

ALASKA LEGISLATURE COMMITTEE FILES 1987-1988 8672

5247 SHES SB 32

819

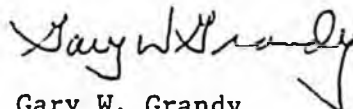
Representative John Sund, Robin Taylor
Senator Lloyd Jones
Juneau, Alaska

Page 2.

I believe these innocent newborns have a God-given right to start life without being in subjection to problems created by their mother's marijuana habits.

I will not repeat the many comments made in the hearings but I did hear a majority of testimony in favor of SB #32. I also believe that the majority of citizens in Petersburg and Alaska support SB #32. You will receive or the Hess Committee will receive a petition from people in Petersburg who support SB #32. Therefore, I solicit your vote in favor of SB #32 when it reaches the floor of the legislature.

Sincerely,



Gary W. Grandy
Administrator

cc: Hess Committee - Recriminilization of Marijuana
Ben Grussendorf, Senator
Ed Malewski - Sitka Community Hospital
Frank Sutton - Mt. Edgecume Hospital

Incidentally, I have just learned that Senator Ben Grussendorf may attempt to retain SB #32 in Committee. bluntly, that stinks and I resent any important legislation being retained in Committee. Politically, those actions can hurt legislators as the majority of people in a democratic society want those issues debated and voted upon.

CITY OF KETCHIKAN

RESOLUTION NO. 87-1498

A RESOLUTION OF THE CITY OF KETCHIKAN, ALASKA, SUPPORTING REPEAL OF A.S. 11.71.070 AND AMENDMENT OF A.S. 11.71.060(a) TO MAKE MARIJUANA ILLEGAL AND ESTABLISHING AN EFFECTIVE DATE

WHEREAS, Alaska is the only state in the union with a permissive statute for personal possession of marijuana, and

WHEREAS, findings of local, state and federal authorities conclude that marijuana is detrimental to the health, welfare and public safety of all people and of all ages, and

WHEREAS, the Supreme Courts of other states and the U.S. Supreme Court have upheld state statutes prohibiting the use and possession of marijuana, and

WHEREAS, current Alaska state statutes are not in conformity with federal drug enforcement laws controlling drug abuse, and

WHEREAS, the conflict between federal and state law pertaining to marijuana causes unnecessary barriers for local police and Alaska State Troopers in protecting the public from drug abusers, and

WHEREAS, Ketchikan Youth Services, Families in Action and other concerned local citizens have expressed concern over the drug abuse problem in the community, and

WHEREAS, representatives of sixty (60) Alaskan high schools at the Alaska Association of School Governments' Annual Fall Conference held on October 18, 1986, unanimously passed a resolution to repeal the current marijuana law and make the drug in all its forms illegal in Alaska.

NOW, THEREFORE, BE IT RESOLVED BY THE COUNCIL OF THE CITY OF KETCHIKAN, ALASKA as follows:

Section 1. The City Council of the City of Ketchikan, Alaska hereby petitions the Governor of the State of Alaska, the Alaska State Legislature and the Alaska Supreme Court to take immediate steps to repeal statutory and constitutional protections for use and possession of marijuana in the State of Alaska in order to promote the general health, welfare and public safety of the citizens of Ketchikan and the State of Alaska.

Section 2. The City Clerk is hereby directed to send copies of this resolution to Governor Cowper, Senator Jones, Representative Taylor, Representative Sund, the Attorney General and the Alaska Municipal League.

Section 3. This resolution shall become effective immediately upon passage.

PASSED AND APPROVED this _____ day of _____, 1987.

Ted Ferry, Mayor

ATTEST:

Karen Miles, CMC
City Clerk



KETCHIKAN GATEWAY BOROUGH SCHOOL DISTRICT

Darroll Hargraves
SUPERINTENDENT

Resolution No. 210
Ketchikan Gateway Borough School District

A REQUEST FOR CHANGING THE STATE STATUTES TO MAKE THE POSSESSION AND USE OF MARIJUANA ILLEGAL

WHEREAS, the State of Alaska allows legal private possession and use of marijuana,

WHEREAS, Alaska's present statutes regarding possession and use of marijuana appear to be in conflict with the laws of the United States, and

WHEREAS, the problem of drug and alcohol abuse in our schools and our society appears to be on the rise, and

WHEREAS, the President of the United States initiated a national crusade to counter the current