showed extensive abnormalities in their tracheal biopsies similar to those previously noted, whereas these abnormalities were found in only two of seven individuals who smoked hashish alone, in one of the three subjects who smoked tobacco alone and in none of the non-smokers. These findings suggest, therefore, that combined use of cannabis and tobacco may be more harmful than the use of either substance alone.

In contrast to the above observations, a Greek study (Boulougouris et al., 1976) failed to find a higher prevalence of bronchitis among 44 chronic hashish users (who also smoked tobacco) compared to tobacco-smoking controls, although cough and throat irritation were common complaints among the hashish smokers. In this study, tracheal biopsies were not obtained. The discrepancy between these findings and those in the U.S. soldiers could be due to differences in the design of the two studies: in the Greek study, subject selection forced exclusion of those with incapacitating illness, whereas the American study was conducted among individuals seeking treatment for respiratory complaints, thereby favoring the inclusion of those with more severe respiratory diseases. It is also possible that the discrepant results of these two studies were due to differences in the smoking techniques employed by the Greek and American hashish users: the rapid, deep and prolonged inhalation technique favored by Americans might lead to greater deposition of irritating particulates in the larger airways and greater exposure of the peripheral airways to the more deeply penetrating and longer-retained gaseous irritants in the smoke.

There are no data from human studies concerning the risk of death from lung cancer in relation to marijuana smoking. However, the presence of known carcinogens in marijuana smoke and the findings in the central airways of heavy hashish smokers of microscopic abnormalities that have been correlated with the subsequent development of lung cancer in long-term tobacco smokers raises the strong possibility that chronic heavy users of marijuana and hashish may be predisposed to the development of lung cancer, particularly if they also smoke tobacco. Although not a single case of lung cancer has yet been attributed to chronic marijuana smoking in this country, the possibility cannot be ignored that chronic, heavy marijuana smoking, like chronic tobacco smoking, may be a risk factor for the development of lung cancer and that the risks of developing lung cancer as the result of combined marijuana and tobacco smoking could be additive or even synergistic. With regard to the relative carcinogenic effects of marijuana and tobacco, one might conjecture that tobacco smoking poses a greater risk for the development of lung cancer than does marijuana smoking simply because many more tobacco cigarettes are generally smoked per day than marijuana joints. On the other hand, differences in the amounts of carcinogenic material deposited at certain sites in the airways (possibly related to different techniques of smoking) could magnify the carcinogenic potential of marijuana smoking compared with tobacco smoking.

Since marijuana smoking, at least in Asia and the Near East, is an older custom than tobacco smoking, it might be argued that if a real causal relationship between the development of lung cancer (and COPD) and marijuana smoking existed, it should have become apparent by now, as it has for tobacco. However, we must consider that the serious health consequences of tobacco were not well documented until the 1950s and 1960s, some four decades after the custom of regular daily smoking of moderate to heavy quantities of tobacco cigarettes was adopted by a substantial fraction of the population of the developed countries of the Western world where health is fairly closely monitored. Similarly, heavy consumption of marijuana on a regular daily basis is still relatively infrequent in our society and of more recent occurrence (past 10-20 years) than is the case with tobacco (past 60-65 years). Therefore, with respect to an appreciation of its health effects, marijuana may now be at the equivalent stage to that of tobacco cigarette smoking in the 1920s and 1930s, when the risks of tobacco smoking were not recognized due to the latency period before illness appears and the failure of diagnosticians to make the connection.

Extensive pulmonary macrophage infiltration of the lung has been documented in animals and by biopsy in humans. A recent investigation described autopsies of 13 known marijuana smokers who died suddenly from trauma. Morris (1985) reports moderate to severe infiltration of the pulmonary alveolar spaces with pigmented macrophages leading to a fibrous tissue response and ulceration. The pigmentation was due to deeply inhaled marijuana smoke. Tobacco smokers of similar age (15-41 years) show little macrophage infiltration, and they do not develop the fibrosis and inflammatory changes until after many years of smoking. This speaks for the development of chronic obstructive pulmonary disease in heavy users. One heavy marijuana smoker, 28 years old, had dyspnea on exertion due to alveoli completely filled with macrophages.

Central Nervous System

Brain wave changes from cannabis generally consist of an increase and slowing of alpha waves. This is consistent with a state of drowsiness. Although scalp electroencephalogram (EEG) records show minimal alterations, electrodes implanted in deep brain structures like the septum, a center for emotionality, obtain marked changes in electrical activity (Heath et al., 1979). In monkeys these abnormal tracings occur after smoking the equivalent of three marijuana cigarettes a day for three months and may persist for many months after discontinuance of the drug. Heath et al. (1979) reported ultra-structural changes in the septal area when monkeys received the equivalent of two cigarettes a day for six months, were withdrawn from marijuana for six months, and then autopsied. Controls did not manifest the alterations which included widening of the synaptic cleft (the space between nerve cells), clumping of the synaptic vesicles and other microscopic deviations from normal structure.

In an earlier study Campbell et al. (1971) reported cerebral atrophy in a series of young cannabis users, employing pneumoencephalography to obtain cerebral ventricular size. These subjects had used other drugs and alcohol so that the findings could not be considered definitive. In addition, two investigations utilizing computerized tomography (CT) scans could not confirm Campbell's work (Co et al., 1977; Keuhnle et al., 1977).

More recently, McGahan et al. (1984) using high resolution computerized tomography scanned three groups of monkeys. One was a control group, a second was given 2.4 mg/kg of the tetrahydrocannabinol (THC) a day by mouth for two to ten months, and a third group received a similar daily dose over a five-year period. The dosage was considered the equivalent of smoking one joint a day. The groups receiving THC were not studied until a year after discontinuing the drug. Statistically significant ventricle enlargement in the frontal and caudate areas of the brain in the five-year treated monkeys as compared to the control and short-term THC groups were found. This finding suggests that the frontal and caudate portions of the brain can atrophy after long-term administration of THC in amounts relevant to human exposure as measured by CT.

The findings revealed by the depth EEG, and the ultra-structural changes found in septal areas, are suggestive that long-term, heavy use of marijuana or THC may produce microscopic changes. The possibility of macroscopic changes in the form of cerebral atrophy remains open, and additional imaging studies must be done.

Weller and Halikas (1985) re-examined 97 regular marijuana users and 50 controls six to seven years after an original psychiatric evaluation. The members of the experimental group were not particularly heavy users with only 12% using the drug almost daily. High levels of depression and alcohol abuse were present in both groups during both examinations. The only impressive difference was an increase in diagnosable antisocial personality disorders in the marijuana group from 6% in the initial evaluation to 21% in the follow-up. The figures for the control group were 0% initially and 2% at follow-up. The authors make no attempt to explain the difference.

The possibility that cannabis interfered with antipsychotic medication was raised by Knudsen and Vilmar (1984). Ten schizophrenics controlled by depot antipsychotic drugs were acutely impaired functionally following cannabis use. The authors postulate that the cannabinoids may have an antagonistic effect upon antipsychotic medication.

Psychomotor Functioning. A wide range of intellectual performance impairment due to marijuana intoxication is known. Cognitive tasks, such as digit symbol substitution, complex reaction time, recent memory and serial subtractions, are all performed with an increased error rate as compared to the sober state. These abilities are all generally recognized to be necessary to perform skilled tasks. Marijuana interferes with the transfer of information from immediate to short-term storage. Less demanding tasks such as simple reaction time are performed as well as during the non-drug condition. A major unresolved question is whether long-term use produces irreversible effects.

In order to determine the role of alcohol and other drugs in fatal auto crashes, blood samples from deceased males between 15 and 34 years of age were obtained in four California counties. Driver responsibility for each fatal accident was determined. The blood was analyzed for 23 drugs or drug groups. The sample consisted of 440 drivers; slightly more than half were killed in single-vehicle accidents. In all, 88% of the 440 drivers were considered responsible for the crash. Only 19% had no drugs present in their blood; 81% were found to have one or more drugs present (Williams et al., 1985). Alcohol was detected in 70% of the drivers, cannabinoids in 37%, cocaine in 11%, diazepam and phencyclidine in 4%, and others in 3% or less. Fifty-two percent of those who had alcohol present, had blood alcohol concentrations (BACs) of 0.1 to 0.19%, and 30% had BACs of .2% or more. THC or its acid

metabolite were present in 0.2 to over 50 ng/ml concentrations in blood. THC was found alone in 12%, in combination with alcohol in 81%, and with other drugs in 7%.

Although alcohol is the prime cause of automotive accidents, marijuana and cocaine are currently being found frequently enough to constitute potentially significant problems. It is established that marijuana and alcohol have additive effects upon driving skills. Since marijuana metabolites were found in more than a third of the drivers, impairment due to marijuana is contributing to the problem.

The pure marijuana user is hard to find. When a small group of such individuals is identified in outpatient treatment centers, they are either quite young, or they turn out to be multiple drug users who have a primary complaint relating to their marijuana usage (Wish and Deren, 1985). Therefore, heavy marijuana users are either in a state of transition toward the use of other mind altering substances, or they are already multiple drug abusers who happen to believe that marijuana is producing difficulties that require treatment. The concerns are related to panicky feelings, especially about changes in time sense, difficulty in sensing how other people were responding to the individual, fear of losing control or inability to stop using.

Performance decrements are another source of complaints by some marijuana smokers. Low energy levels, impaired school or job performance and loss of interest in other activities are mentioned in surveys of high school seniors and others (Johnston, et al. 1986).

Weller et al. (1984) compared alcohol and marijuana use in 97 regular alcohol and marijuana users, a very common form of multiple drug use. Alcohol use preceded marijuana use by three years. Both drugs were used in social situations with about 10% meeting the criteria for alcoholism and the same number for marijuana abuse. Significant problems associated with alcohol included blackouts (20%) and self reports of overuse (27%). The significant complaints about marijuana were panic reactions (22%) and feeling addicted (14%). Of interest was the fact that only 6% of those interviewed reported traffic arrests while drinking compared to 15% while using marijuana.

A chronic cannabis syndrome sometimes follows heavy daily use, particularly in adolescents and young adults. Since it is so variable in presentation and importantly influenced by magnitude and premorbid psychopathology, its existence remains somewhat controversial. In some persons the drug is used as self-medication for a variety of dysphoric states. Chronic cannabis syndrome consists of loss of energy, reduced levels of drive and motivation, apathy, some degree of depression and agitation, and a withdrawal from previous interests. Lethargy, loss of ambition, and loss of goal directedness persist during the interval between marijuana intoxications. After months of abstinence, the anergic condition is reversed, although some clinicians insist that they have encountered permanent brain dysfunction.

In a five-year follow-up of regular marijuana users, it was found that the continued use of the drug was associated with a decrease in certain pleasurable effects (Weller & Halikas, 1984). Users who had earlier reported positive feelings of relaxation, peacefulness, enhanced sensitivity, floating sensations, self-confidence, subjective impressions of heightened mental power, and other sought-after effects now said that these effects had significantly diminished. The undesirable aspects of the experience, however, persisted essentially unchanged. It should not be assumed that the decreased pleasure over time leads to a discontinuance of cannabis use. The persistence of a well established conditioned response without particular positive rewards is also seen with regular use of other drugs such as cocaine, tobacco, phencyclidine, and heroin.

The effects of cannabis on pre-existing serious psychiatric conditions such as schizophrenia have been reviewed by J.C. Negrete (Arif & Archibald, 1981). Sufficient clinical experience is available to recommend abstinence from marijuana for schizophrenics in remission because of the possibility of precipitating a relapse. Although infrequent, other psychiatric problems can emerge. Acute anxiety and panic states from use of the drug are known, especially in persons who have never used marijuana before. Acute paranoid states will occur at times in experienced smokers who have previously used the drug without untoward reactions. Paranoid thinking tends to reverse itself upon discontinuance of the drug.

A shift in cerebral hemispheric dominance was postulated because of the dream-like, imagistic, nonlogical type of cognitive patterns induced by marijuana. It was speculated that the shift was determined to be caused by impaired left hemispheric functioning, with no alteration in right hemispheric performance (Hecht, 1980).

Learning ability during marijuana intoxication is diminished because of the perceptual changes and the fact that immediate recall is intermittently impaired. In addition, the lack of motivation to learn and the attenuation of logical thinking abilities make the acquisition of new information difficult. The incapacity to order sequences of events in time (temporal disorganization) (Tinklenberg et al., 1970), and the lack of rehearsal time associated with episodes of marijuana intoxication, tend to retard learning.

Gonads

It is now generally believed that the effects of cannabinoids on the hormones that modulate the reproductive process originate within the brain by changes in neurotransmitters like dopamine, norepinephrine and serotonin. These amines alter the secretion of the releasing hormone (Tyrey, 1984). A principal site of action of THC is in the hypothalamus where the gonadotropin releasing hormone is suppressed, which in turn inhibits the secretion of leutinizing hormone (LH), follicle stimulating hormone (SH) and prolactin in the pituitary (Smith & Asch, 1984). In turn these changes induce decreases in the female sex hormones, estrogen and progesterone, interfering with ovulation and other hormone-related functions. With discontinuation of cannabis use these effects are reversible. After chronic administration of the drug, tolerance to the reproductive effects of THC is observed. Therefore, the disruptive effects of the THC upon the non-human primate's reproductive functioning is only initially impaired. Its impact on human females requires further study.

Regular marijuana use during at least two phases of development can be detrimental: during fetal existence and during adolescence. The fetal risks will be discussed later. The endocrine events associated with puberty are strongly dependent upon a properly functioning hypothalamic-pituitary axis.

As indicated, many of the endocrine effects caused by the chronic treatment of animals with THC are reversible or demonstrate tolerance development. Still, many questions remain regarding the long-term consequences of use, for example, sperm formation, psychosexual maturation and sex organ function. Until these and other issues are resolved, it is questionable whether marijuana should be consumed by adolescents or males with marginal fertility (Harclerode, 1984).

Immune System

Although additional information regarding the reduction of immune responsibility has become available, the evidence that marijuana smoking in humans decreases resistance to infections remains inconclusive. The question is of particular importance since THC is used as a treatment for cancer chemotherapy side effects. The cancer chemotherapeutic chemicals, themselves, are severely immunosuppressive, and if THC adds to the depressed immune state, it would not be favorable. Another speculation is the possibility that certain drugs could be cofactors in producing Acquired Immune Deficiency Syndrome (AIDS). Marijuana use is often correlated with AIDS, but whether it contributes to its development is not known.

THC does decrease host resistance to herpes simplex virus, type 2, in the guinea pig. This occurs in a dose-related fashion in amounts equivalent to human consumption (Cabral et al., 1985). THC also appears to inhibit both B- and T-lymphocyte production, especially the former. Other preliminary reports suggest that THC modifies lymphocyte membranes and prostaglandin production *in vitro*. It should be recalled that AIDS is caused by a destruction of T4 lymphocytes. One *in vitro* study has shown that small doses of THC resulted in marked inhibition of macrophage spreading and phagocytosis (Lopez-Cepero et al., in press). If confirmed in animals or humans, a further mechanism of immune inhibition might be established.

Fetal Development

Additional information has accrued relating to the effects of maternal marijuana use upon fetal development. This is a complicated subject with many variables like nutrition; alcohol, tobacco, and other drug use; socioeconomic status; etc., impinging upon fetal health, and these variables must be equalized or controlled. Large numbers of mother/child pairs are necessary if infrequently occurring disorders are to be studied.

Three studies have examined samples of sufficient size to adequately parcel out the confounding effect. Hingston et al. (1982) studied 1,690 mother/child pairs. Marijuana in varying amounts was used by 234 mothers during the pregnancy. Marijuana use was found to be associated with lower infant birth weight and length compared to non-users. Women who used marijuana less than three times a week delivered infants who averaged 95 grams less, and those who used more than three times a week delivered babies 139 grams less than the non-using group. Maternal marijuana use was the strongest independent predictor of whether the infant had features compatible with the fetal *alcohol* syndrome (FAS). It was a better predictor of the FAS than alcohol use.

Gibson et al. (1983) sampled 7,301 births for abnormal infant characteristics. Maternal marijuana users were significantly more likely to deliver premature infants with low birth weight. The relationship of marijuana use to perinatal death did not achieve statistical significance, but it was suggestive (p=.12).

The largest study to date is that of Linn et al. (1983). Of 17,326 women who gave birth at the Boston Hospital for Women, 12,718 were interviewed to determine the impact of marijuana and other risk factors on the newborn. Of the 10 independent variables analyzed (which included tobacco and alcohol), marijuana use was the most highly predictive of a congenital malformation.

Hingston et al. (1984) noted that tobacco and marijuana smoking, alcohol and other drug abuse all tend to occur frequently in the same women. Therefore, some of the adverse consequences on fetal development attributed to maternal drinking or smoking may be due to an interaction with marijuana and other psychochemicals. It may be that when a number of these toxic substances are consumed together, their toxic effects on the fetus are additive.

From Downstate Medical Center in Brooklyn, Qazi et al. (1985) reported on five infants of mothers who had smoked two to 14 joints of marijuana a day prior to and during pregnancy. All denied the intake of alcohol or other psychoactive drugs except for one who had consumed a pint of rum a week. Three women smoked a pack or less of cigarettes a day during pregnancy. Each infant had a low birth weight, small head circumference, tremors at birth, abnormal epicanthic folds, posteriorly rotated ears, a long philtrum (the groove on the upper lip), a high arched palate and abnormal palm creases—all stigmata of the FAS. Why do not all heavy marijuana smoking pregnant women have abnormal offspring? Morishima's work (1984) indicates that about 5% of ova are damaged by THC exposure. It may be that a selective vulnerability to injury is present even in the same tissue.

Gross malformations in human infants due to prenatal exposure to cannabis are not yet completely proven. In mice, major malformations occur following exposure to THC, cannabinol and cannabidiol. Mice also have an increased fetal death following maternal cannabinoid administration. Prenatal effects of cannabinoids reliably decrease birth weight in most animal species. When factors like drug-related maternal malnutrition and the residual effects of cannabinoids during the nursing period are eliminated, the fetal weight loss is not large (Abel, 1985).

Infant rats given THC show damage to the hypothalamic cells that produce the gonadotropic releasing hormone. It is possible that this change is irreversible. Amounts of THC equivalent to 2.5 joints a day disrupt the processing of high energy sugars in the testes of young adult male rats.

Cannabinoid levels were found to be 2.5-6 times higher in maternal plasma than in umbilical cord plasma at time of delivery. Although the cannabinoids are certainly found in the human fetus, a partial protection may exist (Blackard & Tennes, 1984). In another investigation (Tennes, 1984), no particular effects upon the newborn were found except a decrease in length and an increase in male infants delivered in the marijuana group.

Fried (1985) found that newborn nervous system alterations in regular maternal marijuana users apparently are not manifested by poorer performance on cognitive and motor tests at one-and-one-half to two years of age. Whether this means that neurological disturbances present at birth are transient, or whether the tests used at one-and-one-half to two years of age have a decreased sensitivity, is unknown.

CONCLUSION

It is reasonable to conclude, as the Institute of Medicine report (1981) did that "what little we know for certain about the effects of marijuana on human health—and all we have reason to suspect—justifies serious national concern."

The following statements about the long-term effects of cannabis can be made.

1. Protracted use causes inflammatory changes of the upper airway and appears to play a role in chronic obstructive lung disease. The question of the carcinogenicity of marijuana must await further study.

2. An amotivational syndrome, especially among adolescents and young adults, is quite well established clinically. Whether chronic usage impairs psychomotor skills during the unintoxicated period has hardly been studied. Permanent macroscopic brain changes cannot be ruled out at this point. People with psychotic states, active or in remission, may do poorly with this drug.

3. The reproductive effects of marijuana are not yet firmly established, but indications of decreases in estrogen and follicle stimulating hormone are frequently reported. Testosterone levels in animal and some human studies show a decrement in most studies.

4. Although numerous reports of decreased immune responsivity are available *in vitro* and in small animal studies, the clinical significance of these findings remains to be established.

5. The teratogenicity of cannabis seems likely but its incidence and exact manifestations remain to be worked out in further investigations.

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The addictive potential of cannabis*

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ABSTRACT

The author reviews the literature on the dependence potential of cannabis. Case studies and experiments of tolerance to cannabis as well as psychological and physical dependence on cannabis are presented in man and in laboratory animals. Some effects common to both species are also recorded. Although the addictive potential of cannabis is often compared with the addictive potential of alcohol and tobacco, the author concludes that the characteristics of cannabis tolerance are similar to those of opiate dependence.

Introduction

Although cannabis as a psychoactive drug has been used by man for many centuries, its addictive potential has only recently been recognized. Eddy and others in 1965 described the main features of dependence for several drug types and their views on the characteristics of the cannabis-type dependence found general acceptance [1].

However, since 1965, new scientific knowledge has been acquired. The identification of Δ-9-tetrahydrocannabinol (Δ-9-THC) as the main active substance of cannabis and its synthesis [2, 3] contributed enormously to knowledge on the pharmacology of cannabis. Moreover, an explosive increase in cannabis consumption has stimulated laboratory, clinical and epidemiological research on cannabis in many countries.

The author of this paper reviewed tolerance to and dependence on cannabis some years ago [4], and this paper presents some additional information.

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Tolerance to cannabis

For a long time it was considered that cannabis did not produce tolerance. Lemberger and others in 1971, after injecting radioactively labelled (C^{14})-Δ-9-THC (0.5 mg) intravenously to chronic marijuana smokers and naive subjects, stated that non-smokers did not indicate any pharmacological effect. In contrast, all of the long-term marijuana smokers reported effects that lasted as long as 90 minutes [5]. They interpreted the results as chronic marijuana users having "reverse tolerance".

At present it is considered that so-called "reverse tolerance" is a misinterpretation [6]. However, there is evidence supporting the view that tolerance develops to many effects of cannabis both in laboratory animals and in man. The diverse effects of cannabis have been described in many species. Ataxia in the dog, ptosis of eyelids in the monkey and tachycardia in man are the most characteristic effects of cannabis use which lose their intensity after repeated administration indicating tolerance development. In most animal and human studies related to tolerance, marijuana (extract or smoke) or Δ-9-THC has generally been used. However, some investigators have also used other pharmacologically active cannabinoids such as DMPH (a dimethylheptyl homologue of Δ-6a(10a)-THC, Δ-8-THC, 11-OH-Δ-9-THC) and a few synthetic derivatives. In the following pages the term "cannabis" will, in addition to plant material, include all active cannabinoids.

Psychological dependence on cannabis

The indication of psychological dependence to any substance in man is a compulsive need to take the substance, or intensive craving for it. As is the case for many substances of abuse, psychological dependence is the basis of cannabis abuse. The continued self-administration of drugs by animals after a period of withdrawal provides evidence of psychological dependence [7]. In this context, in 1971, Deneau and Kaymakçalan [8] succeeded in producing self-administration of Δ-9-THC in monkeys. In 1972 Kaymakçalan, using cocaine, obtained self-administration of this substance in monkeys [9]. The results of these studies have been summarized in an earlier issue of the *Bulletin on Narcotics* [4].

Pickens and others in 1973 reported intravenous self-administration of Δ-9-THC in two monkeys which had previously been self-administering phencyclidine (PCP). After the substitution of Δ-9-THC, the animals continued to self-administer this latter drug [10]. In addition to intravenous self-injection, the same authors produced self-administration of cannabis smoke by inhalation, training two monkeys to smoke hashish from a tube [10].

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Van Ree and others, as well as Takahashi and Singer, were able to induce self-administration of Δ-9-THC in the rat [11, 12]. The former authors produced this effect by intravenous injection following a four-day forced injection period. At the highest dose level (0.3 mg/kg/injection) only 40 per cent of animals initiated self-administration of Δ-9-THC [11]. This percentage and the drug intake were low in comparison with self-administration of amphetamine and narcotics in the rat.

Physical dependence on cannabis

Physical dependence on cannabis in laboratory animals

Although there are reports of CNS hyper-excitability [13, 14] or increased aggressiveness in mice after abrupt withdrawal of Δ-9-THC [15], the most conclusive evidence on the physical dependence of animals to cannabis is obtained from studies of rats and monkeys.

Deneau and Kaymakçalan [8] and Kaymakçalan [9] in experiments in self-administration of Δ-9-THC in monkeys observed a typical abstinence syndrome which was not dissimilar from the opiate abstinence syndrome.

Other investigators also observed withdrawal changes in monkeys receiving either Δ-9-THC or cannabis smoke. Stadnicki and others reported the effects on behaviour and EEG in three rhesus monkeys following chronic oral administration of marijuana extract. The two monkeys that became tolerant after 50 days' treatment with Δ-9-THC (37.5 mg/kg) responded to termination of treatment with withdrawal signs manifested by increased aggressiveness. One of the two exhibited hallucinations and a period of increased EEG desynchronization [16]. Heath studied the effects of cannabis smoke on the EEG patterns taken from electrodes implanted in different parts of the brain of monkeys. After three months' exposure to cannabis there were some EEG changes which ameliorated following administration of an increased amount of cannabis [17]. Snyder and others have trained three monkeys to press a lever on a special schedule for liquid reinforcement. Following a stable baseline performance, two monkeys received 2 mg/kg of Δ-9-THC orally every third day for 90 days, with a placebo administered on intervening days. The third animal received a placebo throughout testing. When the drug was discontinued there was an abstinence effect in the drug-monkeys characterized by a change in performance [18].

Recent studies indicate that the abstinence syndrome of THC-treated rats consists of many signs and symptoms. However, some earlier works suggested the presence of some cannabis abstinence signs in rats. For example, Davis and others injected rats daily with 25 mg/kg Δ-9-THC subcutaneously for 20 days. During the immediate post-drug period a slight but statistically significant elevation of activity occurred on the second day [19]. Similarly, Pirch and others recorded electrocorticograms of rats by

implanted electrodes. During the period of chronic oral administration of marijuana extract distillate to the rats, animals were given 20 mg/kg or 40 mg/kg Δ-9-THC for 9 – 13 days. Upon termination of chronic treatment, a "rebound" increase in integrated ECoG voltage was observed. This "rebound" was maximal on the second and third day following the last dose [20]. The same group of investigators confirmed their earlier reports in a subsequent study increasing the dose of Δ-9-THC to 100 mg/kg in two animals [21]. Another cannabis withdrawal sign in the rat was an increase in grooming which was reported by Sjöden. This author studied the effects of long-term administration and withdrawal of THC (5 mg/kg Δ-8-THC or 2.5 mg/kg Δ-9-THC) on open-field behaviour in rats. During the two-week injection period a depressant effect of both isomers was noted on ambulation, rearing, grooming and latency. At drug withdrawal most open-field measures slowly returned to control levels, whereas the rate of grooming showed a definite increase [22].

Hirschhorn and Rosecrans in 1977 reported that Naloxone precipitated a narcotic-like withdrawal syndrome in rats treated for five weeks with increasing doses of Δ-9-THC, the highest dose being 32 mg/kg given during the last three weeks. The main withdrawal symptoms were diarrhoea, teeth chattering, wet-dog shakes, salivation and ptosis [23]. Kaymakçalan and others in 1977 confirmed the above and showed that abrupt withdrawal of chronic injections of Δ-9-THC can cause an abstinence syndrome. They injected 10 rats subcutaneously with Δ-9-THC daily for five weeks in increasing doses. During the last three weeks the rats received 40 mg/kg Δ-9-THC at each administration. Ten control rats received the same amount of the vehicle by the same route for the same period. The administration of Naloxone on the 22nd and 31st days and the termination of drug administration on the 35th day caused an opiate-like abstinence syndrome [24]. The most common signs of abstinence in THC-treated animals were ptosis, teeth chattering, piloerection, defecation, urination, complete palpebral closure, dyspnea and grooming. Other signs observed in less than 50 per cent of the animals were chewing, tremors on the face, rearing, abnormal posture, yawning, escape behaviour, ear blanching, eating of objects, wet-dog shakes, jumping, biting of fingers and sniffing. During abstinence, increasing locomotor activity was recorded in THC-treated animals by an activity-meter. Both abstinence scores and increased motility exhibited a peak at the 48th hour of withdrawal [24].

Taylor and Fennessy reported a chlorimipramine-induced withdrawal syndrome in the rat after chronic treatment with Δ-9-THC [25]. Chlorimipramine, which is a potent inhibitor of serotonin uptake, may antagonize some effects of Δ-9-THC in the rat. Therefore, precipitation of an abstinence syndrome with this chemical in Δ-9-THC-treated rats is considered somewhat similar to the action of Naloxone in opiate-dependent animals. The rats received increasing doses of intravenous Δ-9-THC twice daily for 10 days. The highest dose was 120 mg/kg, twice a day administered

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days 6 – 10. On day 11, some of the rats were injected intraperitoneally with 5 mg/kg chlorimipramine. Quantifiable changes in behaviour consisted of writhing, wet-dog shakes, jumping and backward kicking of the hind legs. Other symptoms included front paw tremor, ptosis, chewing movements, excessive grooming, yawning, squealing, ataxia, unsteadiness in gait and sitting up on the posterior for long periods. Reporting these findings, on another occasion, the authors stated that "Δ-9-THC is capable of inducing a state of physical dependence" [26].

Physical dependence on cannabis in man

A close survey of the literature reveals that several authors have described cannabis withdrawal symptoms in man. Most publications on this subject, with a few exceptions [27 – 29], appeared after 1970.

Observations on abstinence symptoms in man refer mainly to those countries where potent forms of cannabis (ganja, dagga, hashish) are available. However, even in the United States of America where until recently weak preparations of cannabis were being used, a detailed description of marijuana withdrawal symptoms was reported by Marcovitz and Myers in 1944 based on 35 "confirmed marihuana addicts" who were admitted to a military hospital [27]. In the same decade, Fraser in India reported on soldiers who had been ganja smokers for some years and after joining the army exhibited severe withdrawal symptoms due to difficulty in obtaining cannabis [29]. Some recent studies from India also confirmed the dependence liability of cannabis. Chopra and Jandu, in their investigation of 275 chronic cannabis users, found that a large percentage of heavy users developed physical dependence [30]. In a research project sponsored by the World Health Organization (WHO) and carried out by the Department of Forensic Medicine of Banaras Hindu University in 1976, the long-term effects of cannabis were studied in 50 cannabis users, and a comparison was made with the data obtained from 25 non-user controls. It was found that the majority of users (98 per cent) felt uncomfortable if they were unable to obtain their daily supply or dose of cannabis and in addition to a strong craving for the drug (86 per cent), the majority also showed mental irritability and feelings of anxiety (74 per cent), as well as profound lethargy and physical weakness (60 per cent). As many as 70 per cent of the users reported some kind of physical discomfort in the absence of the drug [31].

Middle Eastern and east Mediterranean countries are historically known to have a relative high hashish consumption. Kielholz and Ladewig observed withdrawal symptoms which lasted three to seven days in three young chronic hashish smokers who came to Switzerland from the Middle East [32]. According to Miras, writing on chronic hashish smokers in Greece, "there is definitely a dependence risk, although much less serious than with opiates" [33].

In South Africa also, cannabis dependence has been reported. In five young South Africans, Bensusan reported marijuana withdrawal symptoms which persisted for one to three days. The disappearance of withdrawal symptoms coincided with the possibility of obtaining cannabis [34]. The same author observed two other similar cases of acute withdrawal symptoms from cannabis smoking. Morley and others collected information on the subjective effects of cannabis from 150 individuals who had used it on at least five occasions. Fourteen reported withdrawal symptoms [35]. Levin, in a paper delivered at the First South African International Conference on Alcoholism and Drug Dependence, reported that cannabis use elicited psychiatric complications in 33 per cent of 137 cannabis users. In 5 per cent of the total group, these complications were related to drug withdrawal [36]. Again, in South Africa, Schweitzer and Levin described a case of acute brain syndrome due to cannabis withdrawal in a patient who had been hospitalized for multiple fractures [37].

Current epidemics of marijuana use among young persons have redirected the attention of psychiatrists, family physicians and paediatricians to the possibility of physical dependence on marijuana. Teitel (1977) reported three cases of manic-depressive illness which followed withdrawal of marijuana after prolonged use [38]. Manatt indicated that heavy users of cannabis experienced a mild flu-like withdrawal syndrome [39]. Lantner reported that marijuana develops tolerance rapidly, is physically addictive and many smokers report withdrawal symptoms [40].

In addition to the withdrawal symptoms in cannabis users described above, some experiments have been carried out using cannabinoids on volunteers. Williams and others in 1946 applied Parahexyl (a synthetic cannabinoid having marijuana-like effects and also known as Synhexyl) to six patients between the ages of 26 and 33 who were former marijuana smokers. The drug was given in self-chosen doses at self-chosen intervals for a period of 26 to 31 days. The daily dose ranged from 60 to 2,400 mg and was taken orally in one to eight individual doses. On the third day, after abrupt discontinuation of the drug, most patients exhibited some symptoms of withdrawal [28].

In other experimental studies the main active component of cannabis, Δ-9-THC, has been used. Some investigators were interested in the withdrawal changes in sleep patterns and in the EEG of volunteers after Δ-9-THC administration. Freeman, using all-night polygraphic recordings, studied the effect of cannabis on the sleep patterns of two young women. At night they took 20 mg/kg Δ-9-THC in fruit juice. It was noticed that physiologic withdrawal effects occurred after only four nights of Δ-9-THC use, and the author concluded that these findings support the view that marijuana does cause physical dependence [41]. In a subsequent study, Freeman administered 20 mg Δ-9-THC orally at bedtime to five volunteers, who slept for 8 – 15 consecutive nights in the laboratory. He monitored EEG, chin EMG and eye movements, and noted that Δ-9-THC decreased the REM phase of

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sleep. As in the first study, abrupt withdrawal of the drug after four to six consecutive nights of use produced mild insomnia [42]. In another study, Freeman and Al-Marashi (1977) followed the EEG patterns in sleep of two volunteers who spent 30 consecutive nights in the laboratory. The patients received 20 mg Δ-9-THC orally for 12 nights on days 7 to 18. During the first five withdrawal nights sleep latency increased more than twofold. Also, during the withdrawal period, there were a greater number of eye movements during REM sleep and a large decrease in slow wave sleep. Many changes in polygraphic sleep patterns persisted for at least 12 days following discontinuation of Δ-9-THC [43]. Feinberg and others studied the influence of orally administered Δ-9-THC on the sleep patterns of seven male volunteers. During withdrawal, total sleep time was significantly reduced, and this change was entirely due to increase in sleep latency. In addition, both REM sleep and eye movements increased; the rebound effect being greater for eye movement [44].

The work of Jones and others, carried out by oral administration of Δ-9-THC to volunteers, is the most convincing evidence that cannabis can produce physical dependence in man. The volunteers, after a gradual increase in dose, received a fixed dose of 180 – 210 mg Δ-9-THC per day for 11 to 21 days, and were then abruptly switched to a placebo for 5 – 9 days. During this period all subjects showed a variety of abstinence signs and symptoms [45]. The main objection to this work was the amount of the drug given daily to the volunteers. The term "elephant doses" has been used for this regimen [46]. However, considering that in some parts of the world daily doses of 240 – 360 mg of Δ-9-THC are not unusual, daily amounts of 180 – 210 mg may represent a human dose [47].

Some symptoms of cannabis withdrawal syndromes common to man and animals

Signs and symptoms	*Man*	*Monkey*	*Rat*
Hyperactivity	+	+	+
Increased excitability	+	+	–
Aggressiveness	+	+	–
Tremors	+	+	+
EEG changes	+	+	+
Hallucinations	+	+	?
Photophobia or palpebral closure	+	+	+
Yawning	+	+	+
Salivation	+	–	+
Anorexia	+	+	–
Diarrhoea	+	–	+
Piloerection	–	+	+
Abnormal posture	–	+	+
Licking or biting of fingers	–	+	+
Eating unusual things	–	+	+
Masturbation	+	+	?
Craving for cannabis	+	+	?

+ = present; – = absent or not checked; ? = difficult to assess

Nevertheless, the wealth of findings leaves little doubt about the existence of a cannabis withdrawal syndrome, confirming the possibility of physical dependence in man. The most frequently observed cannabis abstinence symptoms in man are excitation, irritability, agitation, restlessness, tremors or tremulousness, anxiety, depression or suicidal tendency, insomnia or sleep disturbances, sweating, abdominal distress, nausea, anorexia or decreased appetite, general malaise and muscular aches.

It is interesting to note that some of the cannabis withdrawal symptoms in man are also observed in laboratory animals (see table).

Discussion and conclusion

The demonstration of tolerance and of the dependence-producing properties of cannabis may have important academic and practical implications. In experimental animals the initiation, degree and duration of cannabis tolerance show great similarities to the characteristics of opiate dependence. There are also similarities between cannabis and opiate withdrawal symptoms in the monkey and the rat. Cannabis can potentiate some of the effects of morphine and there is cross-tolerance between the two substances. Furthermore, several common pharmacologic actions are induced by cannabis and opiates [48, 49]. The addictive potential of cannabis is often compared with the addictive potential of alcohol and tobacco. It seems that the development of dependence to any of these three most widely abused substances is related to such factors as dose (potency), frequency, duration of use as well as some possible individual factors. However, the pharmacokinetic and pharmacologic properties of the three substances are very different. Whereas alcohol and nicotine are easily destroyed or eliminated from the body, active cannabinoids remain in the tissues for a long time. In addition, the spectrum of pharmacologic effects of cannabis is so large that they cannot be compared with the effects of alcohol or nicotine.

In the future, if the availability of potent forms of cannabis becomes widespread, dependence on cannabis may create more serious problems to society.

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CHAPTER 168

Marijuana

Jack H. Mendelson

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Marijuana smoking is the most frequent form of illicit drug use in America. Although there is evidence that a gradual decline has occurred in marijuana usage by young adults in the United States from 1975 through 1984 (53), it is estimated that at least one in every 20 high school seniors smokes marijuana on a daily basis. The health benefits associated with a decline in the age of onset of marijuana smoking (100) may be offset by an increase in the potency of marijuana available in many locations in the United States (109,113). The importance of marijuana use in the causation of derangements in health, psychological status, and social function remains a subject of controversy. In this chapter we review and attempt to evaluate some pertinent biomedical and psychosocial factors associated with marijuana abuse and dependence. Because of space limitations, this review is necessarily selective. However, a number of extensive and excellent critical reviews on the effects of marijuana on biologic and behavioral function are currently available for readers who wish to obtain more detailed information (29,78,113).

CHEMISTRY AND PHARMACOLOGY

An extensive review of the chemistry, pharmacology, and toxicology of cannabis compounds was described by Harris in *Psychopharmacology: A Generation of Progress* published in 1978. Over 400 compounds in addition to the psychoactive agent Δ^9-tetrahydrocannabinol (THC) have been identified in marijuana cigarettes. The usual marijuana cigarette, prepared from the leaves and flowering tops of the plant *Cannabis sativa*, contains 0.5 to 1 g of plant material. The THC concentration in typical marijuana cigarettes may range between 5 and 20 mg, but concentrations as high as 100 mg per cigarette have been detected. Hashish is prepared from concentrated resin of *Cannabis sativa* and contains a THC concentration between 8 and 12% by weight. "Hash oil," a lipid-soluble plant extract, may contain a THC concentration as high as 25 to 60%. "Hash oil" has been added to marijuana cigarettes in order to increase the concentration of THC. During pyrolysis of a marijuana cigarette, over 150 compounds in addition to the THC are present in smoke and fumes.

Following marijuana cigarette smoking, THC is quickly absorbed from the lungs and is then sequestered rapidly from blood into body tissues. The THC is metabolized chiefly in the liver, where it is converted to 11-hydroxy-THC, a psychoactive compound, and more than 20 other metabolites. The THC metabolites are excreted via the feces at relatively slow rates.

Although many investigations of the effects of marijuana smoking on behavior (including determinations of levels of intoxication and the subjective "high") have been reported, it has been difficult to establish good correlations between clinical effects and plasma THC levels (8,34,110–112,118). In general, peak levels of intoxication occur later and persist longer than peak levels of THC in plasma. Undoubtedly, one problem in establishing covariance between behavioral effects and plasma THC levels is the complex pharmacokinetic profile of THC in humans (46). However, recent data indicate that more sophisticated analysis of pharmacologic response and plasma THC levels with compartmental models and phase plots may yield significant correlations (17). Chiang and Barnett (17) have reported that the effect compartment for psychologic high is directly coupled to the central (plasma) compartment. These inves-

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tigators concluded that "the effect is directly proportional to mean THC levels from approximately 1 to 4 hr after the start of smoking a marijuana cigarette." When data obtained in previous studies (112) were reanalyzed with the model proposed by Chiang and Barnett, good correlations were obtained between rapid behavioral and physiologic effects after marijuana smoking and plasma THC levels (17).

Delayed physiologic and pathophysiologic effects of marijuana smoking may be caused by accumulation of critical plasma levels of a major metabolite, 11-nor-COOH-THC (9-carboxy-THC) (135). Good correlations have been reported between radioimmunoassay analysis and gas chromatograph–mass spectroscopy analysis of THC and 9-carboxy-THC in plasma obtained from men and women following marijuana smoking (112), and no differences between men and women have been observed with respect to conversion of THC to 9-carboxy-THC (135).

Hunt and Jones have noted that if THC in biological fluids were confined only to blood, 99% of an intravenous dose (and presumably a similar dose administered via inhalation) would be metabolized in less than 30 min (46). However, the swift decline of THC in plasma is associated with a very rapid intake of the drug into tissue compartments. It has been calculated that approximately 70% of the THC in plasma following an i.v. dose rapidly enters the tissue compartment, and 30% is converted to metabolites. Hunt and Jones (46) state that "after approximately 6 hr the rate-limiting step for elimination of unchanged THC is not metabolism as implied by Lemberger et al. (71) but rather is a slow return to plasma of THC sequestered in tissues."

EFFECTS ON BEHAVIOR: SENSORY PROCESSES AND PERCEPTION

Since automobile accidents are a major cause of death and disability in America, marijuana effects on perceptual and sensory functions that are essential for driving are of considerable importance. Early studies (47) showed that heavy marijuana smokers often experienced distortions in the sizes of objects and also had impaired distance perception of objects and their rate of approach. Marijuana smoking reduces accurate detection of peripheral light stimuli as a consequence of impaired ocular motor control (103). Decrements in visual reaction time (104), ocular motor tracking function (4), and color discrimination have also been reported (4). Impairment in auditory function such as auditory reaction time and auditory signal detection occurs after marijuana smoking (102).

A number of investigators have reported a unique marijuana-related aberration of perceptual processes: distortion of time sense (15,36,47,132,137). Impairment of time sense perception following marijuana smoking may not only increase risk for automobile accidents but also contribute to disturbance of ideational states under nondriving conditions (83,98).

There is a strong positive correlation between the dose of marijuana used and degree of driving impairment (60,70,123). The duration of marijuana effects on driving function may persist for over 2 hr (117). Since marijuana smoking impairs driving ability, it is not surprising that the drug also adversely affects a pilot's performance during simulated instrument flying (13,49,50). Moreover, pilot performance has been shown to be impaired as a consequence of marijuana hangover effects. Recent studies have shown that significant impairment in a pilot's function may persist for as long as 24 hr following acute marijuana smoking (141).

COGNITIVE FUNCTION

Marijuana effects on cognitive function are dependent on the dose of marijuana used, the route of administration, plus the demand characteristics of the task such as difficulty, complexity, and familiarity or practice. A significant correlation between dose effects and task difficulty and complexity has been established by a number of investigators (14,115,116,140). Complex cognitive tasks are especially sensitive to marijuana effects (14,116). The acquisition of new information that requires systematic study and learning is also compromised by marijuana use (1,119,126,134). It has also been reported that marijuana use may impair short-term memory function (10,21,22,69,82,121).

MOTIVATION

Perhaps one of the most controversial purported adverse effects of marijuana use is the "amotivational syndrome" (81). Although some investigators have concluded that amotivation and loss of interest in conventional social goals is an indirect concomitant of marijuana use (107), others believe that marijuana directly impairs motivation and achievement (25,27,52,77). A major problem inherent in evaluation of clinical reports of "amotivation" is the reliability and validity of procedures employed to measure motivation.

Several studies have attempted to assess effects of marijuana smoking on motivation to obtain socially desirable goals such as money reinforcement (84,85,88,90,91). These studies indicated that marijuana smoking (including heavy marijuana smoking) did not significantly suppress operant acquisition of either marijuana cigarettes or money. However, the operant task employed in these studies, as well as those utilized by other investigators (99), was relatively easy to perform. Adverse effects of marijuana on personal achievement cannot, at present, be explained by a specific and unique drug effect on motivation.

PSYCHIATRIC DISORDERS

Marijuana-induced intoxication is similar to intoxication caused by ethanol. Marijuana users usually report enhanced mood states following smoking, but there are also reports of anxiety, depersonalization, and dissociation after marijuana smoking (19,47,58,83,107,127). Popular folklore has

argued that marijuana use facilitates aggressive behavior, but objective clinical observations have not supported this notion. Some experts have suggested that poor impulse control and enhanced aggressive behavior may occur in a minority of individuals either during active use (2,54) or during drug withdrawal (29).

Although marijuana smoking does not induce *de novo* psychiatric disorders, there is considerable evidence that marijuana smoking may aggravate preexisting illness. Paranoid symptoms as well as affective disorders may be exacerbated during marijuana use (18,37,106,127). Anxiety and panic reactions have also been reported following marijuana use in susceptible individuals (98,109,138).

TOLERANCE AND PHYSICAL DEPENDENCE

Significant tolerance develops to marijuana effects during chronic use. This process is associated with the tendency to increase dose and/or frequency of marijuana use through time (84,85,88,90,91). As tolerance progresses, psychological dependence may occur (32,113). Evidence of overt physical dependence in males has been reported by Jones et al. (57,59). The marijuana abstinence syndrome consists of anorexia, anxiety, agitation, depression, restlessness, irritability, tremor, as well as severe insomnia (56). There have also been recent reports of physical dependence on marijuana by women who were studied under controlled research ward conditions. Abrupt cessation of marijuana use following 21 days of heavy smoking caused an abstinence syndrome consisting of sweating, exaggerated deep tendon reflexes, lateral gaze nystagmus, tremulousness of the tongue and extremities, anxiety, dysphoria, insomnia, and anorexia. Onset of withdrawal signs and symptoms occurred 10 hr following cessation of marijuana smoking, and symptom intensity was greatest 48 hr after smoking. The dose of THC sufficient to induce dependence was 3.2 mg/kg body weight per day for 3 consecutive weeks (94).

PHYSIOLOGIC EFFECTS

Respiratory System

Because the most common route of self-administration of marijuana is through inhalation of pyrolyzed material, it is not surprising that respiratory disorders are common in chronic marijuana smokers. Clinical reports have implicated marijuana smoking in the causation of persistent rhinitis, dyspnea, and decreased exercise tolerance (40). Marijuana smokers are also at increased risk for developing chronic cough and bronchitis (3,129). Pulmonary function studies have shown that marijuana may produce a significant impairment in vital capacity and ventilatory function (40,86,105,128). Recent studies of pulmonary function in women who smoke marijuana revealed a striking reduction in gas diffusion across the surface of lung cell membranes (131). Women who smoked marijuana plus tobacco cigarettes had even greater impairment of lung function than those women who smoked marijuana only. Since there is evidence that women are increasing both cigarette smoking and marijuana smoking, it is reasonable to anticipate that the prevalence of pulmonary disease in women smokers will increase in future years.

Cardiovascular System

One of the most consistent effects observed in humans following marijuana smoking is tachycardia (5,9,20,35, 51,55). Electrocardiographic studies have shown that elevations of the S–T segment, increase in amplitude of the P wave, and inversion or flattening of the T wave occur following marijuana smoking (9,24,62,120,139). High doses of marijuana can induce premature ventricular contractions (62).

Blood pressure changes following marijuana smoking are variable. Increased and decreased pressure responses as well as marijuana-induced postural hypotension have been reported (11,12,55,114,136). Although no cardiovascular-related deaths directly attributable to marijuana use have been reported, it is probable that chronic marijuana smoking may exacerbate cardiac problems in individuals with preexisting cardiovascular disease (78).

Central Nervous System

Marijuana is used primarily to induce changes in mood states and behavior, but the neural mechanisms underlying this process remain to be determined. Marijuana smoking produces changes in the electrical activity (EEG) of the brain, principally a reduction in peak power of the α rhythm, a decrease in β rhythm activity, and an increase in the amplitude of the contingent negative variation (30,31,43,56,61,65,75,76). The relationship between marijuana-induced changes in the EEG and neurophysiologic impairment is unknown. Marijuana-induced structural damage to the central nervous system has not been observed in postmortem studies. Previous impressions that gross structural changes occur in the intact brains of heavy marijuana smokers have not been confirmed by studies utilizing CAT scan procedures (23,68).

Reproductive System

Marijuana-induced decrements in plasma testosterone levels observed in one laboratory (24,63,64) have not been confirmed by a number of other studies (28,38,87,89,92,122). However, marijuana smoking has been reported to cause a decrease in sperm cell count and motility (39). Marijuana-induced abnormalities in sperm cell morphology have also been reported (39,48,101).

Experimental animal studies have consistently shown that relatively small doses of THC may have adverse effects on reproductive hormones in females (6,7,16,45,66,67,79, 108,124,125). Marijuana smoking affects reproductive hormones in women differently at different phases of the menstrual cycle (95–97). Paradoxically, marijuana stimulates

the luteinizing hormone (LH) surge during the periovulatory phase of the menstrual cycle and thus may increase probability of ovulation (96). But marijuana smoking during the luteal phase of the menstrual cycle suppresses LH (96) and enhances risk for a shortened luteal phase and compromises optimal conditions for maintenance of pregnancy. If pregnancy is sustained, adverse effects of marijuana on LH and uterine function may increase the probability for occurrence of fetal abnormalities. Taken together, these data suggest that acute marijuana smoking may stimulate ovulation but that maintenance of pregnancy may be compromised and, if pregnancy is sustained, there is increased risk for damage to the fetus. Marijuana-induced changes in reproductive hormones may be one important factor that contributes to congenital malformation and behavior disorders that have been reported to occur in newborns whose mothers were chronic marijuana smokers (74).

Acute marijuana smoking suppresses prolactin levels in women (97), a finding that is consistent with data reported in studies with female rodents and monkeys (7,16,44,45,66, 67,133). Marijuana-related suppression of plasma prolactin levels appears unique for women, since marijuana has not been found to suppress prolactin levels in men (64,72,93). Although it remains to be determined if marijuana-induced suppression of prolactin occurs in lactating as well as nonlactating females, inhibition of prolactin secretion during lactation could impede adequate nurturance of newborns who are maintained on schedules of breast-feeding. It is also possible that marijuana-induced prolactin suppression in women could have therapeutic applications for the management of neoplastic disease associated with prolactin hyperstimulation. More precise delineation of the sites of marijuana action on neuroendocrine function should be carried out with provocative tests that have been shown to be efficacious in clinical medicine for identifying hypothalamic and pituitary dysfunction (80).

There have been a number of reports of adverse effects of marijuana smoking on fetal growth and development. A high frequency of low-birth-weight children has been reported for women who chronically use marijuana during pregnancy (130). Prospective studies with large population groups revealed that there was a significant inverse relationship between number of marijuana cigarettes smoked by pregnant women and birth weight of their children. The lowest birth weight of newborns occurred in women who were the heaviest marijuana smokers. Longitudinal studies also revealed that a number of prominent features of the fetal alcohol syndrome were also commonly observed in the offspring of heavy marijuana users (42). Behavioral evaluation of newborns whose mothers smoked marijuana heavily showed that these infants had a higher frequency of tremor and startle responses in comparison to offspring of women who never smoked marijuana (33,74).

POTENTIAL THERAPEUTIC USES FOR MARIJUANA

Because marijuana is classified as a drug that has no applications for medical use (FDA schedule I), few investigations have been carried out to assess any possible therapeutic uses. In 1976, Cohen and Stillman edited a volume that highlighted a number of possibilities for therapeutic potentials of marijuana (26). Unfortunately, few effective therapeutic uses for marijuana have been discovered and confirmed in controlled clinical trials. One exception is the development of synthetic cannabis compounds that appear to be efficacious for reduction of nausea and vomiting associated with chemotherapy for neoplastic disease (41,73).

SUMMARY

Although recreational use of marijuana by young adults in the United States is decreasing, millions of persons consistently abuse the drug. Since inhalation of pyrolyzed marijuana leaf remains the most common route of administration, marijuana-induced pulmonary disease is likely to become a major public health problem. At present, considerable evidence for marijuana-related impairment of pulmonary function has been well documented in clinical studies. Many specialists in pulmonary medicine believe that marijuana smoking, similar to cigarette smoking, enhances risk for development of lung cancer. Persons who appear to be at greatest risk are women who smoke both marijuana and tobacco cigarettes.

Initial reports that marijuana suppresses testosterone levels in males have not been confirmed, but marijuana use does reduce sperm cell motility and function. The significance of these effects on male fertility have not yet been determined.

Marijuana smoking produces significant changes in female reproductive hormone function. In addition, low-birth-weight children and fetal abnormalities have been reported in the offspring of mothers who regularly smoke marijuana during pregnancy.

Persons who constantly use marijuana in high dosage often have concomitant social, occupational, and interpersonal problems. These individuals are also at greater risk for developing polydrug abuse disorders. However, the specific and unique antecedent biologic, psychologic, and social factors that enhance risk for marijuana or other drug abuse disorders have not been discovered.

Although much has been learned about the chemistry and pharmacology of marijuana and other cannabis compounds, their mechanism of action in the central nervous system is not well understood. Similar to other self-administered intoxicating agents (e.g., alcohol), tolerance and dependence (psychologic and physiologic) on marijuana may occur in men and women.

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Health Aspects of Cannabis*

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I. Introduction

THE MODERN era of research into the effects of cannabis in man began less than 20 years ago. Many issues about its health hazards, as they are with all drugs, remain controversial and ambiguous. Many adverse reactions to drugs were not recognized until after much exposure had occurred. Often these are idiosyncratic or allergic reactions. On the other hand, adverse reactions due to extensions of the pharmacological action of a drug may be recognized both early and late. A similar pattern holds for cannabis.

The ambiguity currently surrounding the health hazards of cannabis may be attributed to a number of factors besides those which ordinarily prevail. First, it has been difficult either to prove or to disprove health hazards in man from animal studies. When such studies of cannabis reveal possible harmful effects, the doses used are often large and treatment is generally short. Second, cannabis is still used mainly by young persons in the best of health: Fortunately, the pattern of use is more often one of intermittent rather than regular use, the doses of drug usually being relatively small. This factor might lead to an underestimation of the potential impact of cannabis on health. Third, cannabis is often used in combination with tobacco and alcohol, among licit drugs, as well as a variety of other illicit drugs. Thus, potential health hazards from cannabis may be difficult to distinguish from those of concomitantly used drugs. Finally, the whole issue of cannabis use is so laden with emotion that serious investigations of the health hazards of the drug have been colored by the prejudices of the experimenter, either for or against the drug as a potential hazard to health.

Assessment of the therapeutic potentials of marijuana is also clouded by prejudices, either for or against the drug. Virtually every claim of therapeutic benefit made for marijuana is for a condition for which there are already many effective treatments. Thus, to justify the use of the new agent, it must be subjected to the same elements of proof as a brand-new drug. Thus far, none of the potential indications has been officially recognized.

This report will focus on three main areas: (*a*) acute and chronic effects of cannabis in humans; (*b*) issues regarding its possible adverse effects on health, including its effects on driving ability; and (c) the therapeutic potential of cannabis constituents or synthetic homologs of such constituents.

II. Acute and Chronic Effects of Cannabis in Humans

A. Acute Studies

The availability of synthetic trans-delta-9-tetrahydrocannabinol (THC), the major component of cannabis, and chemical techniques for quantifying its content in cannabis preparations and in blood have made possible for the first time pharmacological studies which provide some precision in dose. When the material is smoked, as it is most commonly used in North America, a variable fraction of THC is lost by smoke escaping into the air or exhaled from the respiratory dead space. Relatively little is lost by pyrolysis, since it is likely that the cannabinoid is volatilized in advance of the burning segment of the cigarette. The efficiency of the delivery of a dose by smoking has been estimated to be about 18%, but frequent smokers obtain 23%, while infrequent users obtain only 10% (110). THC and marijuana extracts are also active by mouth; the systemic bioavailability of oral administration is only about 6%, one-third that from smoking (130).

When smoked, THC is rapidly absorbed, and effects appear within minutes. If marijuana is of low potency, effects may be subtle and brief. Seldom do they last longer than 2 to 3 h after a single cigarette, although users prolong effects by repeated smoking. Oral doses delay the onset of symptoms for 30 min to over 2 h, as well as prolonging the span of action of the drug. These time schedules are consistent with knowledge of the pharmacokinetics of the drug. Smoking is similar to i.v. administration in producing maximum plasma concentrations early, while p.o. administration produces slower rises of maximum plasma concentrations, which are also lower than those for smoking (105, 130). Although the route of administration affects the time course and intensity of cannabis effects in man, the pattern of these effects was well established by early investigators (84, 88).

All observers have commented on the constant increase in pulse rate, often one of the first effects of the drug. Blood pressure tends to fall slightly or remains unchanged; at higher doses, orthostatic hypotension occurs. Conjunctival reddening is also consistently observed. Both this symptom and the increased pulse rate correlate quite well in time with the appearance and duration of psychic effects of the drug, as well as the plasma concentrations of the drug (6). Muscle strength is decreased. Appetite is inconsistently augmented, along with an increased food intake (80). Observed physiological effects have not included changes in pupil size, respiratory rate, or deep tendon reflexes.

Perceptual and psychic changes are biphasic. An initial period of euphoria or "high" is followed by drowsiness. Time sense is altered, hearing is less discriminant, and vision is apparently sharper with many visual distortions. Depersonalization, difficulty in concentrating and thinking, and dream-like states are prominent. Many of these symptoms are similar to those produced by psychotomimetics.

The effects that users derive from cannabis are extremely variable. Some of this variability depends on individual variation in degree of tolerance to the drug, based on prior use. Although it is customary to ascribe some variability to difference in setting, i.e., the type of

conditions and surroundings which prevail during drug use, or to set, i.e., the expectations of the user, proving the effects of either has been difficult. One study indicated that, with pharmacologically active doses of the drug, extreme variations in setting produced little alteration of drug effects, which were clearly different from those produced by placebo (82).

B. Chronic Studies

The effects of chronic use of cannabis are more to the point when considering the issues of its status as a possible social drug. Three large-scale field trials of cannabis users have been implemented, but the results of these trials have done little to allay apprehensions about the possible ill effects of chronic use. Objections have been made about the small samples used, the sampling techniques, and the adequacy of the studies performed.

Jamaica is a country in which cannabis is widely used, under the name ganja. The content of the THC in native cannabis is generally high, estimated at several-fold that of cannabis generally available to users in North America. The average Jamaican user smokes seven to eight cannabis cigarettes a day, such use not being considered deviant in that country. Sixty adult workers, all men, were selected for study. Thirty were ganja smokers, and 30 were not, although the latter may have used cannabis tea. Extensive studies in the hospital revealed no significant physical abnormalities between the two groups. The smokers were found to be at greater risk of functional hypoxia, which might have been due to the fact that tobacco was also used by this group. Smokers claimed to use cannabis so as to work better, but evidence in a selected subgroup supported slightly decreased performance. The small sample and the fact that impairment may be difficult to detect in unskilled workers make it difficult to be sanguine about these generally negative results (147).

A similar study was done in Costa Rica, another country in which cannabis use is prevalent. Two groups of 80 subjects, users of cannabis and nonusers, were compared by a variety of clinical and laboratory examinations. Essentially no difference between the two groups was detected (34). Forty-seven chronic users of hashish in Greece were compared with 40 nonusers, focussing primarily on tests of brain damage. No evidence of abnormality in function as judged by a variety of tests could be detected in the hashish group as compared with the others. The hashish users had a higher prevalence of personality disorders, probably unrelated to their use of hashish but possibly contributing to it (49).

If field studies fail to provide evidence of harm from prolonged use of cannabis, it is unlikely that experimental studies will do better, and such has been the case. The results of a 30-day high-dose cannabis study in which doses up to 210 mg of THC per day were administered p.o. to volunteers were most remarkable in how well the subjects tolerated such large doses (93). Tolerance was probably present in most subjects prior to the study, but it was rapidly augmented during it. Under these conditions, a mild withdrawal reaction was found when the drug was abruptly discontinued. Additional unanticipated findings were weight gain, bradycardia, and an absence of psychotomimetic effects. As the amount of drug absorbed from p.o. administration may be small, these results are only partially applicable to smoking.

A longer experimental study in which cannabis was smoked rather than taken p.o. exposed subjects from 35 to 198 mg of THC daily for 78 days. The unique contribution of this study was the discovery of the effects of cannabis in lowering intraocular pressure. Other effects noted were lowering of serum testosterone levels, airway narrowing after heavy use, lack of chromosomal alteration, and unchanged immune responses (35). Other effects of chronic cannabis use are related in a specific publication of the New York Academy of Sciences on chronic cannabis use (31).

In summary, we have a very good idea of the acute effects of cannabis, although these are tempered by the dose of THC, the route of administration of the previous exposure of the user to the drug, and possibly by their past experiences with it. The effects of chronic use are somewhat less certain. Experimental studies suggest that tolerance develops rapdily, that a mild withdrawal reaction may occur, and that some acute effects may be reversed (for instance, a slow heart rate with chronic use rather than a rapid one as seen with acute use). Field studies have failed to detect any major health consequences from chronic heavy use of cannabis, but these studies have many deficiences, most studies being far too small to pick up unusual or rare consequences that could be of great importance. Nonetheless, one is forced to conclude that cannabis is a relatively safe drug as social drugs go. To date it compares favorably with tobacco and alcohol, if not with caffeine. One should bear in mind, however, the very long time that it took to determine the ill effects of health of these accepted social drugs.

III. Possible Adverse Effects of Cannabis on Health

A. Immunity

A number of in vitro studies, using both human and animal material, suggest that cell-mediated immunity may be impaired after exposure to cannabis. Clinically, one might assume that sustained impairment of cell-mediated immunity might lead to an increased prevalence of opportunistic infections, or an increased prevalence of malignancy, as seen in the current epidemic of acquired immune deficiency syndrome (AIDS). No such clinical evidence has been discovered. Despite some degree of impairment of immune responses, the remaining immune function may be adequate, especially in the young persons who are the major users of cannabis.

An impairment of cellular immunity in 51 chronic users of cannabis was shown by inhibition of lymphocyte blastogenesis from the mitogen, phytohemagglutinin (171). A decrease in T-lymphocytes was found in 9 of 23 chronic cannabis users, employing rosette formation as a way of quantifying T-lymphocytes; the number of total lymphocytes was not different from nonusers (66). Thus, two early studies suggested that T-lymphocytes might be decreased in number as well as in ability to respond to an immunologic challenge. Immunosuppression was shown in animals by prolonged allogenic skin graft survival, inhibited primary antibody production to sheep erythrocytes, and a diminished blastogenic response (109).

Further studies have tended to confirm an immunosuppressant action of cannabis in animals, whether the material was given p.o. or injected i.p. (144, 185). Mice treated with THC and challenged with gram-negative bacteria showed enhanced susceptibility (19). However, others, using in vitro techniques for studying lymphocytes, have found no alteration in nucleic acid synthesis in the presence of as much as 10.6×10^{-4} M concentrations of THC (137).

Effects of cannabis on T-cells may be transitory. Smoking of cannabis temporarily decreased T-cell function in 13 chronic users as compared with 9 matched nonsmokers, but the effects varied from subject to subject and were closely related to the time at which the blood samples to be tested were drawn (134). Although early T-cell rosette formation was impaired in ten chronic cannabis smokers, despite a normal total of circulating T-cells, the absence of clinical evidence of greater disease susceptibility among such subjects makes this observation of dubious clinical importance (45, 126).

Other studies cast doubt on some of the earlier positive observations of impaired cellular immunity. Dinitrochlorobenzene is used as a skin test for intact delayed hypersensitivity, mediated by cellular immunity. No differences were observed in 34 chronic marijuana smokers as compared with 279 nonsmokers (152). The response of cultured lymphocytes from 12 long-term smokers of cannabis to two mitogens was not impaired as contrasted with lymphocytes from nonsmokers (178). Even the ingestion of cannabis in amounts of 210 mg daily of THC failed to alter the response of the subject's lymphocytes to mitogen stimulation (105).

In summary, evidence is difficult to interpret concerning a possible suppressant effect of cannabis on cell-mediated immunity. If suppression occurs, it may be only transient, in the sense that recovery can occur. Further, the degree may not be clinically significant as the reserve capacity of the body to respond to immune challenge may not be exceeded. We simply do not know how much impairment is necessary to make someone vulnerable. Clinical experience has not yet indicated an increased vulnerability of cannabis users, but further observations of the possible contribution of marijuana use susceptibility to develop AIDS must be awaited.

B. Chromosomal Damage

Adverse effects on chromosomes of somatic cells have been especially controversial. The techniques of human cytogenetic studies still leave much to be desired. Assessing damage to chromosomes is more of an art than a science. Interpretations are highly subjective, and it is often difficult to get agreement between any two readers of the same slide. Further, processing of cells to make the chromosomal preparations may differ from one laboratory to another, so that it is possible to get conflicting results from the same blood specimen even when read by the same reader. One needs only recall the controversy about chromosomal damage from lysergic acid diethylamide (LSD) a few years ago to interpret any reports of chromosomal damage with great caution. As similar types and degrees of chromosomal alteration have been reported in association with other drugs commonly used in medical practice, without any clinical evidence of harm, the significance of such changes remains unclear. Early reports were positive, but more recent reports were negative. A significant increase (3.4 *versus* 1.2%) of chromosomal abnormalities was reported in marijuana users as compared with nonusers (155). Changes were largely breaks or translocations of chromosomes. More of the latter were found in chronic cannabis users than in nonusers, but when breaks were included in the count the differences vanished (76). No increase in chromosomal breaks was found in cells from subjects taking p.o. hashish extract (which contains THC as well as cannabinol), marijuana extract (containing only THC) or synthetic THC (128). After 72 days of chronic smoking of cannabis, no increase in break frequency was found over that which existed prior to the study (116).

Both the retrospective and prospective studies have flaws, and one simply cannot conclude that the issue is settled. For that matter, it has not yet been settled for a variety of drugs, including aspirin, in which an increased number of chromosomal abnormalities have been described. One must conclude for the time being that, even if a small increase in chromosomal abnormalities is produced by cannabis, the clinical significance is doubtful.

C. Pregnancy and Fetal Development

This is another area of great uncertainty about the meaning of data. Virtually every drug that has been studied for dysmorphogenic effects has been found to have them if the doses are high enough, if enough species are tested, or if treatment is prolonged. The placenta is not a barrier to the passage of most drugs, so the assumption should be made that they will reach the fetus if taken during pregnancy (3).

This assumption is well validated for THC, based on autoradiographic studies (87). A high incidence of staining of fetuses was seen in mice treated on day

pregnancy with a single i.p. dose of 16 mg of cannabis resin per kg. No reduction in litter size or apparent malformations were seen. When the same dose was given repeatedly from days 1 to 6 of pregnancy, fetal resorption was complete (133). Treatment of mice from days 6 to 15 of gestation with THC at doses of 5, 15, 50, and 150 mg/kg had no effect on fetal weight, prenatal mortality rate, and frequency of gross external, internal, or skeletal abnormalities (50). Exposure of pregnant rats to either cannabis smoke or smoke from extracted marijuana throughout gestation produced less fertile offspring with smaller reproductive organs in the cannabis-treated animals (12, 54).

Pregnant rabbits treated p.o. with daily doses of THC at 15 mg/kg on days 6 to 18 of gestation delivered infants without visible abnormalities (36). Injection s.c. of doses of THC up to 100 mg/kg daily on days 6 to 15 of gestation had no teratogenic effect (97). Fetal resorption was seen in rats treated with s.c. doses of THC at 100 mg/kg for days 1 to 20 of gestation, but lesser doses had no effect (18).

Clinical studies have also not elucidated the question. An epidemiological study found more meconium staining of the fetus and more disturbances of the duration of labor (either short or long) among 35 users of marijuana as compared with 36 nonusers (63). However, no significant difference was found between 19 moderate to heavy users and many more nonusers in regard to several neonatal outcomes (53). Small sample sizes reduce the confidence in the results of either study. A much larger study involved 12,424 women of whom 1,246 (11%) were marijuana users. Lower birth weights, a shorter gestation period, and more major malformations were found among the offspring of users (111). No changes in serum human chorionic gonadotropin, placental lactogen, progesterone, estradiol, and estriol were found in 13 women who smoked marijuana during their pregnancy, compared with a matched control number who did not (20).

In summary, it is still good practice in areas of ignorance, such as the effects of drugs on fetal development, to be prudent. While no definite clinical association has yet been made between cannabis use during pregnancy and fetal abnormalities, such events are likely to be rare at best and could easily be missed. The belated recognition of the harmful effects on the fetus of smoking tobacco and drinking alcoholic beverages indicates that the same caution with cannabis is wise.

D. Cell Metabolism

Information currently available for the effects of cannabis on cell physiology and metabolism is limited. Smoke from both cannabis and tobacco increased the size of the cytoplasm, nuclei, and nucleoli along with an increase in DNA content of human lung cell explants. Mitotic abnormalities were also noted with an increase of 10 to 25% over those of controls. Combination of both smokes produced greater abnormalities than either one alone. Malignant cell transformation of hamster lung culture was observed after administration of both types of smoke (108). These findings suggest that cannabis smoke is harmful to lung cells in cultures and contributes to the development of premalignant and malignant lesions.

Cannabinoids may also interfere with the normal cell cycle. Experiments with the protozoan, *Tetrahymena*, synchronized in culture, showed a reduction in growth rate during log phase and a lengthening of the mean division time upon exposure of THC. These changes were dose dependent (183). Addition of THC to various human and animal cell cultures has been shown to decrease synthesis of DNA, RNA, and protein (17).

The clinical implication of some of these findings is obscure. On the one hand, exposure to smoke from cannabis may be carcinogenic. On the other, the changes in nucleic acid synthesis, were they to be specific for rapidly dividing cells, such as those of malignancies, might be useful therapeutically in their treatment.

E. Psychopathology

Cannabis may produce directly an acute panic reaction, a toxic delirium, an acute paranoid state, or acute mania. Whether it can directly evoke depressive or schizophrenic states, or whether it can lead to sociopathy or even to the "amotivational syndrome" is much less certain. The existence of a specific cannabis psychosis, postulated for many years, is still not established. The fact that users of cannabis may have higher levels of various types of psychopathology does not infer a causal relationship. Indeed, the evidence rather suggests that virtually every diagnosable psychiatric illness among cannabis users began before the first use of the drug. Use of alcohol and tobacco, as well as sexual experience and "acting-out" behavior, usually antedated the use of cannabis (68). When the contributions of childhood misbehavior, school behavioral problems, and associated use of other illicit drugs were taken into account, it was difficult to make a case for a deleterious effect of regular marijuana use (69). Thus, it seems likely that psychopathology may predispose to cannabis use rather than the other way around.

1. Acute panic reaction. This adverse psychological consequence of cannabis use is probably the most frequent. About one in three users in one high school and one in five in another reported having experienced anxiety, confusion, or other unpleasant effects from cannabis use. These unpleasant experiences were not always associated with unfamiliarity with the drug; some subjects experienced these adverse reactions after repeated use (7). The conventional wisdom, however, is that such acute panic reactions occur more commonly in relatively inexperienced users of cannabis, more commonly when the dose is larger than that to which prior users may have become accustomed, and more commonly in older

users who may enter the drug state with a higher level of initial apprehension (67).

The acute panic reactions associated with cannabis are similar to those previously reported to be caused by hallucinogens. The subject is most concerned about losing control, or even of losing his or her mind. Reactions are usually self-limited and may respond to reassurance or "talking down"; in the case of cannabis use, sedatives are rarely required as the inherent sedative effect of the drug, following the initial stimulation, often is adequate. Occasionally one may see a dissociative reaction, but this complication is readily reversible. Depersonalization may be more long-lasting and recurrent, somewhat akin to "flashbacks" reported following hallucinogens; the electroencephalogram shows no abnormality (158).

2. Toxic delirium. Very high doses of cannabis may evoke a toxic delirium, manifested by marked memory impairment, confusion, and disorientation (120). This nonspecific adverse psychological effect is seen with many drugs, but the exact mechanism is not clear in the case of cannabis as it is in the case of *Datra stramonium* smoking, for instance, which produces potent anticholinergic actions. As high does of any drug tend to prolong its action, delirium is self-limited and requires no specific treatment. Highly potent preparations of cannabis are not as readily available in North America as in other parts of the world, so these reactions are less commonly observed in the United States and Canada.

3. Acute paranoid states. It is difficult to gauge the frequency of these reactions. In a laboratory setting, they are frequently encountered. Quite possibly the experimental setting creates a paranoid frame of reference to begin with. That this reaction is not peculiar to the laboratory is evident from reports in which it has been experienced in social settings (96). The illegal status of the drug might contribute in such instances, for while intoxicated, one might be more fearful of the consequences of getting caught. Undoubtedly, the degree of paranoia of the individual is also an important determinant, so that this reaction may represent an interplay between both the setting in which the drug is taken as well as the personality traits of the user.

4. Psychoses. A variety of psychotic reactions have been ascribed to cannabis use. Many are difficult to fit into the usual diagnostic classifications. Two cases of a kind of manic reaction were reported in children who were repeatedly exposed to cannabis by elders. Both required treatment with antipsychotic drugs but ultimately showed a full recovery (16). Hypomania, with persecutory delusions, auditory hallucinations, withdrawal, and thought disorder, was observed in four Jamaican subjects who had increased their use of marijuana (71). Twenty psychotic patients admitted to a mental hospital with high urinary cannabinoid levels were compared with 20 such patients with no evidence of exposure to cannabis. The former group was more agitated and hypomanic but showed less affective flattening, au[illegible] hallucinations, incoherence of speech, and hysteria tha[illegible] the 20 matched control patients. The cannabis patients improved considerably after a week, while the control patients were essentially unchanged (146). Thus, a self-limiting hypomanic-schizophrenic-like psychosis following marijuana has been documented.

Psychoses in a group of East Indian marijuana users were predominantly instances of toxic delirium, but those who had "schizoid" features became overtly schizophrenic during the period of intoxication (30). The aggravating effect of marijuana on preexisting schizophrenia has been documented (169). However, it was impossible to distinguish retrospectively those individuals who exhibited behavioral changes in association with marijuana smoking from those who did not (114).

A controversial clinical report of 13 adults with psychatric disorder associated with the use of cannabis included some who had schizophrenic-like illnesses and one with depressive features. The majority of these subjects had used only cannabis, which was thought be the major precipitant of their disorders (98). A similar report from South Sweden involved 11 patients observed over a 1-year period. None had previous psychosis or abused other drugs. A mixture of affective and schizophrenic-like symptoms, as well as confusion and pronounced aggressiveness, was observed. The mental disturbances were self-limiting and rare (132).

It is impossible to think of any controlled trial that could be designed to detect adverse psychiatric effects from chronic use of a drug. Thus, clinical reports have long served as the surest way to detect adverse effects of both social and medically used drugs. Imperfect as such reports are, they can never be ignored.

Chronic use of hashish among a group of military personnel was tolerated quite well. Panic reactions, toxic psychosis, and schizophrenic reactions were infrequent occurrences among this group of 720 smokers, except when hashish was used in conjunction with alcohol or other psychoactive drugs. Rather, these 110 subjects who used the highest doses (over 50 g/month) developed a chronic intoxicated state characterized by apathy, dullness, lethargy, as well as impaired judgment, concentration, and memory (163).

The paranoid psychosis associated with long-term cannabis use was contrasted with paranoid schizophrenia in groups of 25 Indian patients with each syndrome. The cannabis psychosis was characterized by more bizarre behavior, more violence and panic, an absence of schizophrenic thought disorder, and more insight than was seen in the clearly schizophrenic group. The psychosis with drug use cleared rapidly with hospitalization and antipsychotic drug treatment and relapsed only when drug use was resumed (164). If there is a true cannabis psychosis, this description is probably the most accurate.

It would seem reasonable to assume that cannabis

[illegible] unmask latent psychiatric disorders and that this [illegible]ion probably accounts for the great variety that have been described following its use. On the other hand, evidence for a specific type of psychosis associated with its use is still elusive. Hallucinogenic drugs have a similar property of unmasking latent illness, but a drug such as LSD, being much more disruptive to mental functioning than cannabis, is much more likely to precipitate a true psychosis or depression. Needless to say, use of cannabis should be discouraged (as would probably be the case with most socially used psychoactive drugs) in any patient with a history of prior emotional disorder (5).

5. Flashbacks. This curious phenomenon, in which events associated with drug use are suddenly thrust into consciousness in the nondrugged state, has never been satisfactorily explained. It is most common with LSD and other similar hallucinogens but has been reported fairly often with cannabis use. At first, it was thought that the phenomenon occurred only in subjects who had used LSD as well as cannabis, but more recent experience indicates that it occurs in those whose sole drug use is cannabis (153). One possibility is that flashbacks represent a kind of *deja vu* phenomenon. Another is that they are associated with recurrent paroxysmal seizure-like activity in the brain. The most unlikely possibility is that they are related to a persistent drug effect. They may occur many months removed from the last use of either LSD or cannabis, so that it is highly unlikely that any active drug could still be present in the body. Further, the interval between last drug use and the flashback is one in which the subject is perfectly lucid. For the most part, the reactions are mild and require no specific treatment.

6. Violence. The myth dies hard that cannabis makes otherwise docile subjects violent. Virtually every experimental study of cannabis that has tried to measure violent or aggressive behavior or thoughts during cannabis intoxication has come to the same conclusion; they are decreased rather than increased. A study of 40 college students focussed specifically on this problem, comparing cannabis with alcohol. Expression of physical aggression was related to the quantity of alcohol taken, but not to any dose of THC (64). Similar findings have resulted from surveys (162). Aggressive and sexually assaultive behavior in delinquent adolescents was more common following use of alcohol, even in those who also used cannabis (168). A review of the whole subject of cannabis and violence came to the consensus that cannabis does not precipitate violence in the vast majority of users. The possibility was entertained that a rare individual with some special predisposition to aggressive or violent behavior may be triggered into expressing such behavior under the influence of the drug (2).

7. Amotivational syndrome. Whether chronic use of cannabis changes the basic personality of the user so that he or she becomes less impelled to work and to strive for success has been a vexing question. As with other questions concerning cannabis use, it is difficult to separate consequences from possible causes of drug use. It has been postulated that the apparent loss of motivation seen in some cannabis users is really a manifestation of a concurrent depression, for which cannabis may have been a self-prescribed treatment (102).

The demonstration of such a syndrome in field studies has been generally unsuccessful. Cannabis use among working men in Costa Rica did not impair to any detectable degree their ability to function (26). Much the same was found among Jamaican laborers. No signs of apathy, ineffectiveness, nonproductiveness, or deficits in general motivation were found (38). Each of these approaches has been criticized on the basis that those surveyed were unskilled workers in whom subtle impairment might be difficult to detect. However, a study of college students came to similar conclusions (117). Little evidence was adduced that dropping out of college was associated with cannabis use. Family background, relationship with parents during high school, and social values were stronger forces than drug use. Thus, in subjects with moderate use patterns of cannabis, no evidence of the amotivational syndrome was detected (18). A similar survey of college students found no significant relationship between marijuana use and achievement, orientation, or actual performance (123).

Laboratory studies have provided only scant evidence for this concept. A Canadian study showed a decrease in productivity following the smoking of cannabis. The decreased building of stools was due to less time worked than lessened efficiency at work (122). Using an operant paradigm, volunteer subjects on a research ward worked less as their consumption of cannabis increased. The decreased work output might have been due to decreased ability to work rather than decreased motivation (119). The former possibility is not suggested by neuropsychological testing of long-term users. No generalized decrement was observed in adapative abilities or cerebral functions (24). Similar results were found in members of a United States religious sect that relies on cannabis use. They showed no impairment of cognitive functions on a number of neuropsychological tests (150).

If this syndrome is so difficult to prove, why does concern about it persist? Mainly because of clinical observations. One cannot help being impressed by the fact that many promising youngsters change their goals in life drastically after entering the illicit drug culture, usually by way of cannabis. While it is clearly impossible to be certain that these changes were caused by the drug (one might equally argue that the use of drug followed the decision to change life style), the consequences are often sad. With cannabis as with most other pleasures, moderation is the key word. Moderate use of the drug does not seem to be associated with this outcome, but

when drug use becomes a preoccupation, trouble may be in the offing.

8. Residual psychomotor impairment. Almost any task, if it is made difficult enough or if a large enough dose of drug is given, can be shown to be impaired by acute administration of cannabis. More to the point is whether following chronic use impairment remains a problem. Experimental studies in rats suggest that it does, but such studies are always difficult to extrapolate to man (47). A comparison of 23 chronic users of bhang (equivalent to about 50 mg of THC daily for at least 5 years) with 11 nonusers revealed some evidence of impairment in the users. The latter had lower intelligence and memory quotients with lower scores on psychomotor tests (179). For whatever reasons, studies of cannabis done in India tend to show more evidence of impairment or other adverse effects than those done elsewhere.

9. Brain damage. The startling report of cerebral atrophy in ten young men who were chronic users of cannabis aroused a great deal of controversy (22). The subjects selected for the study were ones who had come to psychiatric and neurological attention, besides which they had used other drugs. Even the validity of the method of measuring atrophy by comparing pneumocephalograms of the patients with negative controls was questioned. A study in monkeys provided some support for this observation. After 2 to 3 months of heavy to moderate exposure to marijuana smoke, electrographic recording changes were noted in the septal region, hippocampus, and amygdala which persisted 1 to 8 months after smoke exposure stopped. Ultrastructural changes were seen in synapses, as well as destruction of rough endoplasmic reticulum and the presence of nuclear inclusion bodies. No such changes were observed in animals exposed to smoke from extracted cannabis (73).

The advent of computerized tomography reopened the question. Two studies using this technique have effectively refuted the original claim of brain atrophy. Nineteen men with long histories of heavy cannabis smoking were examined, and none was found to have brain atrophy as determined by this sensitive technique (101). A similar finding was noted in the other study (33). On the other hand, alcohol has long been thought to cause brain atrophy, but recent studies suggest that it may be partially reversible (23). As brain atrophy from alcohol requires a substantial amount of use, it is possible that with longer exposure, heavy users of cannabis might show a similar pattern, but at present this seems unlikely.

Thus, the issue of brain damage is not totally resolved, although the original observation of brain atrophy seems to have been disproven. The issue is of tremendous importance and probably can only be settled by some suitable animal model, as studies in man are confounded by too many other variables.

F. Tolerance and Dependence

Tolerance to cannabis has long been suspected to occur during its continued use. Narrative accounts indicate that chronic users of the drug either show very little effect from moderate doses or require very large doses to produce the characteristic intoxication. A pioneer study of subchronic administration of cannabis and synhexyl, a synthetic cannabinoid, suggests at best some degree of tolerance to the euphoriant actions (180). Yet it has only been in the past few years that tolerance to cannabis has been clearly documented experimentally.

The demonstration of tolerance in man was delayed by ethical restrictions on the amount of exposure permissible to human subjects. For instance, in an early study subjects were exposed only to a test dose of 20 mg of THC p.o. and then given the same doses or placebos repeated at bedtime for 4 more days, followed by the same THC dose as a challenge on the fifth day. Using such small doses and relatively infrequent intervals, it was impossible to show tolerance to the psychic effects of the drug, although tolerance to the tachycardia and dizziness produced by the drug were evident (85).

Other early studies likewise suggested tolerance without definite proof. Tolerance to both tachycardia and "high" was reported following 21 days of consecutive smoking of only one cigarette a day by experienced smokers. It was possible that these subjects may have already been tolerant to the drug (46). Another study, in which subjects smoked a cannabis cigarette containing 14 mg of THC for 22 days, revealed a progressive decline in the increase of pulse rate following smoking, an increase in alpha rhythm on the electroencephalogram, and more decrement in the performance of short-term memory and reaction time tasks (49).

A number of other early studies provided less evidence of tolerance. Little evidence of tolerance to clinical effects of cannabis was found from daily smoking of marijuana cigarettes over a period of 10 to 28 days (51, 142). Free choice of marijuana cigarettes for 21 days also provided little evidence to support the concept of tolerance in man (165). Meanwhile, substantial evidence had accumulated that tolerance could be shown in various animal species, especially with high doses of THC given for prolonged periods.

Definite evidence of tolerance to the effects of THC in man was adduced only when it became permissible to use comparably large doses over longer periods of time. Subjects in one 30-day study were given high doses (70 to 210 mg/day) of THC p.o. around the clock. Tachycardia actually became bradycardia, and a progressive loss of "high" was noted (49). Similar tolerance to cannabis smoking was observed in a 64-day study in which at least one cigarette daily had to be smoked with smoking as desired later in the same day. Additionally, in this study tolerance developed to the respiratory depressant effect of THC (13).

The pattern that has emerged in man, therefore, is that tolerance is not a problem when doses are small, or infrequent, or where the pattern of use of the drug is not

prolonged. Tolerance only becomes a major factor with high, sustained, and prolonged use of the drug. It is interesting that no study in man or animals ever revealed any evidence for "reverse tolerance" or sensitization, such as had been reported in an early, rather naive clinical study of marijuana (176).

1. Cross-tolerance. THC has effects which in man somewhat resemble those of hallucinogens and strongly resemble those of alcohol, while in animals it slightly resembles morphine. No cross-tolerance to mescaline or lysergide (LSD) could be shown in rats (151). Rats tolerant to the effects of THC were also tolerant to ethyl alcohol, but when the situation was reversed, less tolerance to the THC was seen in alcohol-tolerant animals (127). Perhaps this difference in sequential tolerance is why THC has never become established as a treatment for alcohol withdrawal, despite some early clinical trials that suggested a favorable effect. Cross-tolerance between THC and morphine has been shown in rats using customary tests of analgesia (95).

2. Physical dependence. Evidence from both animals and man indicates that physical dependence can be induced by abuse of THC. All monkeys given automatic injections of doses of THC of 0.1 to 0.4 mg/kg showed abstinence signs when withdrawn. When monkeys were allowed to self-administer the drug for 3 to 8 weeks, the majority had an abstinence syndrome when the drug was abruptly discontinued. The syndrome appeared approximately 12 h after the last administration and lasted about 5 days. It was characterized by irritability, aggressivity, tremors, yawning, photophobia, piloerection, and penile erections (95).

In man, a somewhat similar, though mild, withdrawal reaction was uncovered after abrupt cessation of doses of 30 mg of THC given every 4 p.o. for 10 to 20 days. Subjects became irritable, had sleep disturbances, and had decreased appetite. Nausea, vomiting, and occasionally diarrhea were encountered. Sweating, salivation, and tremors were autonomic signs of abstinence (49). Relatively few reports of spontaneous withdrawal reactions from suddenly stopping cannabis use have appeared, despite the extraordinary amount of drug consumed. Five young persons experienced restlessness, abdominal cramps, nausea, sweating, increased pulse rate, and muscle aches when their supplies of cannabis were cut off. Symptoms persisted for 1 to 3 days (15). The rarity of reports of these reactions may reflect the fact that they are mild, and seldom is a user completely cut off from additional drug.

Cannabis would have been an exceptional centrally acting drug if tolerance/dependence were not one of its properties. The fact that tolerance was not strongly recognized as an effect of chronic use of the drug until fairly recently was due to the narrative nature of previous accounts of tolerance in man and the lack of systematic animal experimentation. Tolerance has now been proven for most of the actions of THC. It develops at varying rates for different actions, but it is rapidly reversible. Large doses of THC are required over long time periods for tolerance to develop. As most social use of the drug does not meet these requirements, neither tolerance nor dependence has been a major issue in its social use.

G. Endocrine and Metabolic Effects

Changes in male sex hormones have been a source of controversy ever since the first report of a cannabinoid-induced decrease in serum testosterone level. Decreased levels were associated with morphological abnormalities in sperm and with decreased sexual functioning (100). Such changes must require long-term exposure to cannabis, for subchronic studies in experimental subjects have generally failed to confirm these findings (118). During the first 4 weeks of a chronic administration study, no major changes in hormone levels were detected, but with subsequent exposure a decrease first occurred in luteinizing hormone (LH) followed by decreases in testosterone and follicle-stimulating hormone (FSH) (99). Testosterone synthesis by Leydig cells was decreased in rats, both by THC as well as by other cannabinoids (21). A similar finding had been reported earlier (57). A review of the literature on this subject concluded that no significant effect was found in regard to serum testosterone and that sperm production was decreased but without evidence of infertility. Ovulation was inhibited, and luteinizing hormone was decreased. Cannabinoids had no evidence of estrogenic activity, which had been postulated earlier (4).

The meaning of such changes in man is uncertain, as the hormone levels generally remained within the accepted limits of normal. Further, a single hormone level may not be truly representative of the prevailing levels of hormones that tend to be secreted episodically or which are subject to many extraneous influences.

Data on the effects of cannabis on the female reproductive system are sparse. Preliminary unpublished data indicate that women who use cannabis 4 times a week or more have more anovulatory menstrual cycles than do nonusers of the same age. Animal work tends to support this observation. THC administered to rats suppressed the cyclic surge of LH secretion and of ovulation (11).

Gynecomastia has been thought to be a complication of cannabis use, especially when it was also possible to stimulate breast tissue development in rats with THC (72). Eleven soldiers with gynecomastia of unknown cause were matched with 11 others with similar characteristics except for gynecomastia. No difference in cannabis use was found between the two groups (27). Such a finding does not disprove the relationship between cannabis and gynecomastia. Indeed, if cannabis increases peripheral conversion of testosterone to estrogens, then it is possible that the increased estrogens could stimulate breast tissue in a few susceptible men. Increased estro-

gens might also account for some reports of diminution in sexual desire or in performance in men.

These endocrine changes may be of relatively little consequence in adults, but they could be of major importance in the prepubertal male who may use cannabis. At least one instance of pubertal arrest has been documented. A 16-year-old boy who had smoked marijuana since age 11 had short stature, no pubic hair, small testes and penis, and low serum testosterone. After stopping smoking, growth resumed and serum testosterone reached the normal range (41). As recent surveys of cannabis use indicate that some boys (and girls) may be exposed to it even as early as the prepubertal years, this question is of more than academic interest.

Although cannabis has been said in the past to cause hypoglycemia, this error has been pointed out in numerous studies. On the contrary, some subjects showed impaired glucose tolerance following experimentally administered i.v. doses of 6 mg of THC. Such a dose is probably greater than one generally attains from usual cigarettes but might be obtained from high-grade hashish. The deterioration of glucose tolerance was accompanied by increased levels of plasma growth hormone, as well as by a normal plasma insulin response. These findings suggested that growth hormone might be interfering with the action of insulin (83). A study in rabbits indicated that blood glucose was increased by single doses of THC but that this increase could be prevented by adrenalectomy. Increased release of epinephrine following THC was postulated as a possible cause for the hyperglycemia (70). Although large doses of THC might aggravate diabetes, the rarity of this phenomenon in clinical practice may be due to the lower doses of THC used socially or the development of tolerance to this specific pharmacological effect.

H. Lung Problems

Virtually all users of cannabis in North America take the drug by smoking. As inhaling any foreign material into the lung may have adverse consequences, as is well proven in the case of tobacco, this mode of administration of cannabis might also be suspect Smoking is a most efficient method for administering the drug, due to the enormously high lipid solubility of THC. The pulmonary surfactant is a perfect trap for THC which is then rapidly absorbed into the blood. The kinetics of the THC administered by smoking are similar to those of its i.v. administration.

Heavy use of hashish by soldiers produced a number of bronchopulmonary consequences, including chronic bronchitis, chronic cough, and mucosal changes of squamous metaplasia, a precancerous change (74). Although at first THC was thought not to be a respiratory depressant, more careful studies indicated that it was when given p.o. in doses of 22.5 mg (14). Thus, its use in any form by patients with impaired pulmonary function would be hazardous. Young, healthy volunteer subjects in a chronic smoking experiment had pulmonary function tests before and after 47 to 59 days of daily smoking of approximately five marijuana cigarettes a day. Decreases were found in forced expiratory volume in 1 s, in maximal midexpiratory flow rate, in plethysomographic specific airway conductance, and in diffusing capacity. Thus, very heavy marijuana smoking for 6 to 8 weeks caused mild but significant airway obstruction (161).

Quite possibly such dramatic early changes are not progressive with continued smoking (171). Compared with tobacco, cannabis smoking yields more residue ("tar"), but the amount of smoke inhaled is very likely to be considerably less. The study in which five cigarettes were consumed daily represented heavy use of the drug, compared with 20 to 40 tobacco cigarettes which might be consumed by a heavy tobacco smoker. Low values for specific airway conductance were found in marijuana smokers, a change not observed in tobacco smokers. This change indicates mild impairment of large airway function. No differences were found between marijuana smokers and nonsmokers in spirometric indices, closing volumes, or nitrogen concentrations between 750 and 1250 ml of expired air (159). Marijuana smoke inhibits pulmonary antibacterial defense systems, mainly alveolar macrophages, in a dose-dependent manner. The cytotoxin involved is not related to any psychoactive component (86). One would assume that marijuana smokers might be more susceptible to bacterial infections of the lung, yet such increased susceptibility has not been clinically documented.

The issue of damage to lungs from cannabis is somewhat confounded by the fact that many cannabis users also use tobacco. As yet, it is far easier to find pulmonary cripples from the abuse of tobacco than it is to find any evidence of clinically important pulmonary insufficiency from smoking of cannabis.

I. Cardiovascular Problems

Tachycardia, orthostatic hypotension, and increased blood concentrations of carboxyhemoglobin from cannabis smoking would undoubtedly have deleterious effects on persons with heart disease due to arteriosclerosis of the coronary arteries or congestive heart failure. Although a slight trend toward increased use by persons over age 30 years has been detected in recent epidemiological studies, it is unlikely that many persons with serious heart disease will be exposed to this hazard from cannabis use.

Tachycardia is a consequence of almost every acute dose of cannabis, although some degree of tolerance develops to this effect. Evidence suggests that it is mainly due to an inhibition of vagal tone (32). Increasing the heart rate and thereby cardiac work might be harmful to patients with angina pectoris or congestive heart failure. A direct test of the effects of marijuana smoking in exercise-induced angina proved this harmful effect of the drug. Smoking one cigarette containing 19 mg of THC

decreased the exercise time until angina by 48%. Smoking a marijuana placebo cigarette decreased the exercise time until angina by only 9%. Thus, smoking marijuana increased myocardial oxygen demand and decreased myocardial oxygen delivery (9). A subsequent study compared the effect of this type of marijuana cigarette with that of a high nicotine cigarette. The marijuana cigarette decreased exercise time to angina by 50%; the nicotine cigarette decreased the exercise time to angina by 23% (10). Clearly, smoking of any kind is bad for patients with angina, but the greater effect of cannabis in increasing heart rate makes this drug especially bad for such patients. Fortunately, few angina patients are devotees of cannabis.

A rapid heart rate might be expected to aggravate congestive heart failure. Actually, little is known about the direct effects of THC on myocardium. A single study using an isolated rat heart reported a negative inotropic effect from THC, i.e., weaker contractibility of the muscle (115). If so, the use of cannabis by patients in congestive heart failure could make matters even worse.

Premature ventricular contractions have been reported following marijuana smoking (91). However, when subjects were continually monitored electrocardiographically while smoking cigarettes containing approximately 20 mg of THC, no increase in such premature beats was found (145). Ventricular premature beats are rarely observed and do not seem to be of any great clinical importance.

J. Eye Problems

Eye complaints of cannabis users are vague and mild. All of 350 cannabis users had some eye complaints. Several consistent findings were (*a*) photophobia and blepharospasms; (*b*) injection of the globe; (*c*) increased visibility of the corneal nerves; and (*d*) accommodative or refractive changes. Visual acuity was preserved, but pupillary reactions were sluggish. Both alcohol and cannabis produced moderately debilitating effects on lateral phoria and abduction. During smoking, lacrimation may be observed along with the characteristic marked conjunctival injection. Despite the fact that numerous and complex changes occur in the eyes of cannabis users, these effects are confined to the anterior segment and in most respects mimic an irritative process of that region. They are transient and not cumulative. They are probably of little clinical significance (60).

Reduction in intraocular pressure is a characteristic effect from cannabis. This action provides distinct therapeutic possibilities and will be discussed later.

K. Contamination of Cannabis

The most definite health hazard was contamination of cannabis, largely of Mexican origin, by the herbicide, paraquat. Inhalation of toxic amounts of this material could lead to severe lung damage, and some instances of acute toxicity have occurred. Paradoxically, this hazard stemmed from efforts to save cannabis users from less well-documented hazards to their health.

Estimates of the amount of contaminated cannabis reaching North America may have been grossly exaggerated due to false positive results in testing for paraquat. Formerly as much as one-third to one-half of Mexican cannabis was assumed to be contaminated. The results of later analyses suggest that only about 10% is contaminated. The problem still remains for the user as to how to identify such a contaminated product.

One thought has been to look for red spots on the marijuana leaves. This approach may be difficult for the leaves usually are available in a finely ground form. A red fluorescence is seen under ultraviolet light, such as is commonly used in discotheques. A similar red fluorescence may be seen on the lips of the smoker of paraquat-contaminated cannabis.

After the experience with paraquat in Mexico, its use was temporarily discontinued. Recently, the possibility that it may be used against cannabis crops in California and Hawaii has resurfaced. One would hope that overzealous law enforcement would not once again pose a serious health risk to marijuana users.

Cannabis is generally harvested like any other crop. The final product of ground leaves and stems look very much like grass cut by a mower. Usual insecticides and fungicides are rarely used, as the plant grows abundantly with minimal care. Other sources of contamination may include insects and fungi.

L. Possible Accumulation of Drug

The major if not the sole active component of cannabis, THC, is highly lipid soluble. As the human body has a high lipid content, which includes not only body fat, but also brain and most cell membranes, lipid-soluble drugs tend to leave the blood rapidly to be distributed to fatty tissues. It is characteristic of such drugs that the action of a single dose is terminated not by the elimination of the drug through metabolic processes, but by redistribution to sites in the body where it cannot act. The prime example of such a drug is pentothal sodium, which rapidly produces anesthesia when given i.v., but which has a very short span of action. The drug still remains in the body, but in places where it cannot act. A similar situation applies to the widely used sedative drug, diazepam.

An early study of the pharmacokinetics of THC examined its tissue distribution following a single s.c. injection in rats. Following a single injection of radiolabeled material, the concentration of THC in fat was 10 times greater than for any other tissue examined, and persisted in this tissue for 2 weeks. Thus, there is good evidence that THC and its metabolites might accumulate not only in fat, but also in brain (107).

Obviously, similar studies could not be done in man. One can measure in man the extraction of cannabis metabolites following single or repeated doses, to get some idea of their persistence. Following both single and

repeated doses (at least single doses for several days), metabolites of cannabis can be found in the urine for varying periods, up to several days following the last dose (94). All of these metabolites are ones that are known to have no mental effects, except for a miniscule amount of unchanged THC which is excreted during the first 4 h following a dose, while the drug is having definite clinical effects. The excretion of these metabolites is not accompanied by any evidence of cannabis-like effects.

We may conjecture that THC rapidly leaves the blood to be sequestered in fatty tissues. It is either gradually metabolized in these tissues to inactive metabolites which are then excreted in the urine, or it may be gradually released from these tissues in small amounts to be metabolized by the liver before attaining effective plasma concentrations. In either case, there is no evidence of a continuing drug effect from this accumulation of drug in the body.

No one has yet reported on the excretion of metabolites following prolonged exceedingly high dose administration of THC. In one study in which doses of up to 210 mg of THC were given p.o., abrupt discontinuation of the drug led quickly to mild signs of a withdrawal reaction (49). As the development of withdrawal reactions is contingent upon a rapid decline to the point of absence of active drug in the body, one must assume that no accumulation of active drug occurred, even under extreme circumstances.

In short, the apprehension about accumulation of THC from repeated use is based on evidence indicating only the accumulation of drug that is either in inactive form to begin with or which is rendered inactive before reaching the circulation in any pharmacologically active amount. We do not know the full toxicity of many of the possible metabolites which might accumulate, but generally toxicity studies of cannabis and its constituents lead to the inescapable conclusion that it is one of the safest drugs ever studied in this way.

M. Effects on Driving an Automobile

If marijuana is to become an accepted social drug, it would be important to know its effects on driving ability. Fully one-half of the fatal car crashes in the United States are associated with another social drug, alcohol. Neither experimental nor epidemiological approaches to the marijuana question have yet provided definitive answers.

Many studies have used acute doses of marijuana or THC to study various psychomotor functions. These can be summarized by saying that, if the dose of drug was high enough or the task difficult enough, impairments were shown. It is difficult to determine how pertinent these tests are to the actual driving of an automobile. Furthermore, it is difficult to relate the effects of acute consumption of marijuana, often in relatively naive subjects, to the effects that may be found in chronic users, who may have developed some degree of tolerance.

Studies on the acute effects of marijuana on simulated driving have shown mixed results. The first compared smoked marijuana (doses uncertain) with ethanol in sufficient quantities to produce alcohol levels of 100 mg/dl. Marijuana increased speedometer errors but produced no deviation from the norm on accelerator, brake, signal, steering, or total errors. Alcohol had a far more deleterious effect (43). Marijuana administered p.o. in doses of 8, 12, and 16 mg was compared with a dose of 70 g of alcohol in eight volunteer subjects performing a simulated driving task. Both marijuana and alcohol increased the time to brake and to start, but these changes were confined to the 16-mg dose of THC (138). Marijuana was smoked with the intention of administering doses of 0, 50, 100, and 200 μg/kg, a most dubious assumption. No significant deviations from the norm were noted in car control and tracking aspects (124).

Actual driving in normal traffic conditions would more closely mimic real-life situations, including the dangers. Sixty-four volunteer subjects smoked cigarettes containing 0, 4.9, or 8.4 mg of THC. Oddly enough, THC had a biphasic effect, causing deterioration of driving skills in some subjects and improvement in others. A recently completed study compared the effects of smoking a marijuana cigarette with or without alcohol, alcohol alone, and placebos for each drug. Actual driving was done over a course rigged with various traffic problems. Both drugs produced impairment of driving performance, the combination being worse than either alone (141).

Fifty-nine subjects smoked marijuana cigarettes until "high" and then were tested periodically by highway patrol officers on the roadside sobriety test. Overall, 94% of subjects failed to pass the test 90 min after smoking and 60% after 150 min, despite the fact that by then plasma concentrations of THC were rather low (81). It appeared that establishing a clear relation between THC plasma concentrations and the degree of clinical impairment will be much more difficult than has been found in the case of alcohol (140). The exact prevalence of persons who might be picked up while driving under the influence of marijuana is uncertain. One survey found at least 5 ng of THC per ml in the blood specimens of 14.4% of a random sample of 1792 drivers detained for erratic driving. Many were also associated with blood levels of alcohol as well (184).

Flying an airplane is much more difficult than driving an automobile, but the general principles of impairment are similar. Ten certified pilots who smoked marijuana or placebo were tested on a simulator. The results were highly variable from pilot to pilot and from skill to skill. It was assumed that the pilots had regained full function after 4 h (90). Somewhat contrary results were obtained in another similar study which found, however, some degree of impairment in flying skills as long as 24 h after an exposure to marijuana. The subjects were unaware of any such impairment (182).

The issue is not clearly settled, but common sense would suggest that it would be unwise to try to drive an automobile soon after exposure to marijuana. In our first study with the drug, the subjects were asked during the period of their intoxication, "Would you be able to drive a car now?" Their uniform answer was, "You've got to be kidding." The biggest areas of doubt are how long the impairment, even though subtle, may last and how to deal forensically with driving while under the influence of marijuana. The best evidence at present would be to assume that any amount of THC more than 10 ng/ml in plasma is presumptive evidence of impairment. Such a decision is arbitrary, but so have been forensic decisions about the presumed level of intoxication with alcohol.

IV. Therapeutic Uses

For many centuries, cannabis was used as a treatment, but only during the 19th century did a particularly lively interest develop for exploiting its therapeutic potential. Cannabis was reported to be effective in treating tetanus, convulsive disorders, neuralgia, migraine, dysmenorrhea, postpartum psychoses, senile insomnia, depression, and gonorrhea, as well as opium or chloral hydrate addiction. In addition, it was used to stimulate appetite and to allay the pain and anxiety of patients terminally ill with cancer (64, 121). However, the advent of modern pharmacology beginning in the 20th century discovered many other drugs more definitely effective in these disorders, with a subsequent decrease in the enthusiasm for cannabis as a therapeutic agent.

Advances in the chemistry of cannabis during the 1940s established tetrahydrocannabinol (THC) as the major active component. A semisynthetic THC-like material, synhexyl, was tested as a therapeutic agent during the late 1940s and early 1950s. Initial trials reported efficacy as an antidepressant and as a treatment for alcohol or opiate withdrawal, but subsequent clinical evaluations were negative (155, 166).

The exact structure of THC was shown in 1964 to be delta-9-trans-tetrahydrocannabinol, which was soon synthesized. The relative abundance of this material permitted extensive laboratory and clinical studies from 1968 onwards. These studies have included potential therapeutic uses.

At the present time, a number of pharmaceutical houses have programs to develop cannabinoids as therapeutic agents. The major problem is to separate the specific desired pharmacological effect from the pronounced mental effects of cannabinoids. A number of reviews of the potential therapeutic uses of cannabis have been published recently (36, 92, 104). We will now discuss some indications of current interest.

A. Antiemetic for Patients in Cancer Chemotherapy

Cancer chemotherapy, especially with the agent cisplatin, produces severe nausea and vomiting, which is extremely difficult to treat with ordinary antiemetic drugs, such as prochlorperazine. This complication is so severe that many patients forego effective cancer chemotherapy. The antiemetic effects of cannabis had been suggested as early as 1972 (6). THC was first tried as an antiemetic in a controlled trial comparing it with placebo in 20 patients undergoing cancer chemotherapy. Fifteen mg were given to some patients and 20 mg to the others in the form of gelatin capsules containing THC dissolved in sesame oil. The initial dose was started 2 h before chemotherapy and repeated 2 and 6 h later. Fourteen of the 20 patients in whom an evaluation could be made reported a definite antiemetic effect from THC, while none was observed from placebo during 22 courses of that drug (149).

Since then, studies have been largely confirmatory but not entirely so. Fifty-three patients refractory to other treatments were studied in an uncontrolled fashion. Ten had complete control of vomiting when THC was administered prior to chemotherapy and for 24 h thereafter. Twenty-eight had 50% or more reduction in vomiting, and only 15 patients showed no therapeutic effect whatsoever. However, four patients were dropped from the study because of adverse effects (113). Fifteen doses of 15 mg of THC were compared with 10-mg doses of prochlorperazine in a controlled cross-over trial in 84 patients. THC produced complete response in 36 of 79 courses, while prochlorperazine was effective in only 16 of 78 courses. Twenty-five patients received both drugs, of whom 20 preferred THC. Of the 36 courses of THC that resulted in complete antiemetic response, 32 were associated with mental effects characterized as a "high" (148). Another comparison between THC in 15-mg doses and prochlorperazine in 10-mg doses *versus* a placebo control was made in 116 patients who received p.o. doses 3 times a day. The THC regimen was equal to prochlorperazine, and both were superior to placebo. However, many patients who received THC found it to be unpleasant (55). A comparison of THC with placebo was made in 15 patients with each patient acting as his or her own control. Fourteen of the 15 patients given THC obtained more relief of nausea and vomiting than from placebo during a course of high-dose methotrexate chemotherapy (28). Best results were obtained when plasma concentrations of THC were more than 120 ng/ml. Such concentrations would ordinarily be expected to produce rather definite mental effects. THC was compared with two other antiemetics, thiethylperazine and metoclopramide, in a controlled cross-over trial. No difference was found between the antiemetic effect of these three agents. However, adverse effects of THC were sufficiently greater than those from the other two drugs, which raised questions about its clinical utility (37). When THC was compared with prochlorperazine and placebo, the latter two treatments were not found to differ, but THC was superior to either one (131).

In summary, it would appear that THC has definite

antiemetic effects, that these are comparable to many other commonly used antiemetic agents such as prochlorperazine, thiethylperazine, and metoclopramide, but that the major disadvantage of the drug is the mental effects produced by the doses given.

A synthetic homolog of THC, nabilone, was developed in 1972 and has been tested extensively for antiemetic activity. A cross-over study comparing nabilone with prochlorperazine in 113 patients revealed significantly greater response rates following nabilone therapy. However, side effects from nabilone were also more common (77). Although it was hoped that nabilone separated the antiemetic effects from the mental effects of THC, this goal was not totally achieved. Levonantradol and BRL 4664 are two other synthetic THC homologs which showed antiemetic effects in open studies (43, 154). The exact role of synthetic homologs of THC as antiemetic agents remains to be determined.

Currently, a large amount of data on the clinical use of THC as an antiemetic is being accumulated in therapeutic situations monitored by the Food and Drug Administration. Unfortunately, this massive amount of clinical experience has no control, so that it may be impossible to conclude more than what is already known. Meanwhile, extremely promising results have been obtained with larger than usual i.v. doses of metoclopramide. When this drug was compared with prochlorperazine and placebo, it was more effective than either, the only disturbing side effect being sedation (59). The doses used of metoclopramide were 1 mg/kg i.v. before treatment with cisplatin (perhaps the most emetic anticancer drug) and several times after treatment. Protection was total in 48% of courses and major in another 23% (157).

This experience with metoclopramide suggests that the whole issue of the antiemetic effects of THC may become moot, as there are other drugs such as domperidone, which may also be effective in this situation.

B. Glaucoma

Discovery of the ability of cannabis to lower intraocular pressure was more or less fortuitous. Intraocular pressure was measured as part of a multifaceted study of the effects of chronic smoking of large amounts of cannabis. Intraocular pressure was found to decrease as much as 45% in 9 of 11 subjects, 30 min after smoking (75). Lowered intraocular pressure lasted 4 to 5 h after smoking a single cigarette. Its magnitude was unrelated to the total number of cigarettes smoked. The maximal effect on intraocular pressure was produced by the amount of THC absorbed in a single cigarette containing 19 mg of THC. When patients with ocular hypertension or glaucoma were tested, 7 of 11 showed a fall of intraocular pressure of 30%. Confirmatory evidence was obtained from a trial in which i.v. injection of THC in doses of 22 μg/kg and 44 μg/kg produced an average fall in intraocular pressure of 37%, with some decreases as much as 51% (40). Many experiments done in rabbits using various routes of administration, including instillation of cannabinoids into the eye, have confirmed the ability of cannabis to reduce intraocular pressure.

Topical administration would be especially desirable for treating glaucoma as with the other drugs used for this purpose. Smoking cannabis or taking THC i.v. would be totally unsuitable for ptients with glaucoma. Rabbits have been used traditionally for studying topical eye medications. The lipid solubility of THC has been overcome by using mineral oil as the vehicle for its instillation into the eye. The degree of lowering of intraocular pressure is at least as great as with conventional eye drops, such as pilocarpine, and the duration of effect is often longer. Some minimal systemic absorption of the drug occurs when it is applied to the conjunctivae, but it is of no consequence in producing mental effects. Other cannabinoids besides THC, such as cannabinol or 8-alpha- and 8-beta-11-dihydroxy-delta-9-THC, have also produced this effect in rabbits (62). These agents have no mental effects, which makes them of considerable interest for this therapeutic use.

An extract of nonpsychoactive components of cannabis whose composition is still uncertain has been tested both alone and in combination with timolol eye drops in patients with increased intraocular pressure. The effects of the two agents are additive and are said to be effective when other measures have failed (177). BW 146Y, a synthetic THC homolog, has been given p.o. to glaucomatous patients. Unfortunately, mild orthostatic hypotension and subjective effects were noted in addition to reduced intraocular pressure (167).

No psychoactive component of cannabis can be considered as a feasible therapeutic agent in this situation. Intraocular pressures, although they are reduced acutely, have not been shown to be reduced following long-term treatment, nor has there been any demonstration that visual function is preserved by the use of cannabinoids in glaucoma. Some of the problems associated with the development of cannabinoids as treatment for glaucoma have already been cited (61). The exploitation of cannabinoids for treatment of glaucoma will require much further developmental work to ascertain which cannabinoid will be lastingly effective and well tolerated. The potential benefits could be great, as present-day glaucoma treatment still does not prevent blindness as often as it might. If the effects of cannabinoids are additive to those of other drugs, the overall benefit to patients may be greater than is currently possible with single drugs.

C. Analgesia

Smoking of material estimated to deliver 12 mg of THC increased sensitivity to an electric shock applied to the skin (78). Single p.o. doses of 10 mg and 20 mg of THC were compared with codeine (60 mg and 120 mg) in patients with cancer pain. A 20-mg dose of THC was comparable to both doses of codeine. The 10-mg dose, which was better tolerated, was less effective than either

dose of codeine (129). THC given i.v. in dose of 44 μg/kg to patients undergoing dental extraction produced an analgesic effect, which was less than that achieved from doses of 157 μg of diazepam per kg i.v. Several of these patients actually preferred placebo to the dose of 22 μg of THC per kg because of anxiety and dysphoria from the latter drug (139).

The apparent paradox is that THC both increases and decreases pain. Traditionally, aspirin-like drugs, which work peripherally by inhibiting the synthesis of prostaglandins, are used to treat pain derived from the integument. The initial mental stimulation from THC might increase sensitivity to this kind of pain. Visceral pain, such as that of cancer patients, is usually treated by opiates, which have both peripheral and central sites of action. Recent evidence suggests that opiates may act directly on pain pathways in the spinal cord as well as reducing the affect that accompanies pain. Cannabis could conceivably modify the affective response. Thus, when the two types of pain are distinguinshed from each other, the apparent paradox is solved.

THC, nantradol, and nabilone shared some properties with morphine in the chronic spinal dog model. Latency of the skin twitch reflex was increased, and withdrawal abstinence was suppressed. Naltrexone did not antagonize these actions, suggesting that they are not mediated through opiate receptors (56). Levonantradol i.m. was compared with placebo in postoperative pain, and a significant analgesic action was confirmed. No dose-response relationship was observed, and the number of side effects from levonantradol was rather high (89). It seems unlikely that any THC homolog will prove to be an analgesic of choice, when one considers the present array of very effective new analgesics of the agonist-antagonist type. It is too early to be sure, however.

D. Muscle Relaxant

Patients with spinal cord injuries often self-treat their muscle spasticity by smoking cannabis. Cannabis seems to help relieve the involuntary muscle spasms that can be so painful and disabling in this condition. A muscle relaxant or antispastic action of THC was confirmed by an experiment in which p.o. doses of 5 or 10 mg of THC were compared with placebo in patients with multiple sclerosis. The 10-mg dose of THC reduced spasticity by clinical measurement (135). Such single small studies can only point to the need for more study of this potential use of THC or possibly some of its homologs. Diazepam, cyclobenzaprine, baclofen, and dantrolene, which are used as muscle relaxants, all have major limitations. A new skeletal muscle relaxant would be most welcome.

E. Anticonvulsant

One of the first therapeutic uses suggested for cannabis was as an anticonvulsant. Such an effect was documented experimentally many years ago (112). Subsequent studies in various animal species have validated this action. THC in cats temporarily reduced the clinical and electrographic seizure activity induced by electrical stimulation of subcortical structures (175). Mice were protected by cannabidiol against maximal electroshock seizures but not against those caused by pentylenetetrazole. Its profile of activity more resembled that of phenytoin than that of THC (170). THC and cannabidiol both potentiated the anticonvulsant effects of phenytoin against electrically induced seizures in mice. The two cannabinoids in combination produced the most effect (29). Kindling involves the once-daily appliction of initially subconvulsive electrical stimulation to culminate in generalized convulsive seizures. THC given chronically to rats prevented the kindling effect (174).

Clinical testing has been rare, despite all these various lines of evidence supporting an anticonvulsant effect of cannabinoids. Better control of seizures following regular marijuana smoking was reported in a not very convincing single case (39). Fifteen patients not adequately controlled by anticonvulsants were treated with additional cannabidiol in doses of 200 or 300 mg or placebo. Cannabidiol controlled seizures somewhat better than the addition of placebo (25). Cannabidiol has little if any psychoactivity, making it a good candidate for this use.

F. Bronchial Asthma

A general study of the effects of marijuana on respiration revealed a bronchodilating action in normal volunteer subjects. Marijuana smoke was calculated to deliver 85 or 32 μg of THC per kg. A fall of 38% in airway resistance and an increase of 44% in airway conductance occurred in the high-dose group. The low-dose group showed lesser changes, but they were still significant as compared with baseline. The sensitivity of the respiratory center to carbon dioxide was not altered by either dose, indicating no central respiratory depression (172).

Asthma was deliberately induced by either inhalation of methacholine or exercise in asthmatic patients. They were then treated with inhalation of placebo marijuana, of saline, of isoproterenol, or of smoke derived from marijuana containing 1 g of THC. Both marijuana smoke and isoproterenol aerosol effectively reversed both methacholine- and exercise-induced asthma, while saline and placebo marijuana had no effect (160). Aerosols of placebo-ethanol, of THC (200 μg) in ethanol, or of salbutamol (100 μg) were tested in another study of ten stable asthmatic patients. Forced expiratory volume in 1-s forced vital capacity, and peak flow rate were measured on each occasion. Both salbutamol and THC significantly improved ventilatory function. Improvement was more rapid with salbutamol, but the two treatments were equally effective at the end of 1 h (181).

Both delta-8 and delta-9-THC have bronchodilating effects, while neither cannabinol nor cannabidiol has such actions. Thus, this action resides only in the psychoactive material. No evidence of tolerance to this effect developed over 20 days of continual administration (58).

The treatment of asthma is much more chronic; further studies of tolerance will be needed.

Some patients might experience bronchoconstriction following THC. Doses of 10 mg p.o. produced mild and inconsistent bronchodilator effects as well as significant central nervous system effects. One patient of the six studied developed severe bronchial constriction (1). Mild but significant functional impairment, predominantly involving large airways, was found in 74 regular smokers of cannabis. Such impairment was not detectable in individuals of the same age who regularly smoked tobacco (64).

THC would best be administered by aerosol for this purpose, but whether effective doses would avoid the mental effects is uncertain. The mechanism of action by which THC increases airway conductance may be different from the usual beta-adrenergic stimulants. Resistance to repeated applications of beta-adrenergic stimulants does occur. Another type of bronchodilator might help some patients. The recent introduction of highly effective steroid aerosols, such as beclomethasone, meets that need to a considerable extent.

G. Insomnia

THC does not differ from conventional hypnotics in reducing rapid eye movement (REM) sleep (136). THC in doses ranging from 61 to 258 μg/kg produces in normal subjects increments in stage 4 sleep and decrements in REM sleep, but without the characteristic REM rebound which follows chronic treatment with hypnotics. When THC was administered p.o. as a hydroalcoholic solution in doses of 10, 20, and 30 mg, our subjects fell asleep faster after having mood alterations consistent with a "high." Some degree of "hangover" the day following was noted from larger doses (42). Another sleep laboratory study showed that a dose of 20 mg of THC given p.o. decreased REM sleep. After four to six nights of use, abrupt discontinuation of THC produced a mild insomnia but not marked REM rebound (52). REM rebound may not be apparent after low doses of THC. However, very high p.o. doses (70 to 210 mg) reduced REM sleep during treatment and were followed by marked REM rebound after withdrawal (48).

The sleep produced by THC does not seem to differ much from that of most currently used hypnotics. Side effects before sleep induction as well as the hangover effects make the drug less acceptable than currently popular benzodiazepines. It seems unlikely that THC will supplant existing hypnotics in the treatment of insomnia.

H. Miscellaneous Uses

1. Hypertension. Orthostatic hypotension occasionally follows use of THC (5). A dimethylheptyl side-chain derivative has more profound and constant effects on blood pressure. In man, this compound showed a marked orthostatic hypotensive effect, as well as tachycardia and some mental symptoms resembling those of THC. [illegible] the latter are less than from THC in proportion to [illegible] blood pressure-lowering effect, a definite separation of pharmacological effects has not really been attained (106).

Effective antihypertensive drugs have been one of the outstanding achievements of pharmacology over the past 30 years. A new antihypertensive based on orthostatic hypotension, perhaps the least desirable mode of lowering blood pressure, is hardly very enticing (8). The issue seems hardly worth pursuing further.

2. Abstinence syndromes due to central nervous system depressants. Synhexyl, the first THC homolog to be synthesized, was tested as a treatment for withdrawal reactions from opiates and alcohol with little evidence of efficacy. Withdrawal symptoms experienced by rats following morphine pellet implantation, followed by subsequent injection of naloxone, were reduced by THC. Cannabidiol, without any direct effect itself, augmented the action of THC (79).

This relatively weak effect of cannabinoids in opiate dependence is unlikely to be of clinical use. Detoxification programs using methadone have been highly successful and acceptable.

3. Antineoplastic activity. Both the delta-8 and delta-9-THC isomers, as well as cannabinol, have some antineoplastic effect on transplanted lung tumors in animals, as well as on tumors in vitro (125). THC may have a general ability to reduce the synthesis of nucleic acids, which may account for the reported immunosuppressant effects as well. Many agents are available that inhibit nucleic acid synthesis, so the possibility that THC or other cannabinoids might be advantageous seems rather unlikely.

4. Antimicrobial action. Both THC and cannabidiol inhibit and kill staphylococci and streptococci in vitro at concentrations of 1 to 5 μg/ml (173). Such concentrations are well above those reported for use of THC in man, even at the highest tolerated doses. Thus, this effect seems to have little practical application.

5. Migraine. This indication has not been studied systematically in recent years, although it has a long history. In one patient I treated, the mental effects sought socially caused the patient to abandon treatment. Innumerable successful treatments for migraine have been reported at one time or another.

6. Appetite stimulant. Most antipsychotic agents will stimulate appetite, but few other drugs do. THC as compared with ethanol and dextroamphetamine produced a variable response on appetite, both in fed and fasted subjects. The majority had increased appetite and food consumption as compared with placebo (80). Anorexia nervosa might be helped by an appetite stimulant. A test of the presumed appetite-stimulating properties of THC in patients with anorexia nervosa failed over a 4-week period. Doses of THC ranged between 7.5 and 30

mg/day and were compared with 30 mg of diazepam per day and placebo. Three of the 11 patients treated with THC experienced severe dysphoria (65).

7. Alcoholism. Cannabis users are said not to drink, but most do. The prospect of changing an alcoholic into a cannabinolic has some appeal. A study showed that cannabis was not very attractive to alcoholics. Little difference in retention occurred among those given no medication, or a cannabis cigarette, or disulfiram or the combination of the cigarette and disulfiram (143).

V. Summary

Marijuana seems firmly established as another social drug in Western countries, regardless of its current legal status. Patterns of use vary widely. As with other social drugs, the pattern of use is critical in determining adverse effects on health. Perhaps the major area of concern about marijuana use is among the very young. Using any drug on a regular basis that alters reality may be detrimental to the psychosocial maturation of young persons. Chronic use of marijuana may stunt the emotional growth of youngsters. Evidence for an amotivational syndrome is largely based on clinical reports; whether marijuana use is a cause or effect is uncertain. A marijuana psychosis, long rumored, has been difficult to prove. No one doubts that marijuana use may aggravate existing psychoses or other severe emotional disorders. Brain damage has not been proved. Physical dependence is rarely encountered in the usual patterns of social use, despite some degree of tolerance that may develop. The endocrine effects of the drug might be expected to delay puberty in prepubertal boys, but actual instances have been rare. As with any material that is smoked, chronic smoking of marijuana will produce bronchitis; emphysema or lung cancer have not yet been documented. Cardiovascular effects of the drug are harmful to those with preexisting heart disease; fortunately the number of users with such conditions is minimal. Fears that the drug might accumulate in the body to the point of toxicity have been groundless. The potential deleterious effects of marijuana use on driving ability seem to be self-evident; proof of such impairment has been more difficult. The drug is probably harmful when taken during pregnancy, but the risk is uncertain. One would be prudent to avoid marijuana during pregnancy, just as one would do with most other drugs not essential to life or well-being. No clinical consequences have been noted from the effects of the drug on immune response, chromosomes, or cell metabolites. Contamination of marijuana by spraying with defoliants has created the clearest danger to health; such attempts to control production should be abandoned.

Therapeutic uses for marijuana, THC, or cannabinoid homologs are being actively explored. Only the synthetic homolog, nabilone, has been approved for use to control nausea and vomiting associated with cancer chemotherapy. While little doubt remains that marijuana, THC, and nabilone are effective for this use, the advent of other drugs that are equally effective but with fewer adverse effects may make this use moot. Use of marijuana to reduce intraocular pressure in patients with glaucoma requires a feasible topical preparation of cannabinoids. Although some cannabinoids have analgesic activity, the abundance of new opioid analgesics with little dependence liability provides tough competition. The use of marijuana as a muscle relaxant, though promising, has not yet been adequately studied. Clinical studies to establish the efficacy of cannabidiol as an anticonvulsant or to compare it with other anticonvulsants are still to be done. Other potential therapeutic uses, such as treatment of bronchitis, asthma, insomnia, hypertension, abstinence syndromes, migraine, anorexia, and alcoholism, are most unlikely prospects.

Compared with other licit social drugs, such as alcohol, tobacco, and caffeine, marijuana does not pose greater risks. One would wonder, however, if society were given a choice based on current knowledge, whether these drugs would have been granted their present status of acceptance. Marijuana may prove to have greater therapeutic potential than these other social drugs, but many questions still need to be answered.

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Chemical Dependency

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Marijuana: An Overview

*Richard H. Schwartz, MD**

Of all illicit drugs popular in the United States and Canada, *Cannabis* (marijuana or hashish) is the most widely used. The potency of ordinary marijuana is now identical to that of hashish sold in the United States, and high-quality sinsemilla (seedless marijuana), much preferred by marijuana afficionados, is twice as strong as hashish.[10] Approximately 60 per cent of graduating high school seniors have smoked marijuana at least one time, and one in eight students who tried the drug even once progress to daily use. Many of these young people will continue to be psychologically dependent on the drug or will also abuse other mood-altering drugs (e.g., cocaine).

In 1985, marijuana was smoked daily by 120,000 (5 per cent) high school seniors nationwide.[15] In the most comprehensive statewide survey in the country, 3.5 per cent, 9.4 per cent, and 12.8 per cent, respectively, of eighth, tenth, and twelfth graders in Maryland smoked marijuana at least several times a week up to once or more per day; 12 per cent of tenth graders stated that they "got high" from an illicit drug more than ten times in 1984.[24] It should be emphasized that 28 per cent of all entering high school freshmen leave high school before graduation,[31] and frequent marijuana use is undoubtedly a significant factor in the decision to leave school.

CANNABIS: PHYSICAL PROPERTIES

Marijuana comprises the crumbled, cured leaves, small stems, and flower clusters of the resin-producing varieties of the hemp plant, *Cannabis sativa*. Indigenous to Asia, the plant originally was cultivated worldwide as a source of hemp fiber, oil, and homeopathic medicines. Varieties of the plant are often 5 to 8 feet tall and branched, with compound leaves composed of seven to nine serrated, slender, spear-shaped leaflets.

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Drug-producing varieties of the plant have glands that secrete a resinous substance containing about 60 unique compounds, called *cannabinoids*, the most psychoactive and prevalent of which is delta-9-tetrahydrocannabinol (Δ9-THC).

The Δ9-THC content of *C. sativa* is influenced by genetic factors, by the place and circumstances of its growth, by the method of storage of the plant material, and by the number of months elapsed since harvest time. The potency of Δ9-THC diminishes with time, especially for hashish.

In the United States, 60 per cent of all marijuana is grown in California, often by the sinsemilla method, which produces high-potency marijuana. Since 1975, the potency of "street pot" in the United States has tripled, from 1.2 to 4.1 per cent. The Δ9-THC concentration of the more potent sinsemilla type averages 7 per cent, but may be as high as 14 per cent.[10]

USE OF MARIJUANA AS A PSYCHOACTIVE DRUG

Mannner of Use

The primary mode of using marijuana or hashish in the United States is inhaling the smoke of marijuana cigarettes ("joints"), made by rolling 500 mg to 750 mg of marijuana in a thin paper. Smoking implements such as hollow smoking stones, miniature smoking pipes (bowls), or air-cooled or water-cooled smoking chambers (bongs) also may be used to cool and "sweeten" the highly irritating marijuana smoke, thus permitting the user to inhale a larger quantity. Adolescents often purchase marijuana in 4- to 5-gm packets, sufficient to make five or six "joints," each costing about one dollar. Prior to use, seeded marijuana must be cleaned of seeds and small woody stems, the combined weight of which is often 50 per cent or more of the "bag" as purchased. This "manicuring" is often done in the young person's bedroom on a smooth surface such as a record album cover; the seeds may then be discarded or may be collected for later cultivation.

To obtain maximal effect from marijuana, users must master a smoking technique somewhat different from that of smoking tobacco cigarettes or pipe tobacco. The experienced user inhales the smoke as deeply into the lungs as possible and holds his breath for 20 to 30 seconds or more in an effort to extract almost all the Δ9-THC into the capillary-rich pulmonary circulation. When this technique is followed, 50 per cent of the Δ9-THC contained in the crude marijuana is delivered into the smoker's bloodstream and practically no Δ9-THC remains in exhaled breath. Marijuana smoke has a pungent smell, resembling the smell of burning wet hay or leaves, and clings to hair and woolen garments. Consumption of the same amount of drug, of the same potency, even by an experienced user, may produce minimal effects on one occasion and, on another occasion, marked effects on cognition, mood, and performance.

"Hash oil" is street jargon for a viscous, black, oily liquid derived from marijuana mash by dissolving it in an organic solvent. Hash oil contains 20 to 30 per cent Δ9-THC, and one drop smeared on a marijuana rolling paper gives a "high" equivalent to one marijuana cigarette. Thus, users of hash

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oil add one drop to a joint to double its potency. Other drugs or chemicals[39] that may be mixed with marijuana to increase its intoxicating effects include phencyclidine, opium, cocaine paste, and even Raid insect spray. Not infrequently, naive marijuana-smoking adolescents may be given these laced joints without their knowledge, leading occasionally to serious psychiatric states of confusion and disorientation, intense anxiety, depersonalization, profound depression, acute paranoia, acute psychosis, or sheer panic.

Pharmacology

The minimal effective dose of Δ9-THC is 5 mg, of which 50 per cent is destroyed in the process of pyrolysis. The intoxicating dose for a 70-kg adult is 0.035 mg per kg. Merely smoking two sinsemilla cigarettes a day exceeds a total daily dose of 40 mg of Δ9-THC per day (considered to be a very heavy dose). Tolerance to the effects of cannabis has been demonstrated conclusively,[32] and experienced marijuana smokers require more potent cannabis, deeper, more sustained inhalations, or larger amounts of the crude drug to achieve the desired degree of euphoria. Mood-altering, intoxicating and cardiovascular effects of the drug become evident within a few minutes after deep and sustained inhalation of marijuana smoke, whereas oral administration of the drug has a 30-minute lag period. The subjective effects last 2 to 3 hours, somewhat longer if cannabis was eaten rather than smoked.

Δ9-THC is carried quickly by way of the bloodstream to the liver, and most of the drug is broken down (by hydroxylation and carboxylation enzymes in liver microsomes) to non–mood-altering carboxyacid analogues of THC (THC-COOH). These are carried by the enterohepatic circulation into the intestinal lumen, to be excreted in the feces (65 per cent), and through the renal circulation into the urine (35 per cent). Because the liver cannot remove all the Δ9-THC during the first pass through the hepatic circulation, and because Δ9-THC is intensely lipophilic, adipose tissues accumulate a substantial amount of the drug, which is then released slowly and unevenly into the bloodstream. The half-life of Δ9-THC is approximately 3 days.

The pharmacologic effects of ingested cannabis begin in 30 to 120 minutes, peak in 2 to 3 hours, and last 3 to 6 hours. About three times as much Δ9-THC must be ingested as smoked to obtain the same effects, and the psychoactive effects are much more variable with ingestion, even when the drug user is experienced.

Cannabinoid metabolites can be detected in the urine (presumably a result of sustained release from adipose tissue) for 2 or 3 days following one casual use of the drug.[17] The drug may be detected up to four or more weeks after monitored abstinence of daily chronic marijuana smokers.[34]

Unlike alcohol intoxication, the "high" of marijuana can easily be [illegible] (masked through) by volition. Thus a person high on marijuana may seem completely normal in appearance, speech and content of speech, and action. After several hours of the "high" this state gradually merges, if the Δ9-THC concentration is sufficient, into a state of mental physical and mental torpitude, irritability easily provoked to anger, drowsiness, and

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sometimes sleep. During this gradual "coming down" phase, there is a very strong hunger for high-calorie food such as cookies or "junk food" (known as the "marijuana munchies"), and an intense craving for sweet drinks such as carbonated beverages. Unlike alcohol intoxication, there is usually no "hangover" after the marijuana "high" is gone.

There are only two consistent physical signs of marijuana use: (1) increased heart rate and (2) conjunctival irritation or dilation. Because many adolescents are proficient users of Visine or other vasoconstrictive ophthalmic drops, the tell-tale reddened eyes following marijuana smoking may not be present.

ACUTE EFFECTS OF CANNABIS

Expected Effects

Primarily, the effect of marijuana depends on the concentration of Δ9-THC that reaches the bloodstream of the user (i.e., the potency of the Cannabis product). What has been termed "set" and "setting" also play a role.

"Set" is determined by the past experience, attitude, expectations of achieving euphoria ("shaping"), and underlying ego strength of the user. Thus, if the novice user is apprehensive and expects to be discovered by authority figures, he or she may experience a high anxiety level or even panic, and fear of losing control of thought processes may lead to intense discomfort instead of a pleasant experience. Adolescents who are known to have unstable personalities, particularly serious affective disorders such as prolonged depression, or a history of non–drug-induced psychosis, are at serious risk for adverse psychological effects from any psychoactive drug, permanent psychosis may be precipitated in such persons.

"Setting" refers to the degree of trust and congeniality between the user and others present, and to the comfort and safety of the surroundings. Marijuana is smoked alone or used with intoxicating amounts of alcohol, stimulant drugs (such as cocaine or amphetamines), other hallucinogenic drugs, phencyclidine, or inhalant drugs. Obviously, the complex pharmacologic interaction of these drugs is highly individual, and although users with an underlying explosive impulse-control disorder sometimes feel less tense and less angry when they smoke marijuana, they often become moody, irritable, and argumentative as the drug-induced euphoria dissipates. Such negative feelings may lead to hostile confrontation if the user is questioned in the posteuphoric state.

Adverse Effects

The acute effects of marijuana are usually pleasant, but adverse effects occur not infrequently, often unpredictably and even when the user is highly experienced.

Psychological Effects. Acute adverse (toxic) effects of marijuana include acute toxic psychosis, acute panic reactions, and flashback phenomena. Symptoms of acute toxic psychosis include excitement, confusion, disorien-

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tation, delusions, depersonalization, visual hallucinations, and full-blown delirium.[35, 41] Acute panic reactions ("bad trips") may be accompanied by abdominal discomfort, headache, anxiety, depression, morbid fear of being "found out," fear of dying, restlessness, uncontrollable feelings of aggression, and paranoid ideation. Panic or psychotic toxic reactions are more frequent in the novice marijuana smoker. The occurrence of flashback phenomena after marijuana use has been reported, but flashbacks are uncommon.

Effects on Coordination and Reaction Time

Safe operation of a motor vehicle is often compromised if the driver is acutely intoxicated by marijuana.[2, 6, 7, 12, 19–21, 25–30, 31, 38, 42, 43, 48] It is estimated that 60 to 80 per cent of marijuana users who are licensed to operate a motor vehicle on occasion do so while intoxicated by that drug. Marijuana can impair motor activity in unpredictable ways, including altering reflex responses to sensory stimuli; decreasing attention to the "gestalt"; altering perceptions of the passage of time, of depth (e.g., distance to a traffic light or a pedestrian), or of colors; and impairing short-term memory. A person under the influence of marijuana also has impaired vigilance: in a recent study, marijuana was shown to cause impairment of eye-tracking skills that was roughly double that produced by alcohol. In addition, marijuana-intoxicated drivers of motor vehicles may fail to respond optimally to visual clues because of preoccupation with drug-induced imagery or music from the car radio or tape recorder.

Impairment of vigilance, coordination, and reaction time may persist for 12 to 24 hours[30] after the euphoria is gone: teenagers who drove after smoking marijuana on at least six occasions per month were 2.4 times more likely to be involved in traffic accidents. This lasting effect of marijuana intoxication has been demonstrated in a test using airline pilots: on a flight simulation, smoking a single marijuana cigarette containing 19 mg of Δ9-THC led 10 experienced, licensed private pilots to perform appreciably less well than before drug use. In addition, the pilots were unaware that they had performed poorly in the flight simulation tests.[48]

Physiologic Effects. Smoking marijuana affects the respiratory system, the heart, the eyes, and the brain (affect and perception). The mouth and throat feel parched, there is a sensation of pounding of the heart, the eyes become red and irritated, and there is a perceptible change in mood. Early effects include disinhibition and garrulousness (spontaneous laughter), and a sense of relaxation, pleasant reverie, and drowsiness. Many marijuana-intoxicated persons overestimate the passage of time and have impaired ability to process newly learned material and remember it a short time later. Auditory and visual enhancement or distortions may occur, particularly in the casual user. Coordination and balance may be impaired.

Aftereffects of smoking marijuana include lethargy, and changes in sleep patterns and in appetite. Adolescents especially may experience changes in mood (depression and irritability), be easily provoked to argumentativeness, and suffer posteuphoria depression.

Pulmonary System Effects. Stinging and burning sensations in the mouth and throat frequently occur after marijuana smoke is inhaled, and a

dry, hacking cough may be present, particularly if an unscreened marijuana pipe or homemade smoking apparatus was used. Frequent hashish smokers occasionally have swollen, inflamed uvulae.[43]

Histologic changes may occur because marijuana smoke contains more carcinogens and more tar than does tobacco smoke; experienced cannabis smokers take longer and deeper draws on the marijuana cigarette and hold each inhalation in the lungs for a longer time, marijuana cigarettes burn at a higher temperature than do tobacco cigarettes, and marijuana cigarettes are smoked down to the very end (called a "roach"), which is more potent in Δ9-THC and polyaromatic hydrocarbons than is the rest of the cigarette. In addition, frequent cannabis smokers may have stuffy noses, bronchitis, and exacerbations of bronchial asthma. Only occasionally are these symptoms severe enough to prompt medical intervention.

Investigators at the University of California at Los Angeles[12] found that nontobacco-smoking heavy marijuana smokers had mild but significant functional impairment of airway conductance, whereas pathology investigations have shown diffuse infiltrations of mononuclear leukocytes into the alveoli and interstitium of the lungs.[27]

Possible Systemic Effects. Many published articles have detailed additional possible harmful systemic effects of marijuana. These include alterations in immune system function, cellular chromosomes, and cell metabolism; abnormalities in the reproductive system or in development of the fetuses of marijuana-smoking pregnant women[2]; cardiovascular system alterations; and changes in brain histology. All of the above findings have been challenged and all remain unproven, however.

CHRONIC EFFECTS OF CANNABIS

The Amotivational Syndrome

"Whether marijuana is a primary or a secondary factor in inducing amotivation is not a crucial issue. A drug that serves to support and reinforce passivity and withdrawal would make it an undesirable agent in predisposed individuals"[6] (e.g., the young, the learning disabled, and the emotionally immature).

There are seven consistent components of the amotivational syndrome: (1) loss of interest, general apathy, and passivity; (2) loss of desire to work consistently and loss of productivity, accompanied by a lack of concern about the poor work performance; (3) loss of energy and tiredness; (4) moodiness, sullenness, and inability to handle frustration; (5) impairment in concentration and in ability to process new material; (6) slovenly habits and appearance; and (7) a life-style revolving around procurement and use of marijuana and other drugs. A series of published studies of Egyptian prisoners,[37, 38] and of educated Nepalese young adults[36] provides strong evidence that links amotivation to heavy marijuana use by persons who perform highly skilled tasks or are employed in jobs demanding concentration and decision making.

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Costa Rica[4] have purported to show that the amotivational syndrome is not associated with frequent marijuana smoking. These studies were usually conducted among uneducated or poorly educated working-class adults, however, and the results were reported in all cases in nonpeer review publications. Thus, they provide no basis for disengaging marijuana use from the amotivational syndrome in marijuana-using American adolescents. Furthermore, in a study conducted in Costa Rica,[4] 41 marijuana-smoking city residents socioeconomically representative of most strata of Costa Rican society were compared to 41 matched controls. Users, when adolescents, had had higher rates of school absenteeism, delinquency, and sentencing to reformatories. Users also were more likely to leave the nuclear family prematurely and become "independent" (not infrequently before age 12 and usually by age 18), and were more committed to running with street gangs during late adolescence.

The Youthful Daily Marijuana Smoker

Marijuana use often progresses in a fairly predictable, stepwise fashion (in approximately one of three marijuana-smoking adolescents), from experimentation, to occasional social use, to regular social use, including actively seeking and buying quantities of marijuana. For some, preoccupation with a life-style focused on use of cannabis develops—the cannabis dependence syndrome.

If an adolescent begins to use marijuana during early adolescence, he or she is likely to use other illicit drugs such as cocaine and hallucinogenic drugs. Of 30 frequent adolescent cocaine snorters in the Straight, Inc. drug treatment program, 80 per cent had been daily marijuana smokers before they abused cocaine. The period of greatest vulnerability for initiation to marijuana is completed for the most part by the age of 22 years, with those who have not experimented with the drug by that age being unlikely to do so thereafter. Overall, patterns are similar for men and women before age 18.

Stepping-Stone Theory of Drug Use. Kandel has identified three stages between nonuse and frequent use of illicit drugs: use of beer or wine, use of cigarettes or distilled beverages, and use of marijuana (cannabis).[16, 17, 18] In almost all cases in that study, adolescents began to use illicit drugs only after becoming users of alcoholic beverages and of tobacco.

Adolescent Daily Marijuana Smokers in Treatment. In a survey of 180 primarily white adolescents in treatment for drug problems (Schwartz RH: unpublished data, 1986), 60 per cent had smoked marijuana on a daily basis. Thirty-seven of these middle class subjects aged 14 to 17 years were chosen at random for an in-depth interview. Approximately 40 per cent had divorced parents: 50 per cent of their fathers were college graduates. The median duration of daily use of the drug by those 37 young people was 1.25 years, and an average of 1.75 oz of marijuana was consumed per month at an average cost of approximately $80 per month.

About 75 per cent of the respondents, after 1 month in treatment, believed that they had experienced significant impairment in coping skills, memory and concentration, self-confidence, judgment, ambition, dependability, and relationships with parents, teachers, and employers as a direct

result of chronic marijuana use. Social consequences of a serious nature began or worsened during the years of chronic marijuana intoxication. These consequences included more than ten violent quarrels with parents (44 per cent), running away for longer than 1 week (30 per cent), being arrested or detained by police (43 per cent), frequent stealing (32 per cent), involvement in an automobile accident while intoxicated (30 per cent), emergency medical care following drug use (27 per cent), and exchanging sexual favors for drugs (girls only–26 per cent).

Despite such significant psychosocial and behavioral problems, less than half of the 37 daily marijuana smokers believed that they had a drug problem on the day of admission to the drug treatment facility. Johnston[14] found that high-school seniors who used marijuana daily represented a cross-section of socioeconomic levels, and that daily use of the drug was only slightly higher among those from broken homes. Daily use correlated with declining grades, and also very strongly with truancy during high school.[14]

Follow-up of the Frequent Marijuana User. Weller et al.[12, 46] interviewed 100 frequent marijuana smokers and 50 nonmarijuana-smoking controls and reinterviewed the same group 6 to 8 years later. The group was composed of young white adults, 60 per cent men, mean age 22 years at the time of the first interview. Thirty per cent smoked marijuana once a week or less, 30 per cent smoked the drug three times a week or more, and only 12 per cent were daily users at the time of the *initial* interview.

At the time of the follow-up interview 20 per cent of the marijuana smokers were daily users. In addition, the proportion who abused alcohol had increased (18 per cent vs 3 per cent initially); furthermore, more subjects had antisocial personality disorders (21 per cent vs 6 per cent), anxiety disorders (11 per cent vs 0 per cent), and depression (44 per cent vs 29 per cent). With time, truly chronic users, instead of experiencing psychedelic effects of marijuana as they had during the earlier years of use, experienced sedative, depressant, or hypnotic effects of the drug as a rule.

CANNABIS ABUSE AND DEPENDENCE

The *Diagnostic and Statistical Manual* (3rd edition) (DSM-III), published by the American Psychiatric Association,[3] defines cannabis abuse as follows: (1) use nearly every day, several times a day, for at least one month, and (2) marked loss of (non–drug-using) friends, absence from work (school), marked loss of interest in (healthy) activities previously engaged in, and legal difficulties other than a single arrest for possession of cannabis.

Cannabis dependence is defined as abuse marked by repeated unsuccessful efforts to control cannabis use, and tolerance to the effects of the drug as evidenced by diminished psychoactive effects on regular use of the same amount of cannabis.

Urine Toxicology Tests for Cannabinoids

Various tests can be used to detect the products of marijuana metabolism in the urine, but they vary in availability, cost, complexity, and

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sensitivity.[35] One of the most often used screening tests is the enzyme multiplied immunoassay technique (EMIT, manufactured by Syva Co.). Two different levels of detection are available for screening for cannabinoids. The 20 ng per ml of urine level is more sensitive than the 100 ng per ml level (i.e., it can detect smaller amounts of carboxy-THC in the urine). The less cumbersome and simpler to use qualitative EMIT test detects recent marijuana use, but its 100 ng per ml level misses many weekend marijuana smokers and as any as 25 per cent of daily marijuana smokers unless the urine specimen is collected within 24 hours of last use. Analysis of 16 urine specimens from marijuana-smoking adolescents followed in a drug treatment program and tested with the EMIT instrument gave a sensitivity of 62 per cent of all proven-positive urine specimens.

A positive test result for marijuana byproducts in urine almost always means that the person used the drug recently. Only 2 of 161 urine specimens analyzed by two different methods by our laboratory had false-positive test results by EMIT tests (Schwartz RH: unpublished data, 1986).

Duration of Positive EMIT Test After Abstinence from Marijuana. Two days after smoking marijuana, more than 30 per cent of infrequent users of the drug will have no trace of carboxy-THC in the urine as measured by the EMITst test, EMIT-dau-100 test or radioimmunoassay-100 test, and by the third day after smoking the drug most novice users will have no carboxy-THC in the urine at all by radioimmunoassay (RIA-20), thin-layer chromatography (TLC), or EMIT-dau-20 tests. In contrast, those who use the drug in moderate amounts (three to four times a week, or 1 oz per month) will often have enough marijuana metabolites in the urine to give positive results on an EMIT test for at least 3 to 5 days after last use. However, we have determined that at least 25 per cent of such users have a negative test when the less sensitive EMIT (100 ng per ml threshold of sensitivity) is used. Chronic users of marijuana (those who smoke more than 2 oz of the drug per month and use it daily) will usually have positive results of the EMIT test for at least 3 days following last use but infrequently may have urine that tests positive for marijuana metabolites for as long as 5 weeks after cessation of drug use.[47] More sensitive toxicology tests, of course, are able to detect lower levels of cannabinoids in a urine specimen for a longer time, but the major variant in duration of excretion of the drug is frequency of its use beforehand.

Because of the level of sensitivity of the test, it is highly improbable or perhaps even impossible that a person who merely inhaled marijuana smoke passively (did not actually smoke the drug himself or herself) would take in enough of the drug to give a positive result on the less sensitive EMIT test.

Methods of Deceiving the EMIT Test. To obtain the highest concentration of marijuana metabolites in a urine specimen from a suspected user of the drug, the specimen should be the first voided urine, which is the most concentrated urine of the day. Specimens should be obtained the morning after likely "party" nights, should be observed for color, and tested for warmth if there is any possibility that the individual diluted it or substituted urine of a non–marijuana-smoking friend. The urine specimen should then be refrigerated, frozen, or even stored at room temperature

for up to 3 days until it can be sent to a reliable and carefully supervised medical laboratory for testing. Cloudy urine from bacteriuria or crystalluria may cause a false-negative EMIT test result. If there is any question that the urine may have been adulterated (by blood, bleach, vinegar, ammonia, table salt, water, or soap solution), the specimen should be obtained under direct observation, as is done in the armed forces.

It is worthwhile to order a urine test for cannabinoids on any adolescent who is depressed, underachieving in school, or argumentative and belligerent, particularly before recommending psychosocial or psychiatric consultation. Although some physicians may disagree philosophically with the importance of such tests, the significant number of adolescents whose psychological problems are related to drug use warrants identification of this component as early as possible.

MARIJUANA AND Δ9-THC AS THERAPEUTIC AGENTS

Nausea and vomiting following administration of many chemotherapeutic drugs debilitate, discourage, depress, and dehydrate cancer patients and interfere with the treatment program.

Synthetic Δ9-THC, generically known as dronabinol, marketed as Marinol, a schedule II drug, is approved for oral use by the U.S. Food and Drug Administration for palliation of cancer chemotherapy-induced nausea and vomiting in patients who have not responded to conventional antiemetics. Dronabinol is definitely effective in precluding postchemotherapy nausea and vomiting, but no more so than metaclopramide administered intravenously. With repeated doses, most patients will experience effects typical of smoking marijuana: mood changes, as well as decreases in concentration, coordination, and ability to estimate time. Adverse physiologic effects include lightheadedness, orthostatic hypotension, tachycardia, conjunctival hyperemia, and dry mouth.

Nabilone and levonantradol are two other synthetic cannabinoids under investigation as antiemetic agents. Glaucoma affects more than one million people in the United States and is a leading cause of blindness. Timolol or pilocarpine can reduce intraocular pressure in 90 per cent of patients with open-angle glaucoma. THC can also reduce intraocular pressure in patients with open-angle glaucoma when administered as a topical eye drop, by the oral route, or when the crude drug marijuana is smoked.[3, 26] For most people, however, THC is much less effective than some of the newer antiglaucoma drugs. In addition, regardless of the route of administration, marijuana or synthetic THC does not cure glaucoma and is not an indispensible palliative treatment for that disease. Furthermore, four to six marijuana cigarettes must be smoked each day to treat glaucoma, and this amount is sufficient to cause chronic marijuana intoxication, with adverse effects on psychosocial development, motivation, memory, motor function, and coordination.

THE PARAQUAT ISSUE

Paraquat (1,1' dimethyl-4,4' bipyridilium chloride) is an herbicide that is diluted and sprayed on plants as a dessicant. Although the chemical is

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CONCLUSIONS

Marijuana is a potent, crude, intoxicating drug that can alter mood and mind. Sinsemilla marijuana, used preferentially by frequent marijuana smokers, is 600 per cent more potent than the marijuana used in the previous decade. In 1985, marijuana was smoked on a daily basis by 120,000 American high school seniors and an unknown number of high school dropouts. Δ9-THC, the primary psychoactive chemical in marijuana, exerts pronounced adverse effects on the estimation of time, on short-term memory stores, and on complex performance tasks.

Experimentation with marijuana even once during adolescence carries with it at least an 8 per cent risk of one's becoming a daily marijuana smoker with attendant psychosocial consequences. For those adolescents with serious underlying genetic and developmental risk factors, the risk of progression from experimental use to the cannabis dependence syndrome appears to be much higher; furthermore, it is highly unlikely that adolescents will try cocaine or hallucinogens without prior experimentation with marijuana.

Parents of adolescents and physicians must be aware that any sustained deterioration in school performance, ethical values, interpersonal relationships, or a combination of these is often associated with frequent use of cannabis. There is also a real risk of serious accidental injury, running away, and suicide attempts in adolescents who develop the cannabis dependency syndrome. Urine toxicology screening tests, in selected cases, can help the physician to diagnose and manage deceptive adolescent drug users who deny or minimize the association of their drug use with their psychosocial problems.

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The Journal of General Psychology, 113(1), 23–55 1986

Marijuana's Effects on Human Cognitive Functions, Psychomotor Functions, and Personality

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ABSTRACT. Marijuana is complex chemically and not yet fully understood, but it is not a narcotic. Like alcohol, marijuana acts as both stimulant and depressant, but it lingers in body organs longer than alcohol. Smoking marijuana can injure mucosal tissue and may have more carcinogenic potential than tobacco. Research has indicated that marijuana intoxication definitely hinders attention, long-term memory storage, and psychomotor skills involved in driving a car or flying a plane. Expectations and past experience with marijuana have often influenced results more than pharmacological aspects have. Marijuana has triggered psychotic episodes in those more vulnerable. Psychological and some instances of physiological dependence on marijuana have been demonstrated. As a psychoactive drug, marijuana surely alters mental functioning. Although it is possible that chronic use of marijuana produces irreversible damage to mind or brain areas, this has not been determined by research.

ADOLESCENT USE OF MARIJUANA has peaked and in some areas declined (Maugh, 1982; Penning & Barnes, 1982; Relman, 1982). In a nationwide sample of 16,000 to 17,000 teenagers, the proportion that had tried marijuana dropped from 51% in 1979 to 42% in 1983, and daily use of marijuana was down from 10.7% in 1978 to 5.5%, according to the poll "Use of Drugs" reported in the *New York Times* on February 12, 1984. Although marijuana has been used since the third century B.C. (Talbot & Teague, 1969), it has become a worldwide problem, and its use may even be increasing with its users' age and among women (Kandel, 1984; Kandel & Adler, 1982; Lamanna, 1981; Lipp, Benson, & Taintor, 1971; Margolis & Popkin, 1980; *Marihuana Research*, 1974; "Marijuana and Health," 1971; Penning & Barnes, 1982; Relman, 1982)

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This review of research was limited to the studies of marijuana's effects, both physical and psychological, on human subjects. One of the methodological problems in research on marijuana is the lack of animal test procedures that adequately reflect many of the pharmacological properties of marijuana intoxication in human subjects, such as euphoria and hallucinations (Carlini, Kamiol, Renault, & Schuster, 1974; Harris, 1971; Thompson & Johanson, 1981).

Many studies have examined physical effects of marijuana, such as its impact on the cardiovascular system (Beaconsfield, Ginsburg, & Rainsbury, 1972; Tinklenberg, Roth, & Kopell, 1976). Tachycardia, for instance, is a consistent physiological effect of marijuana and, as such, is often used as a marker for the presence of marijuana versus placebo in controlled studies (Isbell & Jasinski, 1969; Kiplinger & Manno, 1971; *Marihuana and Health*, 1977). The second focus of this review of research, however, is the effect of marijuana on human cognitive and psychomotor functions and on personality patterns.

What Is Marijuana?

The flower and leaves of the female *Cannabis sativa* plant are the source of marijuana; stem and seeds may also be included in the mixture. *Cannabis sativa* has been grown throughout the world for the fiber that goes into rope, bags, and clothes, and it has been used as a by-product, a stimulant for work and a depressant for relaxation (National Commission on Marihuana and Drug Abuse [NCMDA], 1972). A pure, gummy resin obtained directly from the leaves contains the highest concentration of delta-9-tetrahydrocannabinol (THC; Abel, 1977; Mechoulam, Shani, Edery, & Grunfeld, 1970). Hashish from India is estimated to be 5 to 10 times more potent than marijuana, but estimates of potency of both hashish and marijuana vary with soil, climate, cultivation technique, and mixture (Smith, 1968; Weil, Zinberg, & Nelson, 1968).

Marijuana is a unique mixture of stimulation and depression of the central nervous system that is not mimicked by other classes of drugs (Consroe, Jones, & Laird, 1976). Scientific evidence has shown that marijuana is not a narcotic and should be treated differently from heroin and opiates (NCMDA, 1972). *Cannabis sativa* is one of the oldest intoxicants in use, but less is known about its pharmacology than about any other drug used. Varying mixtures of different parts of the *Cannabis sativa* plant have psychoactive properties that range from sedative in weaker forms and smaller doses to hallucinogenic in stronger forms and larger doses (*Marihuana and Health*, 1977; "Marijuana and Health," 1971). Lack of adequate supplies and of animal test procedures has delayed understanding of this fascinating group of drugs (Harris, 1971).

The marijuana plant is not a single, simple substance but is very complex, containing at least 419 individual compounds; 61 chemicals identified in the plant are specific to the *Cannabis* plant (*Marihuana and Health*, 1977, 1980; Paton, 1975; Zinberg, 1979). The exact chemical configurations of the most active materials did not become known until 1963, and synthesis was not accomplished until 1967.

Delta-9-tetrahydrocannabinol reproduces most if not all of the effects of the plant drug (Galanter et al., 1972; Hollister, 1973; Hollister & Gillespie, 1975; Isbell, 1971; Isbell et al., 1967; Mechoulam et al., 1970). The percentage of THC is a useful guide to the psychoactivity of a drug sample, but other chemical ingredients may prove to be important in modifying THC's effects as well as have their own impact on human physiology (Hollister, Richards, & Gillespie, 1968). Thus, some of the research on THC may prove to be only partially relevant to the effects of the marijuana plant itself (*Marihuana and Health*, 1980).

During the 1920s, marijuana surfaced as an intoxicant among migrant Mexican laborers and became a matter of public concern. In the 1960s, use of marijuana spread among college students and then among secondary school students, and it has been adopted by portions of the established middle class (Braucht, Brakarsh, Follingstad, & Berry, 1973; Penning & Barnes, 1982). In Eastern countries, marijuana has been used to relieve fatigue and to stimulate appetite. In the Middle East and Caribbean Islands, marijuana is mixed in beverages and drunk as tea (Goode, 1975; Haber, 1975; Hall, 1976; "Marijuana Smoking," 1933).

During the 19th century, *Cannabis* extracts were employed in the United States as therapeutics (Ungerlieder & Andrysiak, 1981). Recently, marijuana has proved helpful for some cases of glaucoma (*Marihuana and Health*, 1980; Relman, 1982; Tashkin, 1978), for the nausea associated with chemotherapy for cancer (*Marihuana and Health*, 1980; Relman, 1982; Sallan, Zinberg, & Frei, 1975; *Therapeutic Uses*, 1980), and for a few cases of anorexia nervosa (Zinberg, 1979).

Does marijuana have implications for the health of Americans, especially the young? Smoking marijuana as well as some plants growing with and contaminating marijuana may be hazardous to bronchial tissues and pulmonary systems, even more than tobacco smoking (Chusid, Gelfand, Nutter, & Farci, 1975; Cohen, 1981; Kagen, 1981; *Marihuana and Health*, 1980; Maugh, 1982; Nicholi, 1983; Novotny, Lee, & Bartle, 1976; Relman, 1982; Schwarz, 1973b; Tashkin, 1978; Tashkin, Calvarese, Simmons, & Shapiro, 1980; Tashkin, Shapiro, & Frank, 1973; Tashkin, Shapiro, Lee, & Harper, 1976). Marijuana smoke may contain considerably more potential carcinogens than does tobacco smoke (Cohen, 1981; *Marihuana and Health*, 1980; Nicholi, 1983; Novotny et al., 1976). Marijuana may weaken the body's immunological defenses (Aaronson & Dunn, 1974; Lau et al., 1976; Relman,

1982) and may have a small, reversible suppressive effect on testosterone level and sperm count and motility (Kolodny, Masters, Kolodner, & Toro, 1974; Margolis & Popkin, 1980; *Marihuana Research*, 1974; Maugh, 1982; Mendelson, Kuehnle, Ellingboe, & Babor, 1974; Paton, 1975; Relman, 1982; Stuble & Raven, 1979). Marijuana does cross the placental barrier, and its use during pregnancy should be strongly discouraged because of many unknowns concerning its effects on ovulation, fetal development, and childbearing (Maugh, 1982; Petersen, 1980; Relman, 1982). It also enters into a nursing mother's milk.

The method of administration (oral, intravenous, or smoked) is one source of the variability of effects that limits conclusions in studies of marijuana. Smoking is the most common method of administration in the United States. Most users in the United States have smoked marijuana of relatively low potency, but its potency may be increasing (*Marihuana and Health*, 1977; Nicholi, 1983; Petersen, 1980).

Humans metabolize THC completely. When administered intravenously, THC may persist in plasma for more than 3 days (Lemberger, Silberstein, Axelrod, & Kopin, 1970). It disappears in 28 hr from the blood of experienced marijuana users but lasts for 57 hr in the blood of those unaccustomed to marijuana; metabolites of marijuana are excreted for more than a week in both groups (Dackis, Pottash, Annitto, & Gold, 1982; Lemberger, Tamarkin, Axelrod, & Kopin, 1971; Lemberger et al., 1972). Unlike alcohol, which is largely water soluble and may be washed out within 12 hr, marijuana is fat soluble and remains in the body, lodged in fat tissue, such as the brain, adrenal gland, liver, lungs, ovaries, and testes (Gill, 1976; Margolis & Popkin, 1980; Paton, 1975).

What Variables Must Be Controlled in Research With Marijuana?

Research for 50 years has examined marijuana's effect on human performance, but the variables involved are so complex that conclusions must be carefully stated. The statement of findings may displease those who prefer more forthright condemnation of marijuana lest the unwary, especially the young, might take up its use. It may also displease those who observe correctly that research evidence is not conclusive (Bennett & Milman, 1982; Hollister, 1971b; Kaplan, 1973; Kennedy, 1978; McGlothlin & West, 1968; Margolis & Popkin, 1980; *Marihuana and Health*, 1973, 1975, 1977, 1980; Maugh, 1982; Nicholi, 1983; Relman, 1982; Schwarz, 1973a).

First, there is the question of control of the potency and purity of the substance used as marijuana (Weil et al., 1968). Variation in potency among cannabinoids may reach a factor of 2,000; yet estimates of relative potency and quantitative analyses are difficult to make because of variability among

subjects (Cocchetto, Owens, Perez-Reyes, DiChiseppi, & Miller, 1981; Hawks, 1982; Hollister, 1976; Paton, 1975; Willette, 1976).

Since THC was synthesized, many investigations have employed it because its potency is more easily controlled and quantified (Hollister, 1971a; Hollister et al., 1968). THC reproduces most if not all of the effects of the plant drug (Isbell, 1971; Isbell et al., 1967; *Marihuana and Health*, 1980; Mechoulam et al., 1970; Rafaelsen et al., 1973). When this synthetic drug was administered with the natural marijuana to human subjects, however, the subjective, cognitive, and physiological changes tended to be greater for the natural marijuana. Marked placebo effects were suggestive of a learned subjective marijuana syndrome (Galanter, Weingartner, Vaughan, Roth, & Wyatt, 1973; Hollister, 1976). Recent authors have attempted to control for this factor by reporting the relative potency of the samples used in their studies, but potencies still vary from study to study.

The soil in which marijuana grows influences its potency (Abel, 1977). Carlini et al. (1974) used three samples of marijuana grown in Brazil. Their subjects were 11 physicians and 22 medical students who had never smoked marijuana. Each of the three samples of marijuana was burned in a pipe, and each of the subjects was exposed to the marijuana smoke in a room for 5 to 8 min; their noses were blocked. One sample of marijuana had no psychological effect, but the other two samples disrupted a time-estimation task and had effects two to four times greater than expected from the THC content.

Together with the potency of the marijuana used, the dosage is an important variable in marijuana research (Dornbush, 1974; Dornbush, Fink, & Freedman, 1971). Kiplinger and Manno (1971) and Kiplinger, Manno, Rodda, and Forney (1971) reported dose-related effects of THC. The latter authors had 15 volunteers smoke THC in different doses as well as a placebo dose in a randomized, double-blind design. Larger doses were associated with more interference in verbal tasks and rotor pursuit and unsteadiness on a test of stance. Most other investigations have also found more interference in human functioning traceable to larger doses of marijuana (Evans et al., 1973).

The route of administration—oral ingestion, intravenous injection, and smoking marijuana, which socially is the most common method in the United States—produces different effects (Cohen, 1981; "Marijuana and Health," 1971). The routes of absorption through lungs, digestive tract, or veins may filter the marijuana differently. Some 150 compounds have been identified in the smoke of marijuana; burning possibly transforms some of the chemicals into other compounds (*Marihuana and Health*, 1980). The effects of smoked marijuana appear within seconds to minutes, whereas in marijuana taken orally, the onset of effects is delayed for 30 min to over 2 hr (Hollister, 1973; Lemberger et al., 1972).

Some fraction of marijuana that is smoked may be lost into the air or

exhaled before it is absorbed completely. Many investigations have attempted to standardize the routine of smoking by regulating the size of the cigarette, how long it was smoked, how long it was inhaled, and the number of grams of marijuana it contained, stated in terms of THC potency (Casswell & Marks, [illegible]a). The efficiency of delivery of a marijuana dose by smoking has been e[illegible]nated to range from 20% to 80%; experienced and heavy marijuana users have smoked more efficiently than casual users (Hollister, 1971b, 1973; Lindgren, Ohlsson, Agurell, Hollister, & Gillespie, 1981). Inhaling gaseous and particulate products of *Cannabis* combustion exposes bronchial mucosa to polyaromatic hydrocarbons and other noxious compounds; some authors have been concerned that this may be a prodromal phase of another wave of lung cancer, as occurred with cigarette smoking (Cohen, 1981; Maugh, 1982; Relman, 1982). Potency is increased approximately three times by smoking THC, as compared with oral ingestion of the same material (Isbell et al., 1967).

The amount of marijuana entering the body can be controlled better in oral ingestion. Its fate within the body, however, is less certain because some active material might be lost through decomposition or other metabolic changes (Hollister, 1971b). Lemberger et al., (1972) studied the effects of three methods of administering THC—oral, intravenous, and smoking. The subjects were 12 young male volunteers who were long-term users of marijuana and were paid for their cooperation. Only 50% of the THC content of the smoked marijuana was delivered, but it took [illegible]ffect within 10 to 140 min, averaging at about 70 min. Of the marijuana taken in a cherry-flavored drink, 90% was absorbed, but the peak effect did not occur until 3 hr after the drug was taken. Excretion of marijuana in urine on the first day was similar for oral and intravenous administrations. Psychological effects, measured by a questionnaire and rated in observations at regular intervals, fitted temporally with the plasma levels of metabolites of marijuana ingested and inhaled.

The subjects employed are an important issue in research of marijuana's effects on human cognitive and psychomotor functions and on personality. Auditory thresholds of college students having smoked marijuana, as compared to those having smoked a placebo, were altered significantly on a standard hearing test (Caldwell, Myers, Domino, & Merriam, 1969a, 1969b). Meyer, Pillard, Shapiro, and Mirin (1971) tested six heavy and six casual marijuana users. Generally, research has revealed significant differences between performances of experienced and casual users of marijuana, although the criteria for selecting the two groups have not always agreed (Caldwell et al., 1969a; Greenberg, Mendelson, Kuehnle, Mello, & Babor, 1976; MacAvoy & Marks, 1975; Mendelson, Kuehnle, Greenberg, & Mello, 1976). In a double-blind study, all subjects smoked a placebo, marijuana in a dose fixed for the study, and marijuana in a dose that the subjects themselves selected. The four test sessions were a week apart. Casual smokers experienced more

impairment on a psychomotor task, and their responses to a questionnaire checking their experience of the drug effects indicated that the placebo condition gave them more of a high than did either drug condition. Degree of impairment in a perceptual test was similar for both groups. The casual users made five times as many errors on a divided-attention task when they were smoking the ad libitum dose of marijuana as they did when they were smoking the placebo. Heavy marijuana users did not manifest any increase of errors in the ad libitum dose condition. In a similar study comparing heavy and casual users of marijuana, the heavy users manifested more hostility on the Psychiatric Outpatient Mood Scale and poorer work adjustment and interpersonal relations than did the casual users, although the two groups had been equated in educational background, racial distribution, and social class (Mirin, Shapiro, Meyer, Pillard, & Fisher, 1971).

Jones (1971a; 1971b) tested 100 users of marijuana in drug and placebo conditions. Frequent users (75 of 100 subjects) rated the placebo as higher in potency than did the infrequent marijuana users; the infrequent users significantly distinguished the placebo from the drug condition, but the frequent users did not. The frequent users seemed more likely to respond to cues of familiar taste and smell (i.e., psychological factors) than to the THC content of the cigarettes. Response variability seemed to be a function of users' expectations and their previous experience with marijuana (Carlin, Post, Bakker, & Halpern, 1974; Hollister, 1976; Hollister & Overall, 1975–1976).

The subjects were important considerations in the first research under U.S. auspices on marijuana's effects (Dornbush & Freedman, 1976). The first study examined use of marijuana by soldiers in the Panama Canal Zone. The dose was not specified, and control groups were not included. Appetite was increased, but no serious harm to soldiers' efficiency or corps morale was evidenced (Abel, 1982; "Marijuana Smoking," 1933). The second study, after the Marihuana Tax Act was passed in 1937 in the United States, was the LaGuardia report (*Mayor's Committee*, 1944) which was based on 72 prisoners in New York City, of whom 48 used marijuana. No control groups were described, the marijuana dose was not specified, and the scientific design was faulty ("Marijuana and Health," 1971). Intellectual functioning was impaired, body steadiness was decreased, but basic personality patterns remained unchanged (Clark & Nakashima, 1968; Weil et al., 1968).

The President's Commission on Law Enforcement and Administration of Justice in 1967 stated that no careful and detailed analysis of the experience with marijuana in the United States seemed to have been attempted (Weil et al., 1968). Three studies of those who had used marijuana alone for 10 years or more were conducted in Jamaica, Greece, and Costa Rica (Schaeffer, Andrysiak, & Ungerlieder, 1981). Subjects who had used marijuana exclusively for 10 years could not be identified in the United States. The marijuana users tested in the three other countries came from the lowest, least productive

strata of society, in contrast to the well-educated, middle-class marijuana users who have been the subjects in most research in the United States (Dornbush & Freedman, 1976; Petersen, 1980). Research outside the United States has tended to be mostly anecdotal and deficient in scientific controls (Goode, 1975; Haber, 1975; Hall, 1976; Margolis & Popkin, 1980; Weil et al., 1968).

Both the set and setting must be controlled for consistent findings, but research with these variables has overlapped research with the variable of the subjects employed (Cappell & Pliner, 1974; Galanter et al., 1973; Hollister, 1976; Hollister & Overall, 1975–1976; Jones & Stone, 1970; Lamanna, 1981; Pihl, Shea, & Costa, 1979; Stark-Adamec, Adamec, & Pihl, 1981, 1982; Stark-Adamec, Pihl, & Adamec, 1980; Zinberg, 1979). Setting includes the environmental circumstances of the investigation. Hollister, Overall, and Gerber (1975) studied the effect of setting and found that it had less impact than either the drug effects or the reaction of subjects. Casual users of marijuana (N = 12) smoked cigarettes of either marijuana or placebo. The favorable environment included all the appurtenances deemed desirable by drug users, namely, mystical pictures, visual-centering devices, tapes of drone instruments that were suitable for meditation, burning incense, and small candies. Subjects were invited to remove their shoes and socks and lie on rugs or cushions placed around the room, which was in a private dwelling. The unfavorable environment was an austere laboratory in which were strewn odds and ends of medical equipment in a Veteran's Administration hospital.

Galanter et al. (1974) approached the influence of set and setting on marijuana effects in another way. Experienced users of marijuana (N = 36) joined sensitivity groups; 12 groups of three members each met for 90 min once a week for 26 weeks. The three conditions in the meetings were smoking marijuana, smoking a placebo cigarette, and using no drug. On questionnaires answered in Sessions 9 through 20, subjects' somatic experiences were consistent with the drug condition. The marijuana users had described previous experience with marijuana as happy, friendly, and warm and as occasions when they were not likely to become angry and defensive. Their questionnaire responses, however, did not reflect consistent affective change, increased insight, or increased feelings of cohesiveness in the sessions when they smoked marijuana. In their assessments of their own experience in the group and their perception of the group atmosphere, there were no significant differences between sessions in which they smoked a placebo and those in which they smoked marijuana. The marijuana users did not report themselves as more detached, but observers rated them as less involved with others. Subjective responses of marijuana users were at variance with the experiences they had anticipated in the light of their previous experience with marijuana. A strong learned component in the response to marijuana was suggested by subjective responses to placebo conditions (Galanter et al., 1973; Jones, 1971a, 1971b). To the extent that experienced users of marijuana were able

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to compensate for the effects of marijuana, the decrement in performance might have been less evident (Meyer et al., 1971).

Clopton, Janowsky, Clopton, Judd, and Huey's (1979) findings were in a similar vein. Experienced marijuana users were less aware of the emotions of others in a small-group setting after they smoked marijuana than they were in the placebo session. Their scores on the Affective Sensitivity Scale declined significantly after smoking marijuana. Janowsky et al. (1979) reported similar changes after their male subjects smoked marijuana. Twenty men were selected, all employed in mental health fields. Twenty women, controls, met with the men one-on-one for 25 min, during which they discussed difficult times they had experienced. Then the men smoked a marijuana or placebo cigarette. They returned to discussion for 25 min. After the marijuana cigarette, the men decreased significantly in interpersonal skills and in empathy. This change was noticed by the men themselves in their evaluations of their mood on an affective checklist as well as by judges who rated videotapes of the interviews between men and women.

As a further limitation on the results of investigations, Weil et al. (1968) considered the absence of negative control on placebo treatments one obstacle in marijuana research. For frequent users, the odor and taste of marijuana are so distinctive that an effective placebo is difficult to obtain. Placebo conditions are relatively easier to maintain with those who are unfamiliar with marijuana. Medical, legal, and ethical issues are also obstacles to be overcome if research with marijuana is to be scientifically controlled. Because women have not yet taken up marijuana in the same proportions as men, men predominate as subjects. College, medical, and graduate students also predominate. These factors, together with the small size of groups tested, limit the generality of conclusions from studies of the effects of marijuana (Glynn & Nelson, 1982).

Research Findings on Cognitive Performance

Does long-term substantial use of marijuana lead to impairment of cognitive functions? Intellectual function and immediate memory are impaired by marijuana, according to the statement of the secretary of health, education, and welfare (*Marihuana and Health*, 1975). Answers must usually be qualified in terms of not only the subjects' experience with marijuana, the potency and dosage of the substance used, and the method of administration but also the tasks employed, simple or complex (Cohen, 1981; Dornbush, 1974; Waskow, Olsson, Salzman, & Katz, 1970; Weckowicz et al., 1975; Wetzel, Janowsky, & Clopton, 1982).

Attention was the focus of early investigations of the effect of marijuana on human cognitive functioning. The Goal-Directed Serial Alternation (GDSA) was the task employed in several studies (Melges, Tinklenberg, Hol-

lister, & Gillespie, 1970a, 1970b; Meyer et al., 1971). The GDSA required subjects to simultaneously hold in mind and coordinate information as well as perform mental operations relevant to pursuing a goal. Each subject was assigned a starting number in the range of 106 to 114 and was required to subtract 7 and then add 1, 2, or 3, continuing such alternate subtraction and addition until the number initially selected was attained. Casswell and Marks (1973a) compared nine male casual users and nine male heavy users of marijuana on the GDSA. Both groups obtained lower scores on the GDSA after smoking marijuana. On a vigilance task, Casswell and Marks (1973b) found that their two groups did not differ significantly. Confusion on the GDSA and loss of directedness usually occurred when marijuana was used (Melges et al., 1970a, 1970b). Smoking low doses of marijuana did not influence mental performance of 8 subjects on delayed auditory feedback, addition problems, color naming, or a task similar to the GDSA (Evans et al., 1973). Decrements in performance in connection with smoked marijuana were larger in Casswell and Marks's (1973a, 1973b) studies than were those Melges et al. (1970a, 1970b) found with orally ingested THC. Differences on the Digit Symbol (DS) were not altered significantly by smoking marijuana in Casswell and Marks's (1973a) investigation, in contrast to the significant results Melges et al. (1970a) obtained with THC orally ingested. Casual and heavy users were affected differently on different tasks by marijuana, ingested, smoked, or in the form of THC (Casswell & Marks, 1973a).

In Germany, Dittrich, Battig, and von Zeppelin (1973) also tested the effect of oral ingestion of marijuana on memory as well as on attention. They discovered that the effect of marijuana on attention varied according to the task and concluded that attention should not be considered a unitary trait. On 10 lists of two-syllable nouns, marijuana did not alter the retrieval of information already present in memory, but information stored in short-term memory was forgotten to a greater degree after the marijuana than after a placebo. They judged that their results supported the findings of Abel (1970, 1971) and Melges et al. (1970a, 1970b). Low doses of THC did not alter recall in short-term (6–18 s) memory of consonant trigrams for 10 first-year medical students, but high doses were followed by significant interference, especially in the longer delays. In his investigations of marijuana's effect on memory, Abel (1970, 1971) subjected 49 men and women to two experiments with the following three conditions: smoking marijuana, smoking a placebo, and being in the control group. In the first test, 18 lists of 10 words each were read aloud; 1 min was allowed for verbal recall of the list immediately after the words were presented. On a recognition test for immediate memory, the subjects had to circle 30 words that they recognized from 60 words, 30 from the first 3 lists and 30 new words. They also rated their confidence in the accuracy of their responses. One group smoked a marijuana cigarette for 5 to 10 min, and another smoked a placebo cigarette.

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A second recognition test was made up of 300 items, 150 from the last 15 lists of words and 150 new words. Marijuana and placebo groups did equally well on both recognition tests; the marijuana group tended to be less cautious and to accept more incorrect words. In a second experiment, 10 subjects who were familiar with the effects of marijuana were tested twice, with 1 week between the two sessions; marijuana and control groups were reversed in the two sessions. After they smoked marijuana or the placebo, they were assigned the memory task of 10 lists of 12 words each. After the last list was read, they were given 5 min to write as many words as they could recall. All subjects remembered fewer words in the marijuana condition than they did in the placebo condition.

Marijuana affected recognition and the acquisition processes involved in the storage of information but not retrieval when the free-recall method was employed. In Abel's (1970) early study, eight men and women read through a book twice at their own speed after smoking two marijuana cigarettes. Those who smoked marijuana scored the same as the placebo subjects, but seven of eight marijuana smokers wrote significantly less and included fewer content words. Gianutsos and Litwack's (1976) results showed a significant reduction for chronic marijuana users in the movement of information from short-term memory to a more permanent level of information storage. Their subjects were college students, 25 chronic users and 25 nonusers, similar in sex, age, major, grade point average, and year in school.

Dornbush (1974) replicated the testing conditions of the two experiments conducted by Abel (1970) with 20 male first-year medical students. Specifying the THC content of the marijuana and having a placebo control were additions to Abel's research conditions. The results supported Abel's findings; that is, marijuana disrupted the storage phase of short-term memory (Dornbush et al., 1971). Miller, Drew, and Kiplinger (1972), including a placebo control and specification of the THC content, also replicated Abel's study. Students who were experienced users of marijuana (N = 12), having smoked either marijuana or a placebo in a random, double-blind design, were asked to relate all they could remember of a story read to them and to respond to the Stroop Color-Word Test. Marijuana did not alter performance on the Stroop test. Results on memory for narrative material supported Abel's (1970, 1971) findings but showed, in addition to memory deficits, that irrelevant material was intruded by those who had smoked marijuana, as had been noted in earlier research (Clark, Hughes, & Nakashima, 1970; Tinklenberg, Melges, Hollister, & Gillespie, 1970). Some of the irrelevant material added by those who had smoked marijuana was new and without any basis in the stimulus story, and some was arbitrarily unrelated and so strongly colored emotionally that the original story was altered.

In state-dependent learning research, marijuana intoxication did not alter the ability to accurately assess what information was available in long-term

memory (Darley, Tinklenberg, Roth, Vernon, & Kopell, 1977; Parker et al., 1980). Stillman, Weingartner, Wyatt, Gillin, and Eich (1974) found that subjects recognized pictures better in the marijuana condition (smoking marijuana in a THC dose similar to that required for a social high) than in the placebo-marijuana or the marijuana-placebo condition. Placebo-placebo condition reproduction was substantially better than marijuana-marijuana condition reproduction, and marijuana produced some overall impairment in performance.

Rickles, Cohen, Whitaker, and McIntyre (1973) explored state-dependent recall with male subjects who had smoked two marijuana cigarettes within 20 min or a placebo and then learned paired-association lists. Those intoxicated on marijuana needed significantly more trials to reach criterional learning than did those in the placebo condition. Ten days later, the subjects who had been high on marijuana recalled better the material they had learned. Moderately high doses of marijuana interfered with learning new material in terms of subjects' needing more trials and more failures to reach criterion than did subjects in the placebo condition.

Impaired immediate memory and intellectual performance on a variety of tasks in connection with marijuana has been confirmed experimentally (Relman, 1982). Evidence has indicated that at lower doses, users are able to "suppress the marijuana high." Experimental research has not confirmed the enhanced visual, auditory, and tactual awareness and sensitivity claimed for marijuana by its users (*Marihuana and Health*, 1975).

Research Findings on Psychomotor Performance

Many of the studies in this area began as investigations of marijuana's effect on driving an automobile (Klonoff, 1974). Some researchers have reported that marijuana was associated with errors in estimates of time that might influence driving in traffic (Hollister & Gillespie, 1970; Jones & Stone, 1970; Kaplan, 1973; Melges, Tinklenberg, Hollister, & Gillespie, 1971; Vachon, Sulkowski, & Rich, 1974). Verbal and operative estimates of time, in which subjects press a key for an interval called for by the experimenter, involve functions different from those in reproductive time judgments, in which subjects press a key for 5, 10, or 15 s (Clausen, 1950). Similarly, smoking marijuana seemed to bring on errors in judgments of distance, important in parking and passing cars in traffic (Bech, Rafaelsen, & Rafaelsen, 1973). Tracking tasks and pursuit motor tasks were disrupted more by smoking THC than by taking a placebo, as evaluated by self-ratings and interpersonal judgments (Melges, 1976; Roth et al., 1973). Marijuana smoking affected reaction time and coordination of movements important for operating machinery at work and at home as well as for operating an automobile (Kvalseth, 1977;

Manno, Kiplinger, Haine, Bennett, & Forney, 1970; Manno, Kiplinger, Scholz, Forney, & Haine, 1971; Moskowitz, Shea, & Burns, 1974).

Bech et al. (1973) and Rafaelsen et al. (1973) fed cakes containing THC or a placebo to eight men. Marijuana affected estimates of time and distance in a simulated driving test. The car was equipped with steering wheel, accelerator, brake, and clutch; the men drove for about 25 min. They were asked how far they thought they had been driving. When the wheel was turned, the landscape moved at a speed determined by the drivers' pressure on the accelerator. Marijuana had a more marked effect on the subjective than the objective estimates. Moskowitz, Ziedman, and Sharma (1976) used film depicting moderate to heavy traffic for their investigation; alcohol disrupted visual search more than marijuana did.

Crancer, Dille, Delay, Wallace, and Haykin (1969) studied the comparative effects of marijuana and alcohol on simulated driving performance. Their 36 subjects, who were experienced with marijuana and mostly men, smoked marijuana until they reached a social high. More errors were recorded in the marijuana condition than in the normal condition, for reading the speedometer but not for using the accelerator, brake, or steering. Alcohol produced significantly more errors than marijuana did on driving tasks.

The research of MacAvoy and Marks (1975) in New Zealand also involved comparisons of effects of marijuana and alcohol, in this case on tracking accuracy and recognition of signals. Tasks required pressing a key when a central light signal flashed, breaking the sequence, and pressing a second key when a peripheral red light flashed. Marijuana reduced the accuracy in tracking and recognizing signals and impaired physiological and psychological functions involved in driving skills differently from alcohol.

In Casswell and Marks's (1973b) study, 10 male experienced marijuana users and 10 male nonusers, matched in age and education, were tested with two types of visual signals coming from different sources. Those who smoked marijuana missed significantly more of both the central and peripheral signals. The authors believed that their results applied to driving, which they construed as performing a task while processing information coming from more than one task. Visual-information processing in a tachistoscopic presentation was impaired significantly in 10 male experienced marijuana users after they smoked marijuana but not in a placebo condition (Braff, Silverton, Saccuzzo, & Janowsky 1981).

Clark, Hughes, and Nakashima (1970) studied the effects of oral THC on 18 college students who had never used marijuana. The students were tested on reaction time for four colors, singly or in combination, and on a digit-code memory task. After marijuana, responses to the reaction-time task were markedly inconsistent, especially in the more complex tasks. On the digit-code test, marijuana affected the students' accuracy and significantly reduced their hand steadiness.

Kvalseth (1977) reported an investigation in Norway in which six experienced marijuana users tested on linear and rotary movements made significantly more errors in the marijuana condition than they did in the placebo condition of testing. In two studies, motor performance was significantly decreased for 12 male volunteers who smoked marijuana in a double-blind design; alcohol also interfered with motor tasks of varied complexity; a combination of marijuana and alcohol induced significantly more performance decrement than did either drug alone (Manno et al., 1970, 1971). Both mental and motor performance of 15 male medical students, half of whom had experience with marijuana, showed deterioration after smoking THC, in comparison with the results of the placebo condition (Kiplinger et al., 1971).

Volunteers (N = 25, men and women about equally) responded to the following tasks: addition, subtraction, standing steadiness, pursuit rotor, and reaction time for red and white signal lights (Belgrave et al., 1979). Results were factor analyzed and indicated four factors; THC was associated with significant deterioration on all four factors. Comparisons of alcohol (ethanol) and THC showed that alcohol's effects on performance decrements were slower in onset than THC's but lasted longer. Apparently, the two drugs did not interact, but the combination of drugs as well as each drug alone impaired performance on tasks related to skills involved in driving an automobile.

Janowsky, Meacham, Blaine, Schoor, and Bozzetti (1976a, 1976b), in a double-blind study, investigated the effect of smoking marijuana on simulated-flying performance. Male certified pilots (N = 10, 7 professional and 3 private pilots), all of whom had used marijuana socially, took a simulated-flying test 30 min after smoking marijuana for 10 min; the tests were repeated 2, 4, and 6 hr after they smoked marijuana or a placebo cigarette. All showed significantly decreased flying skill in a 16-min test of flying in a simulated holding pattern sequence, involving straight and level flight and turns, and of instrument flying and navigation. Evaluation continued over the 6-hr period; flying performance was videotaped and analyzed in 10-s intervals for major and minor errors. Performance returned to normal 4 hr after smoking marijuana. Pilots rated the effects of marijuana as equivalent to a social high. They felt that flying was more challenging after smoking marijuana and that they were not able to compensate adequately. Analysis of their performance on videotapes by judges who did not know whether they had smoked marijuana or were in the placebo phase confirmed their self-judgments.

Hansteen, Miller, Lonero, Reid, and Jones (1976) reviewed the studies of marijuana and alcohol effects on automobile driving and psychomotor tracking. They concluded that under certain conditions of dosage and time intervals after smoking, marijuana impaired pursuit-tracking accuracy, hand and body steadiness, time needed to brake, signal detection, perception of danger and risk taking, and susceptibility to distraction or stress. Their own investigation of 16 licensed drivers, 12 men and 4 women, mostly college

students, on driving tests was spread over four weekly sessions and included a high and low dose of marijuana, alcohol, and placebo. Both the doses of alcohol and the higher dose of marijuana induced poorer handling of the automobile. Early reports were more optimistic about driver performance after smoking marijuana than recent evidence (*Marihuana and Health*, 1975). The more complex the task was, the more disruptive the effect of acute marijuana intoxication generally was. Operation of an automobile and complex psychomotor skills are clearly impaired by marijuana (*Marihuana and Health*, 1977; Relman, 1982). In simulated-driving and actual-driving tests, in estimates of time and distance, in alertness to signals at the center of the visual field and on the periphery, and in stability of stance, it appears that marijuana in social doses can impair driving performance and complex psychomotor skills (Paton, 1975; Relman, 1982; Waller, 1965, 1971).

Personality Differences Attributable to Marijuana

Some studies have sought to identify personality traits that might identify those likely to take up drugs, marijuana in particular (Nicholi, 1983). Findings on personality characteristics of contemporary marijuana users indicate a greater diversity of personality patterns than in the more traditional hard-core heroin addicts of past generations (Austin & Lettieri, 1976; Blaine & Julius, 1977; Brill, Crumpton, & Grayson, 1971; Harmatz, Shader, & Salzman, 1972; Murray, 1967; Patalano, 1976, 1978, 1980; Penning & Barnes, 1982; Pope, Ionescu-Pioggia, & Cole, 1981). Gorsuch and Butler (1976), who reviewed the research on the predisposing social and psychological factors, and Sadava and Forsyth (1977) pointed out that a complex interaction of parent-child relationships, parental modeling, involvement with drug-using peers, and availability of illicit drugs made it difficult to distinguish clearly the path leading to initial drug use.

Another approach in marijuana study searched for a constellation of attitudes, values, and behavior representing a rejection of middle-class or establishment norms and activities or behavior reflecting a sense of alienation and dissatisfaction with family and school experience (Dembo, Schmeidler, & Koval, 1976; Ferguson, Lennox, & Lettieri, 1974; Hendin, Pollinger, Ulman, & Carr, 1981; Jessor, 1976; Rooney & Wright, 1982). Several studies employing questionnaires and interviews have looked into behavior patterns that preceded adolescents' use of marijuana (Lettieri, 1975). Family patterns rather than peer pressure appeared to be related to subsequent marijuana use in a study of 180 boys and girls from 13 to 17 years of age (Brook, Likoff, & Whiteman, 1980). Fathers' personalities and child-rearing practices, however, interacted with peer factors in influencing high school students' (Kandel, 1973) and male college students' patterns of marijuana use (Brook, Whiteman, Brook, & Gordon, 1981, 1982). Alcohol, in the form of beer and

wine was often the first step in a sequence leading to tobacco and subsequently to marijuana (Kandel, 1975; Kandel & Faust, 1975; Maugh, 1982). The highest rates of marijuana use were observed in adolescents whose parents and friends both used drugs (Kandel, 1973). Cultural differences contribute to the mix of parental and peer influences on patterns of adolescent drug use (Kandel & Adler, 1982; Winfree & Griffiths, 1983).

In an early description of becoming a marijuana user, Becker (1953) emphasized not antecedent predispositions but the motives and changes in attitudes leading to the use of marijuana for pleasure, not as a compulsive response. It is probable that any excessive use of drugs for pleasure may decrease an individual's motivation. A frequent criticism of marijuana has been that it leads to an *amotivational syndrome* (Hendin, Pollinger, & Ulman, 1981–1982; McGlothlin & West, 1968; Margolis & Popkin, 1980; Miranne, 1979). This passive, inward-turning, amotivational personality change, reflected in rejection of previous achievement-oriented behavior, appeared more often in clinical studies with younger subjects and was more frequent in the late 1960s than recently (Creason & Goldman, 1981; Shean & Fechtmann, 1971; Toohey, Dezelsky, & Baffi, 1982). From their responses to questionnaires, college students' intellectual goals and academic performance seemed less impaired by marijuana than did those of high school students (Hochman & Brill, 1983; Jessor, Jessor, & Finney, 1973; Smith & Fogg, 1976). The question waits for an answer: Does marijuana have any specific capacity for inhibiting motivation not possessed by other drugs (Farnsworth, 1976)?

College students who were users of marijuana appeared to be less responsible, more nonconforming and more open and often possessed higher self-esteem (Cunningham, Cunningham, & English, 1974; Grossman, Goldstein, & Eisenman, 1974; Gulas & King, 1976; Hogan, Mankin, Conway, & Fox, 1970; Knecht, Cundick, Edwards, & Gunderson, 1972; Simon, 1974; Victor, Grossman, & Eisenman, 1973). Campbell (1976), reporting on the Canadian scene, and Mellinger, Somers, Davidson, and Manheimer (1976) found no conclusive evidence that generally moderate patterns of marijuana use produced amotivational symptoms sufficiently serious or long lasting enough to increase the risk of dropping out of college. Evidence connecting heavy use of marijuana to amotivational syndrome did not conclusively show whether the drug was a cause or an effect (Cohen, 1981; "Marijuana and Health," 1971; Relman, 1982).

Campbell (1976), as a member of the Canadian committee investigating the effects of marijuana, reviewed European, Canadian, and North American studies; the evidence did not conclusively support an amotivational-syndrome change in personality traceable to marijuana use. All the changes attributed to use of marijuana could be explained through membership in subcultures that did not stress academic success or the need for planning or through a general decline in motivation. A review of examinations taken and essays

written before and after using marijuana four or five times a week for 4 to 6 weeks, however, revealed a decrease in abstracting and synthesizing ability. After being free of marijuana for 4 months during summer vacation, their ability returned.

Does marijuana lead to violence? Early reports emanating from police records and stories in tabloids accentuated this relationship (Abel, 1977, 1982). Salzman, Van der Kolk, and Shader (1976), Colbach (1971), and Keup (1970) agreed that the setting of a crowd may bring on physical or sexual violence but that violence because of marijuana is rare. Tinklenberg, Roth, Kopell, and Murphy (1976) found that marijuana did not have as socially disruptive effects as alcohol, and no evidence that increase in violent crime was directly related to increase in marijuana use. The consensus is that marijuana does not precipitate violence in most of those who use marijuana and that aggressive behavior is not a common consequence of marijuana use in the United States (Petersen, 1980).

Marijuana intoxication, the high, may approach the hallucinogenic trips of LSD if dosage is high enough (Consroe et al., 1976; Fabian & Fishkin, 1981; Halikas, Goodwin, & Guze, 1971; Tart, 1970). About 17 of 42 (about 40%) marijuana users randomly selected from college students had experienced hallucinogenic ideation (Keeler, Ewing, & Rouse, 1971). Usually, as with other hallucinogens, marijuana users were able to recover as the drug left the system (Gersten, 1980). Hollister and Overall (1975–1976) and Pihl et al. (1979) factor analyzed the responses of several hundred marijuana users regarding their subjective experiences with marijuana; five factors that emerged made it clear that marijuana intoxication effects are multidimensional.

To what extent is the use of marijuana associated with psychotic episodes? Instances in which marijuana interferes with cognitive functioning, such as study or good judgment, have already been discussed, but sometimes these incidents blossom into anxiety states and, though temporary, may cause panic, which is a common reaction to the effects of large doses of marijuana, especially for first-time users (Bailos, 1970; Stanton & Bardoni, 1972; Weil, 1970). Accounts of psychotic episodes attributed to marijuana use have been reported more often in other countries than in the United States (Austin, Macari, & Sutker, 1972; Keup, 1970). Linn (1972) showed that psychopathology was a condition that developed prior to marijuana use.

Do marijuana users experience spontaneous recurrences? Keup (1970) found that 5% to 10% of newly admitted mental patients who had a history of drug abuse reported having had flashbacks after abusing marijuana. Marijuana had frequently been used along with other drugs by soldiers who had experienced flashbacks (Yager, Crumpton, & Rubenstein, 1983). Canadian high school students reported experiencing recurrences of marijuana effects at times when they were not using the drug (Annis & Smart, 1973). Keeler,

Reifler, and Liptzin (1968) described 4 subjects who, in a drug-free state, had recurrences of unusual visual or somatic sensations that they had experienced while using marijuana. The subculture of marijuana users does believe in the reality of spontaneous flashbacks, but in most cases in which marijuana alone was the drug, the users diagnosed the flashbacks themselves, and few were legitimate instances of spontaneous recurrence (Brown & Stickgold, 1976).

Physicians, however, have been concerned with the number of patients who recover from mental illness only to relapse after using marijuana (Gersten, 1980; Nicholi, 1983). Marijuana has been known to push some into mania (Harding & Knight, 1973). Paranoid episodes and hallucinogenic effects occur in connection with marijuana use, especially with large doses and overdoses (Gersten, 1980; Relman, 1982; Treffert, 1978; Weil, 1970). Marijuana is especially ill-advised for those predisposed to schizophrenia (Casswell & Marks, 1973a; Gersten, 1980; Keeler et al., 1971; Keup, 1970; McGlothlin & West, 1968; Melges, 1976; Szymanski, 1981). When marijuana is used to treat nausea associated with chemotherapy for cancer, it sometimes triggers dysphoric reactions (Nicholi, 1983). Normally functioning individuals with no history of psychiatric illness but moderate underlying psychopathology may develop psychiatric disturbances associated with smoking marijuana, but these ordinarily clear up within a short time as the drug leaves the system.

Can marijuana lead to brain damage? Maugh (1974) outlined the arguments and research on the question of whether chronic and heavy marijuana use leads to brain damage. Marijuana seems to pass the blood-brain barrier (Wall, 1971). In England, Campbell, Evans, Thomson, and Williams (1971) reported cases of cerebral atrophy in 10 young men who had been heavy users of marijuana over a period of 2 or more years. Kolansky and Moore (1971, 1972a, 1972b) attributed the deleterious effects of long-time use of marijuana to damaged cerebral cortex. Cohen (1981) judged that long-term heavy use of marijuana and the process's taking so long to reverse itself pointed to organic brain impairment. Evidence in the United States has disputed the earlier judgments ("Marijuana and Health," 1971; Relman, 1982). Computerized transaxial tomography has provided a more comprehensive picture of the brain than Campbell et al. (1971) have. Computerized transaxial tomography of 12 men in St. Louis and 19 men in Boston revealed no evidence of cerebral atrophy (Co, Goodin, Gado, Mikhail, & Hill, 1977; Kuehnle, Mendelson, Davis, & New, 1977; *Marihuana and Health*, 1977; Relman, 1982). Surface electroencephalogram changes during marijuana smoking are minimal, but depth changes go on in the septal and amygdala areas in monkeys exposed to marijuana smoke. As a psychoactive drug, marijuana alters the brain functions of memory and time estimates, but the question to be resolved is whether impaired neurological functioning persists beyond the period of acute intoxication. The weight of evidence so far is that lasting brain impair-

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ment is possible but not inevitably associated with some undetermined level of heavy and chronic use of marijuana (Petersen, 1980).

Marijuana remains a drug with many attendant dangers and is potentially more harmful than was previously suspected (Margolis & Popkin, 1980). Marijuana use is inextricably tied to the use of many other drugs. Those who use drugs, licit and illicit, are far more likely to use marijuana; prior use of alcohol and tobacco by young people is clearly associated with later marijuana use. Heavy users of marijuana are more likely to use other drugs as well (Hochman & Brill, 1983; *Marihuana and Health*, 1975; *Marihuana Research*, 1974).

Discussion

Research supports the statement of the secretary of health, education, and welfare that marijuana impairs human intellectual judgment and short-term memory as well as human psychomotor function, particularly driving an automobile. The complexity of variables involved in research with human subjects' use of marijuana, however, precludes unqualified conclusions. The potency of the material used varies according to the part of the plant used, the soil in which it was grown, the method of cultivation, whether the marijuana is smoked or taken orally or intravenously, and whether the plant material or THC, the potency of which is believed to approximate the potency of plant material, is used. Chronic users of marijuana probably respond differently to marijuana than do casual or naive users.

Still unanswered and crucial to programs of prevention of drug abuse are the questions of why some use marijuana and others do not and why some users of marijuana go on to become addicted to hard drugs and others, similarly at risk, do not (Blaine & Julius, 1977; Cunningham et al., 1974; *Marihuana Research*, 1974). Marijuana is used by groups younger than ever before; today's high school and college students have smoked marijuana longer than those who smoked it when it first became the fad. Marijuana use by women has increased. Will these changes in patterns of marijuana use be translated into damage, physiological or psychological, that was not evident in earlier studies of marijuana smokers (*Marihuana Research*, 1974; Penning & Barnes, 1982)? What effect if any does use of marijuana have on physical and intellectual development in the young, the adolescents and young adults who are prominent among the frequent users of marijuana (Petersen, 1980)? No research has addressed the effect of age in marijuana users. Concern has been expressed that the adolescent users of today may be handicapped later in life by deferring coming to grips with problems of living through frequent use of marijuana (Cohen, 1981; Maugh, 1982). Young people have reported that they fear that marijuana bought on the street might be laced with heroin or some dangerous substances, but assays of street drugs around the country

by the United States government has shown little adulteration (Lamanna, 1981). As youth move into their adult years, will they trade in use of marijuana for traditional adult role behavior? Prediction of the future is more difficult because marijuana use is more widespread than ever before (Glynn & Nelson, 1982).

Because research on long-term physiological and neurological effects of chronic marijuana use remains modest, the information on marijuana's effects has limited relevance to long-term health implications (*Marihuana and Health*, 1977; "Marihuana and Health," 1971; Petersen, 1977). Marijuana has been used popularly in the United States for about two decades; other countries have had longer experience, but the scientific research is lacking (*Marihuana and Health*, 1975). Weller and Halikas (1982) resurveyed about 100 regular users of marijuana after 5 to 6 years; they averaged 27 years of age at the time of the second interview. Comparison of checklist ratings of subjective experiences indicated a decline in the effects initially classified as desirable. Perhaps this decline in experience with marijuana is behind the decline in use noted at the beginning of this report and offers some hope for spontaneous remission in use of marijuana. The major focus for explanations of centrally active drugs is their effects on neurotransmitters and neuropeptides in the brain. Animal studies with marijuana have implicated norepinephrine and serotonin, but the picture is not yet clear (Hollister, 1976; Paton, 1975). Some evidence has indicated that changes in the turnover or degrading effects of the catecholamines might be linked to oral doses of THC, but serotonin levels have been unaffected (Hollister, Moore, Kanter, & Noble, 1970). THC seems to function by an anticholinergic mechanism (Beaconsfield et al., 1972; Drew & Miller, 1974; and Freemon, Rosenblatt, & El-Yousef, 1975; *Marihuana and Health*, 1975; Paton, 1975).

Electrodes implanted in rhesus monkeys' brains may have revealed the brain areas involved in marijuana abuse (Cohen, 1981; Heath, 1973; Petersen, 1980). The hippocampal area of the limbic system of the brain, especially because of marijuana's disruption of immediate memory, has been connected to marijuana abuse through the similarity of behavior changes traceable to marijuana abuse and to the effects of hippocampectomy and temporal lobe resections (Drew & Miller, 1974; Paton, 1975). Perhaps marijuana's impact will be identified through its alteration of the speed of processing pictorial information in favor of the left hemisphere of the brain (Stillman, Wolkowitz, Weingartner, Waldman, DeRenzo, & Wyatt, 1977). Marijuana has chemical properties qualitatively similar to steroid anesthetics (Gill, 1976). Autonomic receptors seem not to explain the effects of THC (Bachman, Benowitz, Herning, & Jones, 1979).

Are there latent consequences of marijuana use due to the complex physicochemical properties of psychoactive cannabinoids? Will research 10 to 20 years ahead reveal consequences of marijuana smoking similar to those dis-

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covered with tobacco? Marijuana is more complex chemically than tobacco, and not all of its effects have been deciphered. Smoking marijuana intoxicates, and tobacco does not; smoking marijuana, unlike tobacco, interferes with intellectual functioning, alters time and distance perception and judgment of dangers, and impairs hand and eye coordination.

Like alcohol, marijuana is a drug, but the effects of the two differ in several respects. Marijuana had more deteriorating effect on some tasks than alcohol did, for example, subjective estimates of time and distance in some simulated-driving tasks (Bech et al., 1973; Crancer et al., 1969; MacAvoy & Marks, 1975). Marijuana's interference with performance was slower in onset than alcohol's but lasted longer (Belgrave et al., 1979). The effect of marijuana in oral form peaked after 30 to 60 min and culminated after 2 to 3 hr, whereas alcohol peaked later, between 1 and 2 hr (Rafaelsen et al., 1973). Marijuana did not have the socially disruptive effects of alcohol, nor was it directly related to violent crimes (Tinklenberg, Roth, & Kopell, 1976; Tinklenberg, Roth, Kopell, & Murphy, 1976). Hollister and Gillespie (1970) found that dextroamphetamines induced changes in behavior different from marijuana and alcohol, whose perceptual effects resembled those of hallucinogens.

Tolerance to some of the effects of marijuana, especially tachycardia and subjective highs, has been demonstrated (Jones, Benowitz, & Bachman, 1976; Mirin et al., 1971; Nowlan & Cohen, 1977; Petersen, 1980; Relman, 1982). Usually, large doses over a long period of time are needed to produce tolerance (Margolis & Popkin, 1980). Moreover, the literature includes a number of experiments where lack of tolerance has been reported (Cappell & Pliner, 1974; Krasnegor, 1978; *Marihuana and Health*, 1975). The following factors could have contributed to the conflicting results: the dosage, the active constituents, and the ingredients' potency (McMillan, Dewey, & Harris, 1971). Tolerance does not develop to all THC effects, and most of the tolerance seems to be lost rapidly. Evidence has not indicated that frequent use of marijuana leads inevitably to escalation of use and dose. Tolerance is not as likely to be reported in outpatient studies, in which drug histories are difficult to control (Jones et al., 1976; Lindgren et al., 1981; Petersen, 1980; Relman, 1982).

Dependence in the sense of experiencing definite physiological symptoms following withdrawal has been shown after heavy use of marijuana but not after the social high (Jones et al., 1976; Nicholi, 1983; Petersen, 1980). Withdrawal symptoms of mild nausea, restlessness, sleeplessness, and loss of appetite have been observed in the heaviest smokers (Lamanna, 1981; Nowlan & Cohen, 1977). Psychological dependence is not unusual (Lamanna, 1981). Where tolerance develops, mild physical dependence seems to be associated, but dosage and schedules of use are important variables (Jones et al., 1976; Petersen, 1980; Relman, 1982). No evidence has indi-

cated that marijuana causes addiction to the extent that narcotics do or that physical dependence plays a significant role in persistent use of marijuana (Jones et al., 1976; Relman, 1982).

Probably no other drug has accumulated so much myth about it and so many unanswered questions. Factors of expectation and past experience with the drug may have influenced findings. The small samples that have been studied—mostly of healthy young male subjects who were well motivated and eager to demonstrate unimpaired performance—are serious limitations to broad conclusions. Until research includes more subjects, particularly those who are older and less healthy and women, the full picture of marijuana's effects will not be clear. Because widespread regular use of marijuana is relatively recent, the consequences of long-term use are less clearly documented than the short-term ones. Much remains to be learned about the effects of chronic use of marijuana. Cause for concern is the widespread use among the young of this drug, usually in addition to alcohol and tobacco, which has harmful known and unknown dangers. Many aspects of marijuana use are unknown. Enough is known, however, to state that use of marijuana is by no means harmless.

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The Chronic Cerebral Effects of Cannabis Use. I. Methodological Issues and Neurological Findings

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Abstract

This paper examines the research evidence relating sustained use of marijuana to chronic cerebral impairment. Evidence from both American and cross-cultural studies is reviewed, with a particular emphasis on methodological problems in the research. The focus of this paper is on neurological findings while another paper focuses on neuropsychological findings. On the basis of available research, it was concluded that there is no evidence that marijuana produces gross structural cerebral changes and little evidence that it leads to functional impairment, although subtle impairment cannot be ruled out.

Mind-altering substances have been used and abused throughout history, and their abuse continues to be a major social problem. Nevertheless, there has been relatively little study of their long-term effects on the central nervous system. Research on this question generally has used only one or two quasi-experimental designs, typically examining identified drug users for neurological impair-

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ment or comparing the performance of drug users and a control group on some assessment instrument. Although these quasi-experimental designs are weak and lack the controls of a true experiment, ethical considerations have severely limited the degree of experimental control that an investigator can exercise. While a few true experiments on the effects of drugs on humans have been conducted (Hill and Belleville, 1953; Isbell, Altschul, Kornetsky, Eisenman, Flanary, and Fraser, 1950), most experimentation on the chronic effects of drug use has been conducted on animals. In the animal research, the issue is not one of experimental control, but rather one of generalizability. Since the cerebral cortex is less highly developed in animals than in man, impairments such as subtle biochemical dysfunctions which may affect only higher-level mental processes might go unnoticed in animals.

In this paper, research on the long-term cerebral effects of marijuana use is reviewed. The large amount of research on marijuana should provide enough data to draw some tentative conclusions and to suggest lines for further research. Only the research with human subjects is reviewed because of the limitations in generalizability already discussed. This review begins with a brief discussion of some methodological considerations in long-term drug effect research before reviewing the research studies themselves. The review ends with several suggestions for new lines of research on this question. A thorough understanding of the risks associated with cannabis is necessary if we are to develop reasoned policies and laws to regulate its use.

METHODOLOGICAL CONSIDERATIONS

Polydrug Use

Studying the chronic effects of any illegal drug presents some very serious methodological issues. Perhaps the most serious of these is the fact that the vast majority of drug abusers are polydrug users. A number of recent studies (Grant, Mohns, Miller, and Reitan, 1976; Grant, Adams, Carlin, Rennick, Judd, and Schoof, 1978; Grant, Reed, Adams, and Carlin, 1979; Judd and Grant, 1975) have provided evidence of neurological or neuropsychological impairment in heavy polydrug users relative to control subjects.

There are many possible factors which may account for these findings. First, the drugs themselves and/or their adulterants may be directly toxic to the central nervous system. Evidence suggestive of such toxicity has been presented for heroin and opium (Hall and Karp, 1973; Richter and Rosenberg, 1968; Schein, Yessayan, and Mayman, 1971; Thompson and Waldman, 1970), amphetamines (Citron, Halpern, McCarron, Lundberg, McCormick, Pincus, Tatter, and Haverback, 1970; Goodman and Becker, 1970; Kane, Keeler, and Reifler, 1969; Weiss, Raskind, Morganstern, Pytlyk, and Baiz, 1970), and inhalants (Grabski, 1961; Knox and Nelson, 1966; Layzer, Fishman, and Schafer, 1978; Prockop, 1977; Prockop and Couri, 1977; Schaumberg and Spencer, 1976; Valpey, Sumi, Copass, and Goble, 1978). Quinine, a substance used to dilute heroin, has been linked to optic atrophy in at least one case (Richter and Pearson, 1975) and is described as having "well recognized tissue toxic effects" (Pearson & Richter, 1975, p. 316).

In addition to the use of other illegal drugs, heavy alcohol use is common among drug abusers (Grant et al., 1979; Institute of Medicine, 1982). Alcohol consumption by drug users must be considered in selecting control groups since there is some evidence of neurological and neuropsychological impairment in alcoholics (for reviews, see Bolter and Hannon, 1980; Kleinknecht and Goldstein, 1972; Parsons, 1977; Parsons and Leber, 1981; Ron, 1977; Tarter, 1975; Wilkinson, 1982).

While the heavy use of alcohol by marijuana users can be addressed by including a control group of heavy alcohol (but not marijuana) users for comparison, there is no comparable way of controlling for the use of other drugs. At least in this culture, finding a group of polydrug users who do not use marijuana to serve as controls is extremely unlikely. An easier approach would be to study marijuana users who are not polydrug users.

Differential Vulnerability

Several authors have suggested the possibility of an interaction between drug effects and a preexisting vulnerability in some subjects. Goodman and Becker (1970) suggested that the hemorrhages in amphetamine users may have resulted from an interaction between the hypertensive and vasoconstrictive effects of the drug and a preexisting neurological vulnerability (such as an arteriovenous malformation or aneurysm which is assumed to have burst under the increased pressure). A recent study of polydrug users (Grant et al., 1978) also raised the possibility that individuals may be differentially vulnerable to drug-related cerebral impairment. Possible interactions between drug effects and some other factor(s) enormously complicate an already difficult research area, although such considerations are probably more realistic than assuming equal vulnerability to drug effects in all subjects. The hypothesis of differential vulnerability seems to be consistent with clinical experience which suggests that the effect of a lesion in a patient with a previous brain injury is often more severe than the same lesion in an unimpaired individual.

Secondary Effects

There are also a number of secondary factors associated with heavy polydrug use that may increase the likelihood of cerebral impairment. Heavy drug

users may have a poor diet, and the resultant long-term nutritional deficiencies may produce impairment. The drug subculture is often violent, resulting in an increased likelihood of traumatic injuries. Falls due to impairment of coordination or loss of consciousness as a result of drug intoxication, overdose, or withdrawal may produce head injury. Head trauma may also result from errors in perception or judgment while in the intoxicated state. Local infections resulting from unsterile injections may spread to the central nervous system. Repeated anoxia resulting from overdose, withdrawal convulsions, or inhalation of solvents may increasingly destroy neurons.

It should be noted that all of the drug studies mentioned earlier as well as the marijuana studies described later in this paper have been retrospective. Thus it is unclear whether drug use predated cerebral impairment or whether the impairment predated drug use. For example, it is possible that the impairment in judgment sometimes seen in individuals with cerebral deficits may prevent them from being fully cognizant of the risks of heavy drug use, thus increasing the likelihood that cerebrally impaired individuals will abuse drugs. Although this possibility has not been studied with respect to marijuana or other illegal drugs, there is some evidence that alcoholics may be more likely than the general population to have been diagnosed as hyperactive or as having minimal brain dysfunction (MBD) in childhood (see Parsons and Leber, 1981, or Tarter, 1976, for reviews).

Even though polydrug use is not an insurmountable problem in marijuana research, there are other related issues which need to be considered. The purity and potency of any given street sample of marijuana may vary widely. Before gaining popularity as a drug in its own right, phencyclidine (PCP, angel dust) was used on occasion to strengthen poor-quality marijuana. Thus the central nervous system effects of PCP are also relevant. Another relevant drug is also one which the user might ingest unknowingly—the herbicide paraquat, which is sprayed on marijuana fields by U.S. Drug Enforcement agents in an attempt to kill the plants. While the central nervous system effects of paraquat are thought to be temporary, insufficient research has been conducted at the present time (Institute of Medicine, 1982).

Degree of Cannabis Use

Estimating the degree of past drug use is difficult since there are no standardized amounts of the drug in street samples. In addition, the self-report of drug users concerning the frequency of drug use is often suspect. In spite of these difficulties, getting some crude estimate of the level of use in the subjects under study is valuable and most studies report such information. However, few studies report how they gathered the information. The validity of such data can be enhanced if the questions used to gather the data are carefully standardized.

Well-worded questions could significantly reduce the effects of response-set biases such as social desirability and acquiescence.

Many studies use subjects who report a wide range of drug use from as little as once a week to as often as several times a day. Since light to moderate users, especially if the use is short term, would be unlikely to demonstrate impairment, their presence in a sample may serve to statistically mask impairment in the heavier users.

In many of the U.S. studies, the subjects were undergraduates or medical students who were often light cannabis users. The use of students as subjects does reduce the likelihood that secondary factors such as differences in motivation between the groups could lead to a false-positive finding of cerebral impairment. However, the likelihood of finding cerebral impairment in a group as select as medical or college students is small regardless of their level of cannabis use. Individuals with cerebral impairment are unlikely to perform as well as unimpaired individuals on standardized aptitude and achievement tests and other measures important for determining admission to college or medical school, and thus would have been selected out of the sample.

Preexisting Group Differences

Other variables provide some unique challenges in the study of the long-term effects of marijuana use. In general, many drug users tend to be transient, making it difficult to do repeated assessments. Many have a life-style that is not work oriented or competitive. Many resent authority figures. As a result, they may be poorly motivated and minimally cooperative during testing, which may produce spuriously low test scores. To the extent that they are isolated from society, they may fail to develop the knowledge and skill necessary for adequate performance on some of the tests. Many of these variables are difficult to control. In addition, lower educational levels, less prestigious occupations, and, in general, lower socioeconomic status are characteristic of adult heavy drug users. Since these variables are related to low scores on many performance measures, special care in selecting a matched control group should be taken.

Psychopathology may present a particularly difficult problem. Schizophrenics often score in the impaired range on neuropsychological measures (Golden, 1978). But often confirming evidence from other observations is lacking, suggesting that many of these low scorers are false positives. If the drug-using group shows more psychopathology than the control group, then drug use and psychopathology would be confounded. Any observed cerebral deficits in the drug users could be the result of either of these variables.

Preexisting group differences are particularly relevant in the cross-cultural studies. Poor nutrition and poor medical care in the cannabis users, and social class differences in the users and nonusers are common. Nonetheless, the cross-

cultural studies are particularly relevant since the users in these studies typically consume considerably more and stronger forms of cannabis than is typical of American users, and polydrug use is less frequent in these individuals. Although there are a number of problems with many of the cross-cultural studies, the majority of the experimental problems would bias the study in favor of finding neurological deficits that are a function of factors other than cannabis consumption. Factors such as poor nutrition and medical care in the users, social class differences, and use of toxic or possibly toxic substances to enhance the effects of the cannabis (such as tobacco, opium, arsenic, strychnine, and dhatura—a poisonous alkaloid) would bias the study toward finding performance deficits in the cannabis users. One problem that might tend to bias the results of the cross-cultural studies in the opposite direction is the selection of the assessment instruments. In many cases the instruments were simply adaptations of tests used in the United States, with little or no normative data on the culture being studied. In some cases items were modified to make the test more relevant to the culture being studied (e.g., Bowman and Pihl, 1973), but those modifications were usually made solely on the basis of face validity. Another problem is the use of tests which are incapable of detecting real differences between groups. Tests which are too difficult (producing a floor effect) or too easy (producing a ceiling effect) may not detect real group differences in performance (Satz, Fletcher, and Sutker, 1976). Pretesting can reduce the likelihood of floor or ceiling effects.

Acute and Withdrawal Effects

Yet another factor is the acute or withdrawal effects of drugs on performance. Unless this factor is controlled, any observed deficit in performance in users might be an acute effect with no long-term consequences. A fairly long period of abstinence is required for some drugs. For example, Hill and Belleville (1953) found continued impairment in fine motor coordination 18 days after the abrupt withdrawal from heavy barbiturate use. Although the behavioral effects of marijuana appear to be short term, tetrahydrocannabinol (THC), the active ingredient in marijuana, remains in fatty tissue for up to 2 or 3 weeks (Mirin and Weiss, 1983). Approximately half of brain tissue is such fatty tissue (Grinker and Sahs, 1966). If the marijuana users use any other drugs, including alcohol, it is necessary to rule out the acute effects of all possible drugs. Behavioral observation is not sufficient since most heavy drug users can easily hide the effects of intoxication (Grant and Judd, 1976). Two ways of dealing with this issue are (1) to routinely use blood and urine screening of all subjects, or (2) to hospitalize drug users as a way of limiting drug use for the duration of the study. Both are expensive and neither is used very often. None of the marijuana studies reviewed in this paper utilized laboratory screening procedures for drugs other than marijuana, and only one study (Schaeffer, Andrysiak, and Ungerleider, 1981) used such a procedure to screen for the presence of marijuana.

Experimenter Bias

A major problem in most studies, and one which could be handled easily, is experimenter bias. The issue of the effects of illegal drugs is as much a social and political concern as a scientific concern, and the current social climate can have many effects on experimenters which can shape their expectations (Zinberg, 1972). Although experimenter bias is known to affect outcome in many experiments (Rosenthal, 1966), the possibility of its occurrence has been virtually ignored in the drug abuse literature. In only one study reviewed (Bowman and Pihl, 1973) were the preconceptions of the investigator stated directly and the possibility of bias considered. A few studies did test their subjects blindly as a way to control experimenter bias, but this was definitely the exception. In two recent reviews of the literature on the chronic cerebral effects of drug use (Grant and Mohns, 1975; Kornblith, 1981), experimenter bias was not even mentioned.

Summary on Methodology

Some of the problems that have been discussed are almost unavoidable given the nature of the problem, the population under study, and the ethical prohibitions which exist against direct experimentation. Some others are easily remedied (e.g., testing blindly to reduce experimenter bias) while others can be effectively dealt with if carefully selected control groups are used. Some control procedures may not be needed at all if preliminary research suggests no differences between users and nonusers since the uncontrolled variables would have likely led to the opposite results. There are times when rigorous adherence to methodological procedures must be sacrificed because of practical considerations and budget constraints. However, some of the methodological errors found in these studies do not seem to be the result of deliberate compromise, but rather seem to stem from oversight or perhaps ignorance. Several studies compared subjects on dozens of measures and, not surprisingly, found a few of them significant. Their interpretation of these results seemed to overlook the possibility that the differences were simply chance events. Satz et al. (1976) have argued that in many of these studies utilizing a variety of measures, a multivariate analysis of the data would have been much more appropriate. Another common error is the overinterpretation of a single or multiple case study (Altman and Evenson, 1973). The major methodological issues described in this paper are summarized in Table 1.

Table 1

Methodological Issues in the Study of Cannabis Users

Characteristics of the subjects:	Polydrug use Differential vulnerability Secondary effects Degree of cannabis use Preexisting group differences
Experimenter factors:	Experimenter bias
Experimental factors:	Acute and withdrawal effects

ASSESSING CEREBRAL DYSFUNCTION

There have been two basic approaches to the study of chronic cerebral effects in drug users: the neurological approach and the psychological-neuropsychological approach. Each has its strengths and weaknesses, and several of the methodological concerns described earlier affect one approach more than the other.

Neurological Approach

In the neurological approach, one or some combination of the following is employed: mental status examination; neurological examination; laboratory tests on blood, urine, or cerebrospinal fluid; electroencephalography (EEG); evoked potentials; echoencephalography (ultrasound); and neuroradiological techniques including skull X-ray, radionuclide brain scanning and flow studies, angiography, pneumoencephalography, and computerized axial tomography (CAT scanning). Most of these assessment techniques require considerable judgment and experience for accurate interpretation. In addition, such techniques have far from perfect reliability and validity (Filskov and Goldstein, 1974; Tsushima and Wedding, 1979), although this is rarely considered in interpreting research which has used these tests to provide evidence of brain impairment in drug users.

The mental status examination consists of clinical observation and questions relating to memory, cognitive processes, judgment, and so on. Many factors other than cerebral impairment, including psychopathology, may influence the results. The questions are not standardized, rating is subjective, and the specific behaviors leading to the conclusions are often not described. Socioeconomic status, race, and age may affect the responses, but these variables are often not taken into account when rating. Responses may also be affected if the individual is experiencing acute or withdrawal effects of drugs.

Table 2

Neurological Findings Organized by Test

Measures	Studies
Neurological examination	Grant et al., (1973) Mayor's Committee (1943/1966) Mendelson et al. (1974) Rodin et al. (1970)
EEG	Karacan et al. (1976) Rodin et al. (1970) Rubin & Comitas (1975) Stefanis et al. (1977)
Echoencephalography	Stefanis et al. (1977)
Pneumoencephalography	Campbell et al. (1971)
CAT scan	Co et al. (1977) Kuehnle et al. (1977)

The neurological examination consists of an assessment of the cranial nerves, reflexes, gait, and so on. Again, rating is subjective since there are no clearly defined empirical norms taking age and other important factors into account.

Laboratory tests may be helpful in the diagnosis of certain neurological conditions, especially those involving infectious processes, but are insensitive to the presence of other conditions, especially disorders in the early stages of development. The EEG, skull X-ray, brain scan and flow study, evoked potentials, pneumoencephalogram, and angiogram are each useful in the diagnosis of only certain neurological disorders. In all of these tests, abnormal findings occur in some proportion of persons lacking other evidence of neurological disorder (false positives). This is particularly true of the EEG (Cobb, 1963; Mayo Clinic, 1963; Vick, 1976) and the pneumoencephalogram (Bull, 1971). Finally, some of these assessment techniques have a significant morbidity and mortality rate, and are thus not appropriate for routine research.

In the late 1970s the CAT scan was developed and rapidly replaced many of the previously discussed tests as a result of its noninvasiveness, increased accuracy, and informativeness. Both the reliability and the validity of the CAT scan are quite high if an experienced interpreter reads the record (Tsushima and Wedding, 1979). Contrast enhancement, which aids in the differentiation of the various types of tissue and fluid, can further increase the validity of the CAT scan.

The neurological techniques that have been described, with the exception of those that assess behavior (i.e., neurological and mental status examinations),

require no more than passive cooperation from the subject. Thus, an unmotivated subject will not present any particular problems in interpretation. Acute or withdrawal effects, psychopathology, or medication of any kind may affect the neurological or mental status examinations and the EEG but do not tend to affect the other tests. With the exception of the mental status examination, factors such as socioeconomic status and membership in a minority subculture should have a negligible effect. Table 2 lists each of the neurological techniques which have been used to investigate the cerebral effects of cannabis use and the investigators who have used them.

Neuropsychological Approach

The neuropsychological approach generally utilizes performance on standardized tests to determine the presence or absence of cerebral impairment. Over the years, there have been considerable changes in the particular tests used and in the signs on these tests thought to be indicative of cerebral impairment. Many of the earliest tests used for this purpose have been found to be invalid indicators of cerebral functioning (e.g., the Rorschach). Many other early tests were based on a unitary view of brain damage (e.g., the Bender Visual Motor Gestalt Test). Today, it is believed that there is no single deficit universally present in cerebral impairment and that proper assessment requires the examination of a wide range of cerebral functions (Golden, 1978). Tests from the unitary approach are now used as part of a comprehensive test battery. One such battery which has been widely used is the Halstead-Reitan Neuropsychological Battery, which has demonstrated reliability and validity comparable to the CAT scan when scored and interpreted by a trained neuropsychologist (Filskov and Goldstein, 1974; Schreiber, Goldman, Kleiman, Goldfader, and Snow, 1976; Swiercinsky and Leigh, 1979; Tsushima and Wedding, 1979). The Wechsler Adult Intelligence Scale (WAIS) and the Minnesota Multiphasic Personality Inventory (MMPI) are generally included in the battery as the WAIS can provide information on cognitive functioning and the MMPI can indicate the existence of factors such as psychopathology that may influence the test scores. For a more complete review of neuropsychological assessment, see Golden (1978) or Parsons and Prigatano (1978).

Neuropsychological testing relies on inferences from behavior to characterize the structural state of the brain. It is more vulnerable than neurological techniques to acute and withdrawal effects and to the effects of such variables as age, educational level, lack of motivation, and psychopathology. In particular, chronic schizophrenia frequently impairs performance on neuropsychological testing (Klonoff, Fibiger, and Hutton, 1970).

Neuropsychological testing can often detect the early stages of a neurological disorder, is sensitive to a wide range of etiologies, has no significant

Table 3

Psychological and Neuropsychological Findings Organized by Test

Type of measure and specific measures	Studies using the measure
Tests of intellectual functioning	
Ammons Full Range Vocabulary	Rubin and Comitas (1975)
Bhatia Battery of Intelligence	Agarwal et al. (1975)
General Aptitude Test Battery (portions)	Soueif (1976)
	Wig and Varma (1977)
Raven's Progressive Matrices	Grant et al. (1973)
	Schaeffer et al. (1981)
	Stefanis et al. (1977)
	Wig and Varma (1977)
WAIS (or portions)	Bowman and Pihl (1973)
	Carlin and Trupin (1977)
	Culver and King (1974)
	Mayor's Committee (1943/1966)
	Mendelson et al. (1974)
	Mendhiratta et al. (1978)
	Rubin and Comitas (1975)
	Satz et al. (1976)
	Schaeffer et al. (1981)
	Soueif (1976)
	Stefanis et al. (1977)
WISC (Indian adaptation)	Wig and Varma (1977)
Neuropsychological test batteries	
Halstead-Reitan (or portions)	Bowman and Pihl (1973)
	Carlin and Trupin (1977)
	Culver and King (1974)
	Grant et al. (1973)
	Mendelson et al. (1974)
	Rochford et al. (1977)
	Rubin and Comitas (1975)
	Satz et al. (1976)
	Schaeffer et al. (1981)
	Soueif (1976)
Tests of abstract reasoning and concept formation	
Embedded Figures	Bowman and Pihl (1973)
Wisconsin Card Sorting	Bowman and Pihl (1973)
Tests of attention and concentration	
Color Cancellation	Ray et al. (1978)
	Wig and Varma (1977)
Digits Backward	Ray et al. (1978)
Goal-Directed Serial Alternation	Grant et al. (1973)
Serial Arithmetic	Ray et al. (1978)
Symbol-Digit Modalities	Schaeffer et al. (1981)

(continued)

Table 3 (continued)

Type of measure and specific measures	Studies using the measure
Tests of memory	
Benton Visual Retention	Satz et al. (1976)
	Schaeffer et al. (1981)
Facial Recognition Memory	Satz et al. (1976)
Knox Cube	Bowman and Pihl (1973)
Paired Associates	Bowman and Pihl (1973)
Recognition	Mendhiratta et al. (1978)
Rey Auditory-Verbal Learning	Schaeffer et al. (1981)
Rey-Osterreith Complex Figure	Bowman and Pihl (1973)
Wechsler Memory Scale	Agarwal et al. (1975)
	Ray et al. (1978)
	Satz et al. (1976)
	Wig and Varma (1977)
Williams Memory Scale	Satz et al. (1976)
Tests of perceptuomotor and motor functions	
Benton Visual-Motor Gestalt	Agarwal et al. (1975)
	Mendhiratta et al. (1978)
	Rochford et al. (1977)
	Rodin et al. (1970)
	Soueif (1976)
	Wig and Varma (1977)
Card Rotation	Culver and King (1974)
Cube Comparisons	Culver and King (1974)
Graduated Holes	Rubin and Comitas (1975)
Hidden Patterns	Culver and King (1974)
Maze Steadiness	Rubin and Comitas (1975)
Minnesota Percepto-Diagnostic	Ray et al. (1978)
	Rochford et al. (1977)
Paper Folding	Culver and King (1974)
Pegboard	Rubin and Comitas (1975)
Pencil Tapping	Mendhiratta et al. (1978)
Pins	Bowman and Pihl (1973)
Reaction Time	Bowman and Pihl (1973)
	Mendhiratta et al. (1978)
	Soueif (1976)
Spatial Orientation	Culver and King (1974)
Speed and Accuracy	Mendhiratta et al. (1978)
Surface Development	Culver and King (1974)
Sensory-perceptual tests	
Distance Estimation	Soueif (1976)
Hooper Visual Organization	Schaeffer et al. (1981)
Laterality Discrimination	Culver and King (1974)
Time Estimation	Bowman and Pihl (1973)
	Mendhiratta et al. (1978)
	Rubin and Comitas (1975)

(continued)

Table 3 (continued)

Type of measure and specific measures	Studies using the measure
Sensory-perceptual tests:	
Time Estimation (continued)	Soueif (1976)
	Wig and Varma (1977)
Personality tests	
Lowenfeld Mosaic	Rubin and Comitas (1975)

medical risks, and provides direct information about behavioral deficits and assets. However, it may have a higher false-positive rate than most neurological techniques. In many ways, neurological and neuropsychological approaches are complementary, with different strengths and limitations. Unfortunately, there are few studies of marijuana (none of them recent) which utilize both techniques. Table 3 lists the various neuropsychological measures that have been used to evaluate the cerebral effects of cannabis and the investigators that have used them.

CHRONIC CEREBRAL EFFECTS OF MARIJUANA USE

Early Research

Until quite recently, little effort had been expended on understanding the effects of marijuana use. Over 80% of the published research on the chronic cerebral effects of marijuana has been conducted since 1970. However, to understand the context in which the current research is being conducted, one needs familiarity with early attempts to study the phenomenon.

The earliest known study of the effects of cannabis is that of the Indian Hemp Drugs Commission of 1893-1894, which had been commissioned by the British government to examine the physical, mental, and moral effects of cannabis use. The commission's report consisted of seven volumes and over 3,000 pages, but its findings have been virtually ignored by most researchers because so few copies of the report exist. In order to provide more access to this material, an article summarizing the findings (Mikuriya, 1968) and a book containing the commission's report while omitting many of the appendixes (Kaplan, 1969) have been published.

The Hemp Drugs Commission was a thorough attempt to study the effects of cannabis, especially considering the lack of auxiliary medical tests available at the time. The commission had no direct contact with the users and conducted very little experimentation. However, its members interviewed 1,193 individuals, including 335 physicians, and reviewed the records of all judicial

proceedings for the previous 20 years in which cannabis had been thought to be a factor in violent crimes. They also reviewed the records of every mental hospital in India and thoroughly studied the files on each of the 222 individuals admitted in 1892 with a possible connection between cannabis use and mental illness.

The commission concluded that the moderate use of cannabis produced no injurious physical, mental, or moral effects, while excessive use was likely to be harmful. This conclusion represented the commission's best guess given the general inadequacy of their data. The commission did not clearly define moderate and excessive use, although it seems likely that even their moderate use would be considered heavy consumption by today's standards. Regardless of amount of cannabis use, however, they found no evidence of residual central nervous system effects, although they readily admitted that their evidence was often inadequate (Kaplan, 1969).

The commission may have been thorough in its work, but it is not clear that it was completely unbiased. For nearly 100 years, opium from India had been a major item in the trade between Britain and China (Hyde, 1973; McCoy, Read, & Adams, 1972). In 1895, 1 year after the report of the Hemp Drugs Commission, the report of a commission on opium was published. Its conclusions about opium were the same as those reported for hemp: that the moderate use of opium was not harmful and that its growth need not be prohibited. The Opium Commission's conclusions may well have been influenced by Britain's vested interest in maintaining the opium trade (Owen, 1934). The Hemp Commission findings may have set the stage for the opium report released the next year.

The next reported study, also conducted in India, was carried out 45 years later (Chopra and Chopra, 1939). Chopra and Chopra examined 1,238 cannabis smokers using interviews, physical examinations, and in some cases, extended behavioral observations. They concluded that moderate use was not harmful to the central nervous system while excessive use did lead to impairment. In a reanalysis of their data 18 years later (Chopra and Chopra, 1957), they questioned whether even moderate use of marijuana might be harmful. However, several problems plagued this study. These included the likelihood of poor nutrition and infectious disease in the sample (it was noted that 2.5% had a "history" of syphilis), and a probable overrepresentation of social deviates since it was unlikely that productive members of a higher social class would be referred to the investigators by medical and local governmental personnel. In discussing long-term central nervous system changes, they primarily reported symptoms that could as readily have reflected psychopathology, such as lability of affect, impairment of judgment and memory, habitual lying, and insomnia. The authors did report that many subjects demonstrated preexisting "neurotic tendencies" but felt that cannabis had been responsible for enhancing

these tendencies. However, they presented no evidence to show that these individuals demonstrated less psychopathology before the onset of cannabis use.

The first study of the effects of marijuana on cerebral functioning conducted in the United States was carried out by the Mayor's Committee on Marijuana, more commonly referred to as the La Guardia Commission, which studied both the medical and psychological consequences of marijuana use (Mayor's Committee on Marijuana, 1943/1966). They studied 72 prison inmates, including 48 users, most of whom were under 30 years of age. User and nonuser subjects were given the Bellevue Adult Intelligence Test before and after the administration of various amounts of marijuana. Although there was a difference in mean score (97 for the user group and 104 for the nonuser group), the investigators felt that this difference could be accounted for by racial and cultural factors since the cannabis group contained a much larger proportion of Black and Puerto Rican subjects who often do more poorly on standardized tests. In addition, the general lack of subtest scatter in the user groups was considered evidence against cannabis-produced cognitive deterioration. More recent research suggests that neither intersubtest scatter nor deterioration in intelligence scores is characteristic of all types of cerebral impairment. Thus their conclusion that marijuana use does not seem to result in impairment appears premature.

In some ways, the La Guardia Commission was a forerunner of the modern marijuana studies. A smaller sample size was used with systematically gathered dependent variables measured for each subject. The conclusions were more clearly data based than in most of the other early studies. In general, the methodology was more in keeping with the empiricism and experimental control characteristic of modern Western science.

Benabud (1957) represents the last of the early marijuana studies. He studied 824 individuals who had been hospitalized for cannabis "addiction," although it was possible that there were additional reasons for their hospitalization. He expressed the opinion that cannabis itself produced a toxic effect which acted as a precipitant for psychosis or dementia, although again, it is not clear that this opinion is based on data.

These early research studies are summarized in Table 4.

Modern Neurological Approaches

Cerebral Atrophy

In the early '70s, a renewed interest in both the short-term and long-term effects of marijuana occurred, partly as a result of the increased use of the drug among high school and college-age subjects. One of the first reported studies, and also one of the most widely quoted, was conducted by Campbell, Evans, Thomson, and Williams (1971). They were the first to link cannabis smoking and

Table 4

A Summary of Early Research on the Effects of Cannabis Use

Author (year) [country]	Sample size and type: user/controls	Findings and comments
Indian Hemp Drugs Commission (1893-1894) [India] Mikuriya (1968); Kaplan (1969)	Medical and government data: ?/0	Moderate cannabis use produces no harmful physical, mental, or moral effects, while excessive use may be deleterious. Based on interview data (N = 1,193) and a review of judiciary and hospital records.
Chopra and Chopra (1939) [India]	"Known addicts": 1,238/0	Moderate use is not harmful to the CNS, while excessive use is harmful. Based on interviews and physical examinations.
Chopra and Chopra (1957) [India]	Mental patients: 600/0	Moderate use may be harmful to the CNS. Based on a study of mental hospital records.
Mayor's Committee (1943/1966) [USA]	Prison inmates: 40/20	A 7-point IQ difference between users and controls was found, but the difference was attributed to racial and cultural differences between the groups.
Benabud (1957) [Morocco]	Mental patients: 824/0	Cannabis may precipitate psychosis or even dementia. Based on interviews and mental hospital records.

cerebral atrophy. They administered pneumoencephalograms (a radiological procedure in which air is used to display the size and position of the cerebral ventricles) to 10 males between the ages of 18 and 28 who used marijuana consistently (not defined). Their results were compared with the pneumoencephalograms of persons of similar age who had been diagnosed as neurologically normal. They noted that all 10 of the marijuana users demonstated cerebral atrophy as determined by enlargement of the lateral ventricles.

However, a number of methodological flaws limit the conclusions that might be drawn from this study. First, the researchers may have been biased since they consistently referred to the users as "addicts," a term with a negative connotation which is generally not used in recent publications to describe marijuana users. The investigators did not report whether the pneumoencephalograms were interpreted blindly, making the bias issue that much more critical. Neither the user nor the control groups were randomly selected. The first four users were known to have abnormal pneumoencephalographic results (the study had been originally undertaken because of these findings), and the others were under psychiatric treatment for drug abuse. The controls were chosen from existing files on the basis of vague neurological complaints with a normal pneumoencephalogram. Thus, they were not actually control subjects, but rather provided a standard by which to compare the results from the users.

Alternative explanations for the cerebral atrophy were ignored by Campbell et al. (1971). For example, all 10 of the marijuana users were in fact polydrug users. All had taken LSD at least once, a few had used barbiturates and intravenous morphine, and seven had admitted the use of amphetamines. In some subjects, other drugs were used at least moderately often, but the investigators dismissed this polydrug use because the subjects used these drugs less often than they used marijuana and because the drugs were more rapidly metabolized than marijuana. In addition, all showed some evidence of psychopathology (Evans, 1974) and 3 of the 10 marijuana-using subjects had histories of head injury. In at least one subject, epileptic seizures began to occur following the injury. However, the investigators also discounted the head injuries as being too minor to result in cerebral atrophy.

A storm of articles followed the publication of the Campbell et al. (1971) study, most of which were critical of the methodology and/or conclusions (Brewer, 1972; Bull, 1971; Cannabis encephalopathy? 1971; Grinspoon 1972; Susser, 1972). However, Campbell et al. (1971) were not without their supporters who felt that "their evidence is amply sufficient to justify the continuation and strengthening of every possible measure to suppress cannabis" (Nattrass, 1971, p. 1314) and that cerebral impairment in cannabis users could also be observed through mental status examinations (Schwarz, 1972). In a second paper, Campbell, Thomson, Evans, and Williams (1972) attempted to justify their procedures and refute earlier criticisms, but their article failed to address the major criticisms of their earlier study.

Because of the risks associated with pneumoencephalography, the Campbell et al. (1971) study was never replicated. However, the development of the CAT scan in the late 1970s, which is painless and noninvasive, enabled investigators to safely test the findings of Campbell et al. Furthermore, the CAT scan is considerably more sensitive and valid than the pneumoencephalogram.

In two separate studies (Co, Goodwin, Gado, Mikhael, and Hill, 1977; Kuehnle, Mendelson, Davis, and New, 1977), the CAT scans of 31 marijuana-using subjects studied were all judged to be normal. These findings are particularly striking since in both studies, the marijuana users were predominantly polydrug users. While a normal CAT scan does not completely rule out the possibility of cerebral impairment, it is less likely than other neurological techniques (such as the pneumoencephalogram) to produce false negatives.

Thus, in spite of the Campbell et al. (1971) report, there seems to be no reason to believe that cannabis use results in cerebral atrophy. Although Campbell et al. is still widely quoted in some circles, its findings have not withstood replication efforts. Since significant cerebral atrophy invariably results in pronounced emotional, behavioral, perceptual, or cognitive deficits, it hardly seems possible that Campbell et al. could have been correct. If they had been correct, our mental and neurological hospitals would be filled with cannabis smokers, given the relatively wide use of the drug today (Zinberg, 1972).

Other Neurological Findings

A variety of other neurological approaches have been employed to study the effects of cannabis smoking. Several investigators found the EEG records to be normal in cannabis users (Karacan, Fernández-Salas, Coggins, Carter, Williams, Thornby, Salis, Okawa, and Villaume, 1976; Rodin, Domino, and Porzak, 1970; Rubin and Comitas, 1975; Stefanis, Dornbush, and Fink, 1977). All but one of those studies (Rodin et al., 1970) were cross-cultural, with users who were long-term, very heavy smokers. The typical cross-cultural study evaluated the cerebral functioning of users who smoked cannabis daily for several years. Stefanis et al. (1977) found no differences between users and nonusers on echoencephalograms, a technique described by the investigators as "a method of estimating ventricular size by a reflection of ultrasound signals" (Stefanis et al., 1977, p. 61). Mendelson, Rossi, and Meyer (1974) reported the only positive finding based on a neurological examination—a lateral gaze nystagmus which was present before, during, and after consumption of marijuana. However, these investigators did not have a nonuser comparison group. Rodin et al. (1970) found no abnormalities on either the mental status or neurological examinations for any of the 10 marijuana smokers in their study. However, their findings are hardly surprising since their subjects were first-year medical students

Table 5

A Summary of Neurological Studies on the Effects of Cannabis Use

Author (year) [country]	Sample size and type: users/controls	Findings and comments
Campbell et al. (1971) [Great Britain]	Neurology and drug abuse outpatients: 10/?	Users were administered pneumoencephalograms and all demonstrated cerebral atrophy indicated by enlarged ventricles. The control group was biased.
Co et al. (1977) [USA]	Paid volunteer users: 12/34	All subjects were found to have normal CAT scans. The control group was biased.
Kuehnle et al. (1977) [USA]	Volunteer users: 19/?	All subjects were found to have normal CAT scans.
Rodin et al. (1970) [USA]	Medical students: 10/0	All subjects demonstrated normal scores on EEG and on neurological and mental status examinations.
Karacan et al. (1976) [Costa Rica]	Heavy users: 32/32	No significant differences were found on sleep EEGs.
Rubin and Comitas (1975) [Jamaica]	Heavy users: 30/30	No significant differences were found on EEGs.
Stefanis et al. (1977) [Greece]	Heavy users: 47/40	No significant differences were found on EEGs or on echoencephalograms.
Mendelson et al. (1974) [USA]	Volunteer users: 20/0	Neurological examination of all users showed lateral gaze nystagmus before, during, and after ingestion of cannabis.
Grant et al. (1973) [USA]	Med students: 29/29	No differences found on neurological examination.

who had recently competed successfully for entrance into medical school. Kolansky and Moore (1971, 1972a, 1972b) did suggest that case study data from their psychoanalytic practice linked cannabis use with psychopathology and with cerebral impairment. However, unlike most of the other studies reviewed in this section, they had no control group and they did not use standard neurological measures in their diagnoses. Therefore, it is difficult to evaluate their contention.

Summary on Research Findings

The research reviewed in this section is summarized in Table 5. The available evidence suggests strongly that there are no gross structural or neurological deficits in marijuana-using subjects, although subtle neurological features (such as lateral gaze nystagmus) may be present. However, the type of deficit most likely to occur would be a subtle, functional deficit which could be assessed more easily with either psychological or neuropsychological assessment techniques. In Part II of this paper (Wert and Raulin, 1986), the research on the long-term effects of cannabis on psychological and neuropsychological functioning is reviewed.

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The Chronic Cerebral Effects of Cannabis Use. II. Psychological Findings and Conclusions

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Abstract

This paper examines the research evidence on the question of whether sustained use of marijuana may produce chronic cerebral impairment as measured by neuropsychological measures. Evidence from both American and cross-cultrual studies suggests that marijuana probably does not produce chronic cerebral impairment, although subtle impairment cannot be ruled out. Several suggestions for new lines of research are discussed including prospective studies, effects of cannabis use on later aging processes, and true experimental studies.

Mind-altering substances have been used and abused throughout history, and their abuse continues to be a major social problem. Research to uncover the risks involved in using drugs is needed if we are to establish reasoned policy on how to regulate these substances. In the first paper of this series (Wert and Raulin, 1986), we discussed some of the problems in studying the chronic cerebral effects of a drug such as cannabis and reviewed the neurological studies conducted to date. In this paper we review the psychological and neuropsycho-

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logical findings on the long-term effects of cannabis and suggest some directions for future study.

MODERN PSYCHOLOGICAL AND NEUROPSYCHOLOGICAL APPROACHES

A number of psychological and neuropsychological studies of the long-term effects of marijuana, including several cross-cultural studies, have been reported. Fifteen studies of the chronic cerebral effects of cannabis have used psychological and neuropsychological assessment measures with varying results. Of the nine cross-cultural studies (Agarwal, Sethi, and Gupta, 1975; Bowman and Pihl, 1973; Mendhiratta, Wig, and Verma, 1978; Ray, Prabhu, Mohan, Nath, and Neki, 1978; Rubin and Comitas, 1975; Satz, Fletcher, and Sutker, 1976; Soueif, 1976; Stefanis, Dornbush, and Fink, 1977; Wig and Varma, 1977), five found some evidence for impairment in the cannabis-using group. However, a closer inspection of the studies suggests that the evidence may not be as strong as these numbers might suggest.

Agarwal et al. (1975) claimed to have found evidence of impairment on three psychological tests (Weschler Memory Scale, Bender Visual Motor Gestalt, and Bhatia Battery of Intelligence) in 40 Indian cannabis users. No control group was used. However, on at least two of these tests, the proportions of scores in the "impaired" range as reported by the investigator are almost exactly what would be expected in a random sample from the general population. On the Bender, nearly half of the subjects received low scores, but without a comparison group it is impossible to determine whether this finding was abnormal for their population.

Stefanis et al. (1977) found four statistically significant differences on WAIS subtests between 47 Greek cannabis users and 41 controls. However, only one of these differences was on a subtest thought to be sensitive to cerebral functioning (Digit Symbol) while the others were on verbal subtests less sensitive to cerebral deficit.

Wig and Varma (1977) studied 27 Indian cannabis users and 11 controls on a number of tests including the EEG, Raven Colored Progressive Matrices, Bender Visual Motor Gestalt, and Indian adaptations of the WISC and the Weschler Memory Scale. Users performed significantly more poorly on 4 of the 8 psychological tests. Interestingly, Satz et al. (1976) found no differences between their 41 cannabis users and 41 controls on a very similar battery, and Rubin and Comitas (1975) found only three differences on a very large battery of similar tests.

Soueif (1976) studied nearly 1,700 incarcerated Egyptian cannabis users and controls, using a wide range of psychological tests (Tool Matching, Marking, Trail Making, Reaction Time, Digit Span, Distance and Time Estimation,

and Bender Visual Motor Gestalt). He found that cannabis users performed significantly more poorly on 10 of the 16 measures. However, the differences were very small and significant primarily because of the extreme statistical power associated with such large sample sizes. They did not seem to reflect clinically significant differences. In addition, place of residence (rural vs urban) and degree of literacy were found to affect test scores at least as much as cannabis use. Finally, the test battery was heavily skewed toward tests of attention, concentration, and psychomotor speed; scores on these tests are heavily influenced by variables such as anxiety, psychopathology, lack of motivation, and acute drug effects (although subjects presumably had little access to drugs since they were incarcerated).

Mendhiratta et al. (1978) also administered a battery consisting primarily of tests of attention, concentration, and motor speed to 50 Indian cannabis users (25 of whom used less potent cannabis) and 25 controls. Groups were matched on age, sex, occupation, education, and level of psychopathology. They reported that one or both of the user groups scored more poorly than controls on 7 of the 9 measures. The authors concluded that chronic cannabis use may lead to deficits in concentration and attention. However, either acute effects (which were not considered) or motivational differences could have accounted for the obtained results.

It is interesting that Ray et al. (1978), using a test battery similarly skewed toward tests of attention, concentration, and motor speed, found only one significant difference between the groups of 30 Indian cannabis users and 50 controls. Ray et al. included a much smaller proportion of illiterate subjects in their sample than Mendhiratta et al.

Bowman and Pihl (1973) found no differences between 30 Jamaican cannabis users and 24 controls on a battery of tests despite the presence of a greater proportion of illiterate subjects in the user groups. The Bowman and Pihl study is distinguished by the use of several techniques to improve the validity of the findings, including a replication of the findings, an attempt to test subjects blindly, and the use of a monetary payment to increase subject motivation.

None of the studies conducted in the United States (Carlin and Trupin, 1977; Culver and King, 1974; Grant, Rochford, Fleming, and Stunkard, 1973; Mendelson, Rossi, and Meyer, 1974; Rochford, Grant, and La Vigne, 1977; Schaeffer et al., 1981) demonstrated statistically significant differences between cannabis users and controls. Rodin, Domino, and Porzak (1970) reported that cannabis users demonstrated "significantly" poorer Bender Gestalt performance (although still within the normal range) than non-drug users. We did not include this study because no results of statistical tests or even means were given, nor was there a mention that any statistical procedures had been performed. We can only conclude that they used the term "significantly" as a figure of speech rather than in the usual sense of *statistical significance.* Culver and King (1974)

Table 1

A Summary of the Psychological and Neuropsychological Studies of the Effects of Cannabis Use

Author (year) [country]	Sample size and type: users/controls	Findings and comments
Agarwal et al. (1975) [India]	Clients of cannabis shop: 40/0	Half of the subjects had abnormally high Bender Gestalt scores; 20% scored in the impaired range on the Wechsler Memory Scale; 25% had IQs < 90.
Bowman and Pihl (1973) Study 1 [Jamaica]	Volunteers with 10+ yr of cannabis use: 16/10	No significant differences between users and nonusers were found on the Embedded Figures, Paired Associates, Wisconsin Card Sorting, Finger Tapping, Digit Span, and Block Design.
Bowman and Pihl (1973) Study 2 [Jamaica]	Same as above: 14/14	The same tests as above were used, plus Time Estimation and Rhythm Tests. Again, no significant differences were found.
Mendhiratta et al. (1978) [India]	Volunteers with 4+ yr of cannabis use: 50/25	Tests used were Digit Span, Design Recognition, Tapping, Design Cancellation, Time and Size Estimation, Word Association, and Bender Gestalt. Users did more poorly on all tests except Digits Forward and Design Cancellation.
Ray et al. (1978) [India]	Rural males; 25% of each group were illiterate: 30/50	Tests used were Backward Digit Span, Serial Addition and Subtraction, Color Cancellation, Minnesota Perceptodiagnostic Test, and the Wechsler Memory Scale. Users scored significantly higher on 1 of the 10 subtests of the Wechsler Memory Scale.
Rubin and Comitas (1975) [Jamaica]	Paid volunteers with 10+ yr of cannabis use: 30/30	Only three significant differences found on a large number of tests including Ammons Vocabulary, Lowenfeld Mosaic, Maze Steadiness, Graduated Holes, Pegboard, and portions of the WAIS and the Halstead-Reitan Battery.
Satz et al. (1976) [Costa Rica]	Volunteers with 10+ yr of cannabis use: 41/41	No significant differences between users and nonusers were found on the WAIS, Benton Visual Retention, Williams Memory, Facial Recognition, Finger Localization, Finger Tapping, and Tactual Performance tests.
Soueif (1976) [Egypt]	Prison inmates: 850/839	Tests used were Tool Matching, Marking, Trail Making, Reaction Time, Digit Span, Distance and Time Estimation, and Bender Gestalt. Significant differences were found on 10 of the 16 measures with cannabis users scoring more poorly.
Stefanis et al. (1977) [Greece]	Volunteers with 10+ yr of cannabis use: 47/40	Gave WAIS and the Raven Progressive Matrices. Differences were found on Verbal IQ, Comprehension, Similarities, and Digit Symbol subtests.
Wig and Varma (1977) [India]	Volunteers with 5+ yr of cannabis use: 23/11	Cannabis users performed more poorly on WISC, Wechsler Memory, GATB Speed, Time Perception, and Bender Gestalt. No differences were found on Raven Colored Progressive Matrices or Color Cancellation.
Carlin and Trupin (1977) [USA]	Volunteers with 2+ yr of cannabis use: 10/10	Tests used were WAIS and Halstead-Reitan Battery. Controls were taken from Reitan's normative population. The control group did worse on Part B of the Trail Making Test.
Culver and King (1974) Study 1 [USA]	College seniors: 14/14	No significant differences between users and nonusers were found on Laterality Discrimination, the WAIS, Cube Comparison, Hidden Patterns, Paper Folding, and the Halstead-Reitan Battery.
Culver and King (1974) Study 2 [USA]	College seniors: 14/14	Tests were the same as above, plus Card Rotation, Spatial Orientation, and Surface Development. No significant differences were found between users and nonusers. Users were only casual users.
Grant et al. (1973) [USA]	Med students: 29/29	Tests used were Raven Advanced Progressive Matrices, Serial Alteration, and portions of the Halstead-Reitan Battery. Users did more poorly on the Location score of the Tactual Performance Test. Subjects were light cannabis users.

(continued)

Table 1 (continued)

Author (year) [country]	Sample size and type: users/controls	Findings and comments
Mendelson et al. (1974) [USA]	Volunteers with 2+ yr of cannabis use: 20/0	Tests included the WAIS and portions of the Halstead-Reitan Battery. No significant differences between casual and heavy users. Upon clinical examination, 2 heavy and 2 casual users showed impairment.
Rochford et al. (1977) [USA]	Med students: 26/25	No significant differences were found on Tactual Performance, Minnesota Perceptodiagnostic Test, and Bender Gestalt. Subjects were light cannabis users.
Schaeffer et al. (1981) [USA & unspecified Caribbean island]	Religious users of cannabis: 10/0	No evidence of impairment using the tests' published norms were found on the Benton Visual Retention, Trail Making Test, portions of the WAIS, Rey Auditory-Verbal Learning, Raven Progressive Matrices, Symbol-Digit Modalities, and Hooper Visual Organization.

conducted two studies with a total of 28 cannabis users and 28 controls, plus a group of LSD users, all of whom were college students. While there were some significant differences between LSD users and other groups, there were no differences between the cannabis users and controls on any of the measures. However, due to the inappropriate use of analysis of covariance (Lord, 1967) to minimize the effects of group differences in alcohol consumption, the results of their second study should be interpreted cautiously.

Carlin and Trupin (1977) compared 10 cannabis users to 10 members of Reitan's normative sample (Reitan, 1966) who had been tested a number of years earlier on the WAIS and portions of the Halstead-Reitan Battery. Clearly, this is not an adequate control group. Still, there were no statistically significant differences between the groups. Rochford et al. (1977) found no performance differences between 26 cannabis users and 25 controls, all of whom were medical students. Similarly, Grant et al. (1973) found only one difference among a large number of tests using medical students as subjects. Mendelson et al. (1974) found no differences between casual and heavy users of cannabis on a variety of neuropsychological measures.

Schaeffer et al. (1981) found and tested what might be considered an ideal experimental group: 10 members of a religious organization in which regular cannabis use was a part of their religious beliefs. Their subjects reported smoking cannabis virtually every waking moment, which was borne out by the observation of cannabis use during the test administration. In many studies, cannabis users were polydrug users and social deviants, often rebellious, resentful of authority, and unmotivated to perform on the basis of the usual social incentives. However, the cannabis-using subjects of Schaeffer et al. denied the use of alcohol and other drugs, and were described as productive members of society, thus minimizing the confounding effects of these variables. Unfortunately, Schaeffer et al. neglected to include a control group.

The following tests were administered: Benton Visual Retention, Trail Making, portions of the WAIS, Rey Auditory-Verbal Learning, Raven Progressive Matrices, Symbol-Digit Modalities, and Hooper Visual Organization. Despite the likelihood of acute drug effects, subjects' performances were not impaired when compared with the tests' published norms. In fact, mean WAIS scores indicated performance in the superior to very superior range.

Schaeffer et al. (1981) were the only investigators who attempted to estimate precannabis performance of their subjects for comparison with the present performance. They obtained early school achievement test scores for two of their subjects and compared the IQ conversion scores of these early tests with the subjects' present WAIS scores. No significant differences were found. While this use of achievement test scores provides only a rough estimate of the subjects' precannabis level of performance, it is a practical way of collecting information which otherwise would require a prospective study. In addition, Schaef-

fer et al. were the only investigators to use a laboratory test to detect recent marijuana ingestion. The use of this test in studies with positive results (i.e., impairment in cannabis users) would have been helpful in ruling out acute effects as the cause of the impairment.

Studies of the psychological and neuropsychological performance of cannabis users are summarized in Table 1.

Summary. Despite the large number of factors biasing most of these studies toward finding impairment in cannabis users (acute effects, polydrug use, poor nutrition, poor medical care, differences in literacy, etc.), only 1 (Wig and Varma, 1977) of the 15 studies found differences which could not be easily explained by these uncontrolled factors. One would expect a larger number of these studies, especially the cross-cultural studies using very heavy, long-term cannabis users, to have shown positive results if cannabis use indeed did produce cerebral impairment.

DISCUSSION

We have seen that the majority of studies have found no clinically or statistically significant differences between groups of cannabis users and controls on commonly accepted neurological and psychological measures of cerebral functioning. This finding is all the more impressive given the number of other variables (such as polydrug use, low motivation, and acute effects) which bias the results toward finding impairment in cannabis-using subjects.

This general finding of no clinically significant differences between cannabis users and controls may be interpreted in several ways. One possibility is that cannabis does not lead to chronic cerebral impairment. A second possibility is that cerebral deficits do develop but that the individual adapts and overcomes them through a process of relearning. It is well known that a chronic or slowly developing lesion will often be masked by the adaptation of the patient to the deficits produced by the lesion (Golden, 1978). A third possibility is that while the vast majority of cannabis-using subjects are not impaired, there may be a very small number of users who are vulnerable to cannabis-produced impairment. Such a possibility could explain the positive findings of a few studies: Perhaps such studies used a larger proportion of vulnerable subjects. The possibility of differential impairment is an interesting one and is discussed later in this section. Fourth, it is possible that cerebral impairment does exist in the cannabis-using subjects, but that the tests are not sensitive enough to detect it. However, given that these same tests have demonstrated impairment in alcoholics (for reviews, see Bolter and Hannon, 1980; Kleinknecht and Goldstein, 1972; Parsons, 1977; Parsons and Leber, 1981; Ron, 1977; Tarter, 1975; Wilkinson, 1982) and heavy social drinkers (MacVane, Butters, Montgomery, and Farber, 1982; Parker, Birnbaum, Boyd, and Noble, 1980; Parker and Noble, 1977, 1980), this does not seem likely.

Directions for Future Research

Virtually all of the studies reviewed in this paper fit into a single research mold. They are all retrospective studies of preestablished groups (cannabis users and non-cannabis users). Although some of the studies made a commendable attempt to obtain suitable control subjects, this is still a very weak and vulnerable research design. In the remainder of the paper, we propose some alternative research designs and discuss their potential usefulness.

Prospective Studies

The greatest weakness of a retrospective study of preexisting groups is that one is never sure if observed differences between the groups are the result of the defining characteristic (in this case, cannabis use) or whether the differences existed prior to any cannabis use. While the experimenter may try to match users and controls on relevant variables, many times the relevant variables are not known or cannot be controlled for or matched. The prospective study, which uses the subject as his or her own control, is a sound method of dealing with many of the issues that cloud retrospective studies. For example, the possibility that cannabis users would have demonstrated poorer performance even before their use of cannabis is eliminated with this design. The notion that impairment might predate drug use has been expressed by some authors with respect to alcoholism (see Parsons and Leber, 1981, and Tarter, 1975, for reviews), although there has been little research to support or refute this hypothesis as yet.

Prospective studies have been recommended by a number of authors (Culver and King, 1974; Rochford et al., 1977; Wig and Varma, 1977; Institute of Medicine, 1982), although these authors have generally failed to address the complexities of such studies. Prospective studies are extremely expensive since a large number of people must be tested (to assure a large enough group of later cannabis users) and followed for a long period of time. The likelihood of maintaining a continuous funding source over such a long period of time is slim. Furthermore, a prospective study does not automatically deal with many of the experimental problems described earlier in this paper. The investigator would still need to control for variables such as polydrug and alcohol abuse, motivational differences, and acute and withdrawal effects. A prospective study, although it does assess precannabis performance, cannot in itself avoid the methodological issues inherent in research in this area.

There is one area where prospective studies could contribute a great deal to our understanding of possible chronic cerebral effects of cannabis. Prospective studies would be one of the few ways to adequately test the hypothesis of differential vulnerability in cannabis users. Such a hypothesis has been raised by a few authors (Carlin and Trupin, 1977; Jones, 1980). It might well be that some

individuals are predisposed to cerebral impairment as the result of cannabis use, either because of structural or biochemical characteristics which accentuate the possible damaging effects of the drug, or because they have little of the "cerebral reserve" that most of us call on when we experience mild cerebral damage. That functional reserve can mask very real cerebral damage (Weiss, 1975). By having pre- and postcannabis performance scores for subjects, we can identify those subjects (if they exist) who show real impairment in functioning. By comparing those subjects who show impairment with those subjects who do not show impairment, we may be able to identify possible risk factors.

In our opinion, the results of the studies we have reviewed do not provide sufficient evidence of impairment to warrant the investment of time and money required for prospective studies. For those interested in ruling out previous impairment, we recommend the use of information that has already been gathered for other purposes such as school achievement or intelligence test scores or preinduction achievement testing for the Armed Forces. We agree with Schaeffer et al. (1981) that such information provides only a rough estimate of precannabis performance, but it would not appear to be cost-effective to gather more precise information through a prospective study. Indeed, a more worthwhile study might be to compare performance on such achievement tests with performance on neurological and psychological tests of cerebral functioning to determine just how "rough" such an estimate really is.

Studying the Effects of Cannabis on the Aging Process

Almost all of the studies reported in this paper used relatively young subjects. Of the 28 studies reviewed, 17 did not include a single subject over the age of 58. In the remaining 11 studies, either the age range was not given or the vast majority of the subjects were under the age of 60. While in most studies the lack of older subjects seemed to be a result of the population the investigators chose to study (students, volunteers recruited through street people, etc.), in at least one study (Agarwal et al., 1975) elderly people were excluded purposely to eliminate the possibility that any impairment seen in subjects was a consequence of aging.

We would like to suggest that the elderly may be the ideal population to investigate the chronic cerebral effects of cannabis use (Smith & Sethi, 1975). This approach has been used successfully in the study of cerebral effects of alcohol use (Blusewicz, Dustman, Schenkenburg, and Beck, 1977; Blusewicz, Schenkenburg, Dustman, and Beck, 1977). The data reviewed in this paper suggest that there are few if any detectable, long-term cerebral effects of cannabis use in young and reasonably healthy individuals. It is reasonable to conclude that any chronic effects that might result from the use of the drug are easily masked by the normal "cerebral reserve." However, the normal aging process

slowly erodes both our functional reserve and, in time, even our primary functional abilities. Chronic cerebral dysfunction is likely to become more noticeable in individuals experiencing additional cerebral deterioration. Thus, a premature intellectual deterioration (senility) might well be expected in long-term cannabis users if cannabis produces even subtle cerebral deterioration. So far, no one has investigated this possibility. Such a study would not be easy since a 60- to 70-year lifetime allows ample opportunity for numerous confounding variables to also affect cerebral functioning. Large sample sizes and some matching of samples on variables known to have chronic cerebral effects would be necessary. However, if any population is likely to show the results of a subtle cerebral impairment, it is likely to be a population of older citizens. Another reason for studying the possible effects of cannabis use on aging is that modern medicine is extending the life expectancy of people. As more people live longer, any variable which increases the level of dysfunction of the elderly will further strain our health care system.

Is It Time to Consider an Experiment?

All of the studies reviewed in this paper used a pseudoexperimental design in which preexisting groups (cannabis users and nonusers) were compared on measures of their cerebral functioning. Any research methods text will describe the weaknesses of such a design. Getting pretest measures (as in a prospective study) strengthens the design somewhat, but there are still numerous confounding variables which could affect the results. The alternative of conducting a true experiment where subjects are randomly assigned to the groups (cannabis users and nonusers) has not been an ethically responsible choice available to investigators. However, it may be time to reconsider the alternative of a true experiment.

We recognize that suggesting an experimental test of the chronic effects of cannabis is controversial, and we want to make it clear that we do not feel that such a test is warranted yet. But if further research were to show little or no effects in vulnerable populations such as the elderly and if the risks to other body systems are shown to be minimal, a carefully designed and executed experiment might add a great deal to our understanding of the long-term effects of cannabis use.

Summary

In this paper we have tried to review the available research on the chronic cerebral effects of cannabis use with a particular focus on methodological issues. Our general conclusion is that the current research does not support the contention that cannabis use results in chronic cerebral impairment. The possibility still

remains that such impairment exists, but it is likely to be either quite subtle or apparent in only a select group of vulnerable subjects. Those studies which did find cerebral effects were either fatally flawed [as in the Campbell et al. (1971) study] or biased in the direction of finding performance differences. For each study where significant impairment was found, several other studies with apparently equal methodological rigor found no impairment.

Any conclusion drawn from the studies reviewed here must be considered tentative because of the limitations inherent in the retrospective design. Although it may be possible to improve on many of the currently available studies in terms of methodology, it would probably make little difference in the conclusions we would draw. Therefore, we have chosen to focus our discussion on new directions for research using alternative designs and/or populations. We do not believe that more retrospective studies, even if they use the finest methodology available, are warranted given the data already available.

The issue of cannabis use is a highly emotional topic with serious political overtones. However, the fact remains that in spite of the illegal status of the drug, its use is widespread. To the extent that potential health risks exist, we have a continuing responsibility to identify them and communicate that information to those affected. Even though the current research does not suggest a risk for cerebral impairment, there are still some areas that have not been adequately investigated. Furthermore, there are areas of risk (e.g., cerebral effects of cannabis use by young children) which have received virtually no study. Now may be the best time to refocus our research efforts and explore these questions.

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THC-negative (No. = 10) (%)
10
0
50
20
20
50
50

produced little change in our results.
is raised by the possibility that
influenced the risk of spontaneous
ult that users who carried long enough
as ours were unrepresentative of users
to interpret the lack of any important
ifferences between the groups as argu-
n that such a phenomenon was respon-
nces observed in labor and neonatal
investigation of this issue is beyond the
owever.
small numbers involved in our study,
is a severe problem. Many differences
by chance alone we might expect statis-
fferences to emerge even if marijuana
observed differences are consistent in
Because of the small size and other limi-
we caution that accurate assessment of
uana use during pregnancy must await
tudies. Such studies will require extreme
duct, and analysis.

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Epidemiology—Principles and

Marihuana Use by Pregnant Women and Effects on Offspring: An Update

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FRIED, P. A. *Marihuana use by pregnant women and effects on offspring: An update.* NEUROBEHAV. TOXICOL. TERATOL. 4(4) 451–454, 1982.—This report is based on a previously described sample of 291 mothers-to- d on an additional 129 subjects. Among these 420 predominantly middle class pregnant women, approximately 3 , cent used marihuana regularly during pregnancy. For assessing the effect of marihuana on pregnancy variables and the offspring, the mothers-to-be were matched in terms of nicotine and alcohol use. Marihuana use was associated with a shorter gestation period and a decreased maternal weight gain. No effect on birth weight, length of labor or difficulty in birth were observed. Consistent with the earlier report, babies born to women who smoked more than five joints per week during pregnancy demonstrated marked tremors and startles and altered visual responsiveness at 2–4 days of age. These symptoms had attenuated by 30 days and no developmental impairments were observed in any of seven babies who had reached one year of age born to women who had smoked 2 joints or more per week during pregnancy.

Marihuana Pregnancy Development Neurobehavior

THE present report is a brief update of aspects of an ongoing study started in 1978 involving the department of Psychology of Carleton University and the Ottawa Civic and Ottawa General hospitals. The purpose of the investigation is to examine, in a prospective fashion, the pattern of use of social levels of alcohol, cigarettes and marihuana during pregnancy and the effects of these drugs on the offspring. Details of the procedure and epidemiological information on approximately 200 subjects have been presented previously [4] and birth data and the results of behavioral testing of babies up to 4 days of age born to the marihuana users among 291 subjects in the Ottawa study have also been described elsewhere [3].

METHOD

The present report is based on a sample consisting of 420 subjects and includes several more infants born to marihuana users. As both the demographic data on the mothers and the results of the newborn are essentially the same as those found in the original cohort [3], the data will be described very briefly. Since the original report, a number of offspring of the marihuana users have been followed up and been examined using the Prechtl neurological examination [5] at nine (±1) and 30 (±2) days and the Bayley Scale of Infant Development [1] at 12 months. Although it is obvious, it must be emphasized that the sample size is small and these longtitudinal results have to be viewed as quite preliminary.

trimesters remaining in their pregnancy. Information obtained included the volume and variability of alcohol consumption, cigarette smoking habits and marihuana intake for the year before pregnancy and each trimester of pregnancy. In addition to this "soft" drug report a general health history, previous pregnancy details, a 24-hour dietary recall and socio-demographic data were obtained.

The categorization for marihuana use for each of the four time periods (year before pregnancy and each of the trimesters) was: non-user; irregular user—one joint or less per week or exposure to the exhaled smoke of others; moderate user—two to five joints per week and; heavy user—more than five joints per week.

RESULTS

The socio-demographic characteristics of the new sample is essentially the same as that of the cohort described previously [4] and therefore will not be dealt with separately. Among the total sample of 420 women the average family income was $29,250±$13,050 and the average age and parity was 29±4 and 0.7±0.9, respectively. The economic figure was very similar to that of the general population of the Ottawa area reported by Statistics Canada and the age and parity figures were consistant with all the women giving birth in 1979 in the participating hospitals. Ninety-four percent of the women had at least a high school diploma and 63 percent had continued their education beyond high school

PULMONARY HAZARDS OF SMOKING MARIJUANA AS COMPARED WITH TOBACCO

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Abstract To compare the pulmonary hazards of smoking marijuana and tobacco, we quantified the relative burden to the lung of insoluble particulates (tar) and carbon monoxide from the smoke of similar quantities of marijuana and tobacco. The 15 subjects, all men, had smoked both marijuana and tobacco habitually for at least five years. We measured each subject's blood carboxyhemoglobin level before and after smoking and the amount of tar inhaled and deposited in the respiratory tract from the smoke of single filter-tipped tobacco cigarettes (900 to 1200 mg) and marijuana cigarettes (741 to 985 mg) containing 0.004 percent or 1.24 percent Δ^9-tetrahydrocannabinol.

As compared with smoking tobacco, smoking marijuana was associated with a nearly fivefold greater increment in the blood carboxyhemoglobin level, an approximately threefold increase in the amount of tar inhaled, and retention in the respiratory tract of one third more inhaled tar ($P<0.001$). Significant differences were also noted in the dynamics of smoking marijuana and tobacco, among them an approximately two-thirds larger puff volume, a one-third greater depth of inhalation, and a fourfold longer breath-holding time with marijuana than with tobacco ($P<0.01$). Smoking dynamics and the delivery of tar during marijuana smoking were only slightly influenced by the percentage of tetrahydrocannabinol.

We conclude that smoking marijuana, regardless of tetrahydrocannabinol content, results in a substantially greater respiratory burden of carbon monoxide and tar than smoking a similar quantity of tobacco. (N Engl J Med 1988; 318:347-51.)

WE have previously shown that the habitual smoking of 3 or 4 marijuana cigarettes a day is associated with the same frequency of the symptoms of acute and chronic bronchitis[1] and the same type and extent of epithelial damage in the central airways[2] as the regular smoking of more than 20 tobacco cigarettes a day. A possible explanation for these findings is that a greater quantity of smoke particulates and noxious gases is delivered to and deposited or absorbed in the lungs by marijuana than by a similar amount of tobacco, possibly as a result of differences in the way each type of cigarette is smoked. To investigate this possibility, we examined the dynamics of smoking a marijuana or a tobacco cigarette and measured the particulates delivered to the smoker's mouth during the smoking of a single cigarette of each type.

METHODS

We studied fifteen men who were habitual smokers (mean age [±SD], 31.5±7.1 years), each of whom smoked both tobacco and marijuana. The subjects smoked an average of 29.9±16.7 tobacco cigarettes per day and had smoked an average of 16.1±12.2 pack-years of tobacco (one pack-year equals one pack of tobacco cigarettes per day times the number of years of smoking); they smoked an average of 16.5±17.1 marijuana cigarettes per week, and had smoked an average of 54.8±34.8 joint-years of marijuana (one joint-year equals one cigarette [joint] of marijuana per day times the number of years of smoking). All were in good general health and had normal or nearly normal values for forced vital capacity (101±8.7 percent of predicted values[3]) and forced expiratory volume in one second (96±14 percent of predicted values[3]). None reported intravenous drug abuse or smoking other illicit substances besides marijuana.

Each subject was studied on a single day after refraining from smoking tobacco for at least one hour and marijuana for at least six hours. During the study session, each subject smoked his own brand of filter-tipped tobacco cigarette, followed, in single-blind fashion, first by a placebo marijuana cigarette (from which nearly all Δ^9-tetrahydrocannabinol [Δ^9-THC] had been extracted, so that the concentration was 0.004 percent) and next by a marijuana cigarette of similar weight containing 1.24±0.06 percent Δ^9-THC. An interval of approximately 30 minutes separated the smoking of each two cigarettes. The tobacco cigarettes weighed 900 to 1120 mg and had a tar yield of 4.6 to 23.1 mg (mean, 12.0±5.7 mg) and a nicotine yield of 0.4 to 1.4 mg (mean, 0.84±0.32 mg) by Federal Trade Commission analysis. The placebo marijuana cigarettes weighed 741 to 940 mg (mean, 840 mg) and those containing 1.24 percent Δ^9-THC weighed 849 to 985 mg (mean, 907 mg); both were supplied by the National Institute on Drug Abuse, were stored at 4°C to minimize chemical degradation, and were maintained in a humidifier at 60 percent humidity and 21°C for 24 hours before the study, to reduce harshness.

The subjects were asked to smoke both the tobacco cigarette and the two marijuana cigarettes in a manner as similar as possible to their usual pattern of smoking tobacco and marijuana. Peripheral venous blood was withdrawn anaerobically immediately before and two minutes after the first two cigarettes were smoked for measurement of the percentage of carboxyhemoglobin saturation, with use of a carbon monoxide–oximeter (Model 282, Instrumentation Laboratory, Lexington, Mass.). After smoking each of the marijuana cigarettes, the subjects were asked to rate their level of intoxication on a scale of 0 to 100 percent, with 100 percent representing the greatest "high" they had ever experienced.

The volume, duration, and number of puffs and the intervals between puffs were measured with a 00 Fleisch pneumotachygraph (linear from 5 to 100 ml per second) connected through a differential pressure transducer (Model MP45-3, Validyne, Northridge, Calif.) (range, ±2 cm of water) to an oscilloscopic recorder with a differential integrator–computer and a rapid photographic writer (Model VR6, Electronics for Medicine, Pleasantville, N.Y.). To prevent the pneumotachygraph screen from becoming clogged by smoke particles,[4] the pneumotachygraph was connected through wide-bore Tygon tubing (length, 70 cm; internal diameter, 1 cm) to the distal end of a glass cylinder (length, 12 cm; diameter, 5 cm) that contained two ventilation ports (each 1 cm in diameter) and was sealed at its proximal end by a rubber stopper. The tobacco or marijuana cigarette was held in a small plastic holder inserted through the rubber stopper. The ventilation ports were left open between puffs to prevent either the extinction of the lighted cigarette or the excessive accumulation of carbon monoxide. During a puff, the smoker covered the ventilation holes with his index and middle fingers so that the entire volume of air drawn through the cigarette could be measured by the pneumotachygraph. The resistance of the pneumotachygraph (0.0068 cm of water per milliliter per second) was considerably lower than that of the cigarette (0.51 cm of water per milliliter per second for tobacco; 0.17 cm of water per milliliter per second for marijuana); therefore, the pneumotachygraph itself was

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not likely to have a substantial effect on smoking dynamics. The duration of a puff was timed from the pneumotachygraphic flow tracing. The interval between puffs was defined as the period between the end of one puff and the start of the next.

To measure "wash-in" volume (the volume of air inhaled), inductive plethysmographic coils (Respitrace Ambulatory Monitoring Systems, Ardsley, N.Y.) were placed around each subject's rib cage and abdomen.[6] A demodulator converted changes in electrical inductance in the coils during respiratory movements into voltage signals proportional to changes in the volume enclosed by the coils. Changes in the volume of the respiratory system were calculated from the weighted sums of the signals from the rib cage and abdomen; the weights were determined by the least-squares calibration method.[7] The accuracy of the calibration was confirmed by comparing the inhaled volumes calculated from respiratory inductive plethysmography with spirometric values; the measurements obtained by spirometry and inductive plethysmography agreed within ±10 percent. The amount of time the inhaled smoke was retained in the lungs (smoke-retention time) was calculated as the interval between the times corresponding to one third of the maximum inhaled volume and two thirds of the maximum volume exhaled following breath holding (Fig. 1). The no-smoking interval was timed from the end of the smoke-retention time to the start of the next puff.

A previously described proportional smoke-trapping device[8] was connected to the apparatus for measuring the volume of puffs in order to measure the amount of smoke particulates delivered to the smoker's mouth. This device consisted of a plastic cigarette holder through which the mainstream smoke was diverted into two parallel pathways, one containing one capillary tube (pathway A) and the other seven parallel capillary tubes (pathway B). A Cambridge filter pad trapped the smoke that passed through pathway A. The tar trapped by the filter was extracted with methanol and analyzed by means of a spectrophotometer (wavelength, 400 nm). A constant fraction of the tar (12.5±0.53 percent) was retained in the filter over a wide range of puff volumes (30 to 60 ml), puff durations (1 to 4 sec), and puff flow rates (20 to 100 ml per second).[8] This apparatus, therefore, permitted the actual quantity of smoke particulates delivered to the mouth to be calculated by multiplying the amount of particulates trapped in the Cambridge filter pad in pathway A by seven. At the end of the period of breath holding after each puff, the subjects turned their heads slightly to one side and exhaled the smoke into the large end (diameter, 26 cm) of an adjacent megaphone device, the distal end (diameter, 4.5 cm) of which was fitted with a high-efficiency filter attached to a vacuum system as described by Hinds et al.[9] After the tar was extracted from the filter with methanol, the exhaled particulates were measured with a spectrophotometer. The amount of smoke retained (deposited) in the respiratory tract was expressed as a percentage of the amount inhaled: percentage deposited = [1 − (amount of exhaled particulates/amount of inhaled particulates)] × 100.

Each subject's measurements were averaged for each cigarette smoked. These mean values, as well as the number of puffs, the quantity of particulates inhaled, the percentage of inhaled particulates deposited, and the increment in carboxyhemoglobin saturation per cigarette, were averaged for all 15 subjects for each type of cigarette smoked. The subjects' ratings of their degree of intoxication after marijuana smoking were also averaged for all subjects for each type of marijuana cigarette (placebo and 1.21 percent Δ^9-THC). Two-way analysis of variance (for subject and type of cigarette) was used to determine the significance of differences in smoking patterns, the delivery and deposition of particulates, and the increase in carboxyhemoglobin saturation among types of cigarette.[10] Pairwise comparisons were then performed using testing for least significant differences[11]; differences were considered significant if P values were <0.05.

Results

Descriptive data about smoking in the group of 15 subjects are shown in Table 1. Placebo marijuana and marijuana containing approximately 1.24 percent Δ^9-THC were smoked in a similar manner. However,

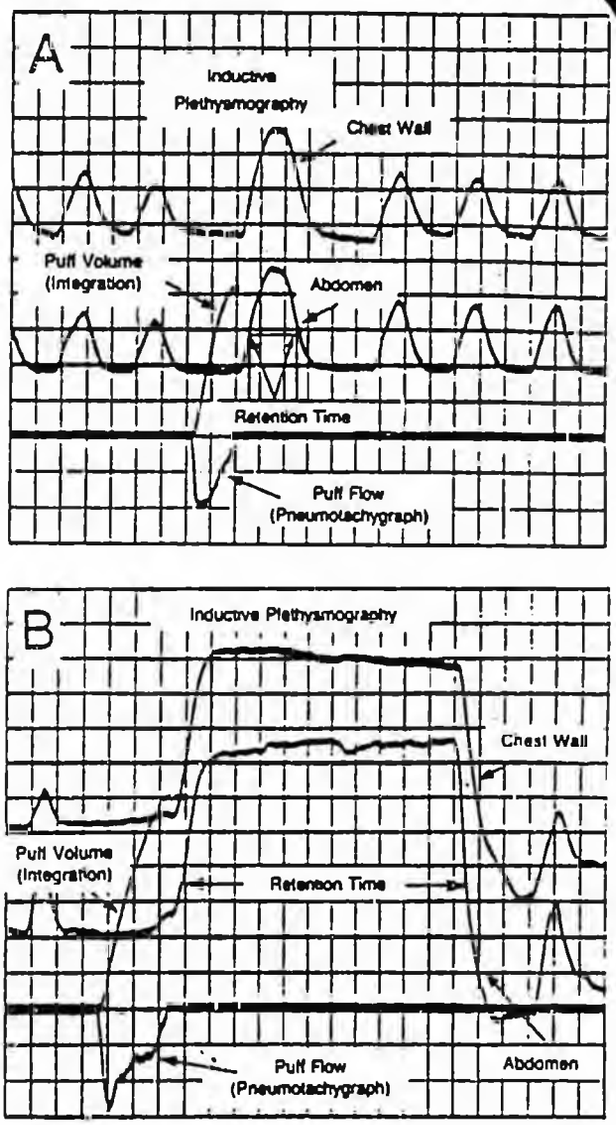

Figure 1. Analogue Tracings of Voltage Signals from Inductive Plethysmographic Coils around the Chest Wall and Abdomen of a Representative Subject and Simultaneous Flow and Integrated Volume Signals from a Pneumotachygraph Incorporated into a Puff-Volume Measuring Device during the Smoking of a Tobacco Cigarette (A) and a Marijuana Cigarette (B).

Note that during marijuana smoking, there is greater amplitude of the voltage signals representing puff volume (measured by the pneumotachygraph) and inhaled volume (measured by the inductive plethysmograph) than during tobacco smoking.

the average volume of puffs was about 70 percent larger ($P<0.001$) and the duration of puffs about 60 percent longer ($P<0.01$) during the smoking of marijuana than the smoking of tobacco, regardless of whether the marijuana contained 1.24 or 0.004 percent Δ^9-THC; significantly more puffs were taken from the tobacco cigarette than from either the placebo marijuana cigarette or that containing 1.24 percent Δ^9-THC ($P<0.001$). Although the interval between puffs was less for tobacco than for marijuana smoking ($P<0.05$), the no-smoking interval, which did not include the breath-holding time after

Table 1. Characteristics of 15 Subjects' Smoking of Tobacco, Placebo Marijuana (0.03% Percent Δ^9-THC), and Marijuana Containing 1.24 Percent Δ^9-THC.*

[illegible]	Tobacco	Marijuana		P Value†
		0.004% Δ^9-THC	1.24% Δ^9-THC	
		mean ±SD		
[illegible]	49.4±15.2	88.3±24.8	78.0±22.8	<0.001
[illegible]	2.4±1.1	3.8±1.9	4.0±2.2	<0.01
[illegible]	13.5±4.0	7.5±2.3	8.5±3.1	<0.001
[illegible]	27.0±8.2	35.3±12.2	37.6±14.5	<0.05
[illegible]	1.31±0.22	1.82±0.66	1.75±0.52	<0.002
[illegible]	3.5±1.3	13.8±9.2	14.7±10.2	<0.001
[illegible]	23.5±8.5	21.5±6.4	23.0±8.8	NS

*All subjects were habitual smokers of both tobacco and marijuana. They smoked their own brands of tobacco cigarettes. †The letters [illegible] analysis of variance; NS denotes not significant.

‡The level of significance of comparisons between tobacco and each strength of marijuana; none of the comparisons between the two different strengths of marijuana (0.004 percent vs. 1.24 percent Δ^9-THC) was statistically significant.

smoke was inhaled, was similar for both substances. The mean inhaled volume was 36 percent greater ($P<0.002$) and the smoke-retention time was four times longer ($P<0.001$) during marijuana smoking than tobacco smoking.

The volume of the portion of the proportional smoke-trapping device through which smoke was delivered was approximately 13 ml. After the first puff, this volume was filled with smoke that was delivered in subsequent puffs; thus, after the first puff, no additional volume of air not containing smoke was included in the measurement of puff volume. When the pneumotachygraph was disassembled from the proportional smoke-trapping device and used to measure puff volume, the difference in the mean volume was negligible (1.2±2.0 ml lower without the smoke-trapping device). Similarly, inhaled volumes determined directly from the cigarette by the inductive plethysmograph, without the attachment of either the pneumotachygraph or the proportional smoke-trapping device, were similar to (within 50 ml) the inhaled volume determined when the subjects smoked through these devices.

The amounts of particulates inhaled, the percentage of inhaled particulates deposited in the respiratory tract, and the differences between the carboxyhemoglobin levels before and after smoking each type of cigarette are shown in Table 2. The major significant difference between smoking marijuana cigarettes containing 0.004 percent Δ^9-THC (placebo) and smoking cigarettes containing 1.24 percent Δ^9-THC was that the latter caused a greater degree of intoxication. In addition, the amount of particulates inhaled from marijuana containing 1.24 percent Δ^9-THC was slightly but significantly greater (20 percent) than that delivered from placebo marijuana ($P<0.05$). In contrast, smoking either type of marijuana was associated with the inhalation of 2.8 to 3.3 times more insoluble particulates (tar) and with the deposition of 32 to 35 percent more of these inhaled particulates than smoking the subject's own brand of tobacco ($P<0.001$). Consequently, marijuana smoking resulted in a tar burden to the respiratory tract that was 3.5 to 4.5 times greater than that produced by tobacco smoking in the same subjects. Furthermore, smoking a single marijuana cigarette caused a fourfold greater increment in carboxyhemoglobin saturation ($P<0.001$) than did smoking a single tobacco cigarette.

Discussion

Long-term adverse pulmonary consequences of tobacco smoking have been shown to be related to dose.[12] For example, the incidence of chronic obstructive pulmonary disease or bronchogenic carcinoma in smokers of fewer than 5 to 10 tobacco cigarettes a day is substantially less than in habitual smokers of more than 20 tobacco cigarettes a day.[13] Although regular tobacco smokers consume more than 15 tobacco cigarettes a day, most current smokers of marijuana smoke less than 1 marijuana cigarette a day.[12] Even among the estimated 6 million daily smokers of marijuana in the United States,[14] smoking more than five marijuana cigarettes a day is unusual. In view of the many similarities in the smoke contents of marijuana and tobacco,[15,16] it has been argued that habitually smoking only a few marijuana cigarettes a day may have a proportionately less harmful long-term effect on the lungs than regularly smoking several times more tobacco cigarettes. This argument assumes that the number of cigarettes smoked is directly proportional to the dose of smoke contents inhaled; however, this assumption ignores the ways in which the characteristics of smoking may influence the delivery of the combustion products of cigarettes.[17,18]

Table 2. Inhalation and Deposition of Particulates, Increases in Blood Carboxyhemoglobin Saturation, and Levels of Intoxication Associated with the Smoking of Tobacco and Marijuana in 15 Smokers of Both Substances.*

Items	Tobacco	Marijuana	
		0.004% Δ^9-THC	1.24% Δ^9-THC
		mean ±SD	
Inhaled particulates (optical density)	4.9±2.0	13.5±6.0†	16.3±6.3†‡
Percentage of particulates deposited	64.0±8.9	84.4±6.9†	86.1±6.7†
Increase in carboxyhemoglobin saturation (%)	0.60±0.52	2.99±1.51†	—§
Degree of intoxication (maximum "high" = 100%)	—	15.3±16.9	63.9±18.3‡

*Δ^9-THC denotes Δ^9-tetrahydrocannabinol.

†Significantly greater than values for tobacco ($P<0.001$ by analysis of variance and testing for least significant difference).

‡Significantly greater than values for marijuana containing 0.004 percent Δ^9-THC ($P<0.05$ by analysis of variance and testing for least significant difference).

§Not measured.

Few studies have been carried out in which the actual dose of smoke contents delivered to and retained in the respiratory tract during natural smoking has been measured. In our study, both the amount of particulate matter that was inhaled and the amount that was deposited in the respiratory tract were quantified during tobacco and marijuana smoking by means of a simple, new, noninvasive device.[8] These measurements allowed us to compare the actual dose to the smoker of particulate matter from the smoke of marijuana with that from tobacco. At the same time, the characteristics of smoking were determined in order to permit the relation between behavioral variables in smoking and the delivery and retention of smoke contents in the respiratory tract for each type of cigarette. The proportional smoke-trapping device had little measurable influence on smoking dynamics.

Findings from the present study indicate that approximately three times as much particulate matter is delivered to the smoker's mouth during the smoking of a single marijuana cigarette than during the smoking of a single tobacco cigarette of the smoker's own brand. These results are similar to those obtained in studies that used smoking machines to simulate conditions thought to be representative of marijuana and tobacco smoking.[19,20] Our results also revealed that approximately one third more of the particulates inhaled from the smoke of marijuana are retained in the respiratory tract than is the case when tobacco is smoked. Consequently, the net respiratory burden of particulates was approximately four times greater during marijuana smoking than tobacco smoking.

Several explanations are possible for the greater burden of particulates to the lungs from marijuana than from a similar quantity of tobacco. First, in all cases, the tobacco cigarettes were more densely packed than the marijuana cigarettes and, unlike the marijuana cigarettes, were filter-tipped; therefore, the filtration efficiency of the tobacco cigarettes was greater. Second, the average residual length of the marijuana cigarettes (23±13 mm) was smaller than that of the tobacco cigarettes (37±12 mm), thereby further reducing the filtration efficiency of the marijuana cigarette. However, because the tobacco cigarettes were initially longer and because the filter tip was excluded in the tobacco butt, the actual quantities of tobacco and marijuana consumed were similar. Third, the subjects' patterns of inhalation in smoking the two types of cigarettes were markedly different; marijuana was smoked with a puff volume that was more than two thirds larger, an inhaled volume one third greater, and a retention time four times longer than the values for tobacco. Although the larger puff volumes for marijuana were partially offset by a smaller number of puffs, this factor may still have contributed to the greater mass of smoke particulates delivered to the mouth in marijuana smoking. The deeper inhaled volumes and, in particular, the severalfold longer retention times during marijuana smoking than during tobacco smoking may have accounted for the greater percentage of the inhaled particulates from marijuana smoke deposited in the respiratory tract.

The four-to-five-times-greater increments in carboxyhemoglobin saturation during marijuana smoking than tobacco smoking were probably due mainly to differences in how the cigarettes were smoked rather than in the amount of carbon monoxide produced, since syringe-simulated puffs of similar volumes and durations from lit cigarettes yielded approximately 25 percent lower concentrations of carbon monoxide from marijuana than from tobacco. This finding is consistent with the more complete combustion of the more loosely packed marijuana. On the other hand, the subjects' deeper inhalations and, in particular, their considerably longer retention of smoke in the lungs during marijuana smoking than during tobacco smoking made possible a greater uptake of carbon monoxide by the pulmonary microcirculation by means of passive diffusion. We measured the increment in blood carboxyhemoglobin after placebo marijuana (from which the cannabinoids had been extracted), and not after marijuana containing Δ^9-THC. However, we would not expect appreciable differences between the effects of real marijuana and those of placebo marijuana on blood carboxyhemoglobin levels, since the smoking dynamics and the carbon monoxide delivery of the two types of marijuana cigarettes were similar. The expected physiologic consequences of the markedly greater boost in carboxyhemoglobin levels from a single marijuana cigarette are a higher degree of impairment in oxygen transfer in the lung,[21] a reduction in the oxygen-carrying capacity of the blood, and impairment in the release of oxygen from hemoglobin in the tissues.[22] Moreover, the Δ^9-THC in marijuana causes dose-related increases in heart rate[23,24] and thus in cardiac work and myocardial oxygen requirements. Therefore, in persons with underlying coronary artery disease who smoke marijuana, the combined effects of a marked rise in the level of carboxyhemoglobin and the cardioacceleration induced by Δ^9-THC could lead to a critical imbalance between reduced myocardial oxygen supply and increased demand.

Interestingly, no significant differences in smoking dynamics were noted between placebo marijuana and marijuana containing 1.24 percent Δ^9-THC, despite marked differences in the subjects' perceived level of intoxication. These findings differ from previous observations in tobacco smokers that puff volume increases when low-nicotine cigarettes are smoked.[25] Our results in marijuana smokers are consistent with data from other studies,[26,27] however, and suggest that the pattern of smoking marijuana is not immediately adjusted to alter the inhaled dose of Δ^9-THC but, instead, probably represents a learned technique based on previous experiences and interactions.

In conclusion, our findings demonstrate that smoking behavior differs markedly between marijuana and tobacco smoking and that these differences are associ-

Table 1. Characteristics of 15 Subjects' Smoking of Tobacco, Placebo Marijuana (0.004 Percent Δ^9-THC), and Marijuana Containing 1.24 Percent Δ^9-THC.*

Index	Tobacco	Marijuana		P Value†
		0.004% Δ^9-THC	1.24% Δ^9-THC	
	mean ±SD			
Puff volume (ml)	49.4±15.2	88.3±24.8	78.0±22.8	<0.001
Puff duration (sec)	2.1±1.1	3.8±1.9	4.0±2.2	<0.01
No. of puffs	13.5±4.0	7.5±2.3	8.5±3.1	<0.001
Interval between puffs (sec)	27.0±8.2	35.3±12.2	37.6±14.5	<0.05
Inhaled volume (liters)	1.21±0.22	1.82±0.66	1.75±0.52	<0.002
Smoke-retention time (sec)	3.5±1.3	13.8±9.2	14.7±10.2	<0.001
Space-smoking time (sec)	23.5±8.5	21.5±6.4	23.0±8.8	NS

*All subjects received all three types of both tobacco and marijuana. They smoked their own brands of tobacco cigarettes. Δ^9-THC denotes Δ^9-tetrahydrocannabinol. NS denotes not significant.

†P values are for the significance of comparisons between tobacco and each strength of marijuana; none of the comparisons between the two strengths of marijuana (0.004 percent vs. 1.24 percent Δ^9-THC) was statistically significant.

smoke was inhaled, was similar for both substances. The mean inhaled volume was 36 percent greater ($P<0.02$) and the smoke-retention time was four times longer ($P<0.001$) during marijuana smoking than tobacco smoking.

The volume of the portion of the proportional smoke-trapping device through which smoke was delivered was approximately 13 ml. After the first puff, this volume was filled with smoke that was delivered in subsequent puffs; thus, after the first puff, no additional volume of air not containing smoke was included in the measurement of puff volume. When the pneumotachygraph was disassembled from the proportional smoke-trapping device and used to measure puff volume, the difference in the mean volume was negligible (4.2±2.0 ml lower without the smoke-trapping device). Similarly, inhaled volumes determined directly from the cigarette by the inductive plethysmograph, without the attachment of either the pneumotachygraph or the proportional smoke-trapping device, were similar to (within 50 ml) the inhaled volume determined when the subjects smoked through those devices.

The amount of particulates inhaled, the percentage of inhaled particulates deposited in the respiratory tract, and the differences between the carboxyhemoglobin levels before and after smoking each type of cigarette are shown in Table 2. The major significant difference between smoking marijuana cigarettes containing 0.004 percent Δ^9-THC (placebo) and smoking cigarettes containing 1.24 percent Δ^9-THC was that the latter caused a greater degree of intoxication. In addition, the amount of particulates inhaled from marijuana containing 1.24 percent Δ^9-THC was slightly but significantly greater (29 percent) than that delivered from placebo marijuana ($P<0.05$). In contrast, smoking either type of marijuana was associated with the inhalation of 2.8 to 3.3 times more insoluble particulates (tar) and with the deposition of 32 to 35 percent more of these inhaled particulates than smoking the subject's own brand of tobacco ($P<0.001$). Consequently, marijuana smoking resulted in a tar burden to the respiratory tract that was 3.5 to 4.5 times greater than that produced by tobacco smoking in the same subjects. Furthermore, smoking a single marijuana cigarette caused a fourfold greater increment in carboxyhemoglobin saturation ($P<0.001$) than did smoking a single tobacco cigarette.

Discussion

Long-term adverse pulmonary consequences of tobacco smoking have been shown to be related to dose.[12] For example, the incidence of chronic obstructive pulmonary disease or bronchogenic carcinoma in smokers of fewer than 5 to 10 tobacco cigarettes a day is substantially less than in habitual smokers of more than 20 tobacco cigarettes a day.[13] Although regular tobacco smokers consume more than 15 tobacco cigarettes a day, most current smokers of marijuana smoke less than 1 marijuana cigarette a day.[12] Even among the estimated 6 million daily smokers of marijuana in the United States,[14] smoking more than five marijuana cigarettes a day is unusual. In view of the many similarities in the smoke contents of marijuana and tobacco,[15,16] it has been argued that habitually smoking only a few marijuana cigarettes a day may have a proportionately less harmful long-term effect on the lungs than regularly smoking several times more tobacco cigarettes. This argument assumes that the number of cigarettes smoked is directly proportional to the dose of smoke contents inhaled; however, this assumption ignores the ways in which the characteristics of smoking may influence the delivery of the combustion products of cigarettes.[17,18]

Table 2. Inhalation and Deposition of Particulates, Increases in Blood Carboxyhemoglobin Saturation, and Levels of Intoxication Associated with the Smoking of Tobacco and Marijuana in 15 Smokers of Both Substances.*

Index	Tobacco	Marijuana	
		0.004% Δ^9-THC	1.24% Δ^9-THC
		mean ±SD	
Inhaled particulates (optical density)	4.9±2.0	13.5±6.0†	16.3±6.3†‡
Percentage of particulates deposited	64.0±8.9	84.4±6.9†	86.1±6.7†
Increase in carboxyhemoglobin saturation (%)	0.60±0.52	2.99±1.51†	—§
Degree of intoxication (maximum "high" = 100%)	—	15.3±16.9	63.9±18.3‡

*Δ^9-THC denotes Δ^9-tetrahydrocannabinol.

†Significantly greater than values for tobacco ($P<0.001$ by analysis of variance and testing for least significant difference).

‡Significantly greater than values for marijuana containing 0.004 percent Δ^9-THC ($P<0.05$ by analysis of variance and testing for least significant difference).

§Not measured.

ated with respiratory burden of smoke particulates and absorption of carbon monoxide that are approximately four times greater in the case of marijuana smoking. These results may account for previous findings that smoking only a few marijuana cigarettes a day (with or without tobacco) has the same effect on the prevalence of acute and chronic respiratory symptoms and the degree of tracheobronchial epithelial histopathology as smoking more than 20 tobacco cigarettes a day (without marijuana). These observations justify concern about the potential long-term pulmonary consequences of the habitual smoking of only a few marijuana cigarettes a day.

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Myocardial infarction during marijuana smoking in a young female

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KEY WORDS: Cannabis, normal coronary arteries.

Although marijuana smoking is popular among young adults, hospital admissions due to adverse effects of this drug are uncommon[1]. We report a case of a young female who developed an acute myocardial infarction while smoking the drug.

Case report

A previously healthy 33-year old secretary was admitted to the Casualty Department with severe central chest pain radiating to both arms. The pain had started one hour before, while smoking marijuana at a party. She had smoked 20 tobacco cigarettes per day for 16 years. There was no past history of cardiac disease, hypertension or diabetes. A paternal uncle had died of myocardial infarction age 59 years. She had taken marijuana on 3 occasions in the previous 3 years with no ill effects. She was not taking the oral contraceptive pill.

On examination, she was euphoric, pale and sweating profusely. Heart rate was 96 min^{-1} and blood pressure 110/70 mmHg. Heart sounds were normal and there were no signs of cardiac failure. The electrocardiograph showed ST elevation in leads 2,3 and aVF with reciprocal ST depression in leads V_2–V_6 (Fig. 1). Chest X-ray was within normal limits.

Fifteen minutes after admission, she developed ventricular fibrillation which responded to a 200 joule DC shock. She then developed 2:1 heart block, followed by complete heart block and a temporary transvenous pacing wire was inserted.

On the first admission day, serum creatine kinase and aspartate transaminase levels were elevated to 883 $IU\,l^{-1}$ (normal 0–180 $IU\,l^{-1}$) and 78 $IU\,l^{-1}$ (normal 6–35 $IU\,l^{-1}$), rising to 1701 $IU\,l^{-1}$ and 208 $IU\,l^{-1}$ on the second day, respectively. There was a corresponding rise in serum creatine kinase (MB) levels to 73 $IU\,l^{-1}$ and 123 $IU\,l^{-1}$ on these days. Blood urea, electrolytes and glucose were normal. Toxicological assay of the patient's urine within 6 h of admission, using a sensitive radioimmunoassay, showed 5·5 ng ml^{-1} of total cross-reacting cannabinoids. Electrocardiographs showed evolving changes of acute inferior infarction over the next week, but there were no further arrhythmias and she was discharged on the twelfth hospital day.

Three months later, she underwent treadmill exercise testing and completed stage 7 of Bruce Protocol, achieving a heart rate of 190 min^{-1} (>85% predicted maximal) with no haemodynamic or electrocardiographic abnormality. Random (non-fasting) serum cholesterol was 6·4 mmol l^{-1} (normal 3·4–7·8) and random serum triglycerides level was 1·58 mmol l^{-1} (normal 0·34–2·26) at this time. Subsequent selective coronary arteriography and left ventriculography showed normal coronary arteries with posterior hypokinesis of the left ventricle.

Comment

Marijuana smoking has been shown to affect the electrocardiograph of normal subjects[2] and a study in patients with ischaemic heart disease showed a significantly decreased exercise time to angina with the drug compared to high-nicotine cigarettes[3]. Two previous cases of acute

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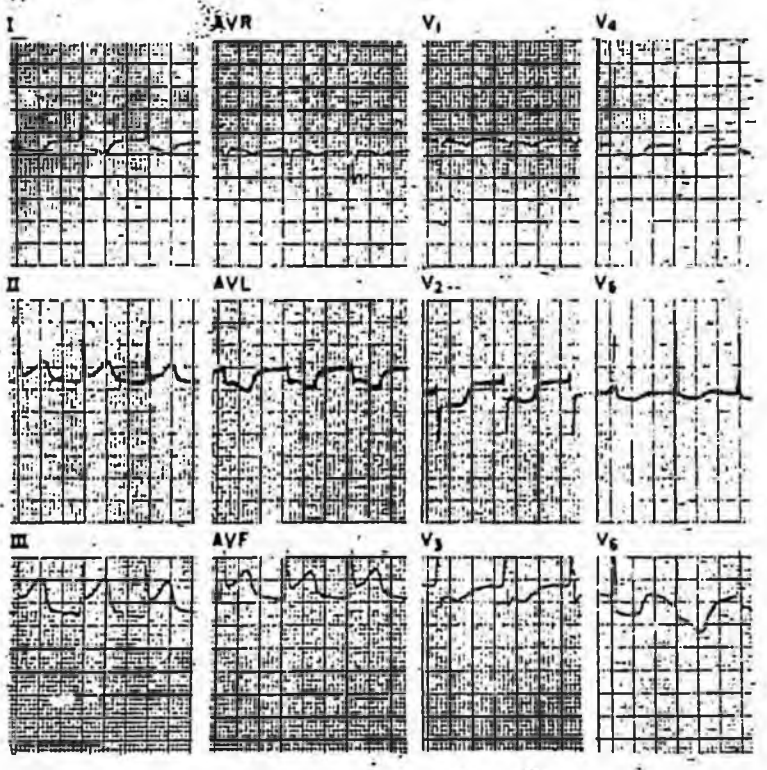

Figure 1 Twelve-lead electrocardiograph on admission.

myocardial infarction in close association with marijuana smoking have been reported[4,5]. In the most recent report, coronary atheroma was demonstrated at post-mortem. In neither case was toxicological evidence of marijuana exposure produced. In this case, the evidence of myocardial infarction is indisputable with classical electrocardiographic change, rise in cardiac enzymes and ventricular wall hypokinesis. The radiologically normal coronary arteries would suggest that coronary spasm was the cause of infarction in this case, in the absence of predisposing causes for thrombosis other than cigarette smoking. It was felt that ergometrine or marijuana challenge during angiography was not ethical in this case. Although the close relationship of drug exposure to acute infarction does not necessarily imply causation, an individual sensitivity to marijuana or an impurity in the preparation may have been present. Further non-invasive methods of investigation of myocardial perfusion in users of the drug would be of interest.

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Fatal coronary artery thrombosis associated with cannabis smoking

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AN unusual case of coronary thrombosis associated with illicit drug use is described. It is suggested that general practitioners and casualty officers should consider the possibility of atypical presentations resulting from drug abuse not made known to the examining doctor.

Case report

A 32-year-old man complained of sudden onset chest pain but was unable to describe his pain in any detail or give any other information. He was distressed, unable to remain in one position for any length of time, and was rolling around his bed and onto the floor. Physical examination was not possible at first owing to lack of co-operation. The patient was sedated with 4 to 5 mg of intravenous diazepam with the remainder of the ampoule given intramuscularly. He became less distressed and was able to co-operate, complaining of central chest pain with tingling in the fingers of both hands. On examination the patient was not clammy, he was hyperventilating, his pulse rate was 100 beats / minute and his blood pressure was normal; there were no signs of cardiac failure. Arrangements were made for the patient to be transferred to a casualty department, but unfortunately he died before the arrival of the ambulance.

Post-mortem investigations gave the following results. The heart weighed 430g; its configuration was normal and the chambers were in proportion. The myocardium was generally flabby in consistency, with early congestion of the anterior two-thirds of the intraventricular septum. There were numerous raised plaques of atheroma throughout both right and left coronary arteries; these were particularly prominent at the start of the circumflex branch of the left coronary artery where there was coarse focal stenosis of the lumen. One centimetre from the start of the descending branch of the left coronary artery one of the plaques showed ulceration of the intimal lining and adherent to it was a dark red thrombus 0.75 cm in length.

It was subsequently learned that the patient had been smoking cannabis earlier that evening.

Comment

This case demonstrates two possible adverse effects of cannabis on a person susceptible to ischaemic heart disease.

First, cannabis has a striking effect on heart rate, inducing a tachycardia up to 160 beats per minute or higher, which is achieved within a few minutes of drug absorption. Thereafter a slow decline in heart rate occurs which may take four hours or longer. Aronow has shown in a study of exercise-induced angina that smoking cannabis causes a decreased exercise time of 48 per cent, until angina is experienced, compared with a placebo reduction of 8.6 per cent.[1] This was ascribed to increased oxygen demand coupled with decreased oxygen perfusion leading to earlier experience of chest pain. Charles described one previous case of myocardial infarction occurring some 30 minutes after smoking cannabis;[2] a 25-year-old patient presented with cardiac failure and the infarction was confirmed by electrocardiography (ECG) and enzyme analysis.

Second, the psychological effects of cannabis appear to run in a continuum from mild dysphoria to acute psychotic reactions. Tart has shown that up to 36 per cent of regular cannabis users experienced symptoms during intoxication of distorted body image, acute pains or hallucinations.[3] Halikas has reported that 16 per cent of regular cannabis users experienced anxiety, fearfulness, confusion or aggressive urges as a 'usual occurrence'.[4] Controlled laboratory investigations have

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shown that acute psychological reactions tend to last up to four hours.

The smoking of cannabis causes changes in the cardiovascular system characteristic of stress. If cannabis were to increase the heart rate in a predisposed individual, it seems reasonable to suppose that angina could be precipitated, resulting perhaps in ischaemic damage. Furthermore, should psychoactive effects of the drug cause the patient to react in an atypical manner, he might not take suitable measures to relieve the angina, thus increasing the risk of damaging the myocardium or of precipitating an arrythmia. The problem of cardiovascular disease associated with cannabis smoking will surely become more common as younger cannabis smokers begin to enter the risk years of ischaemic heart disease.

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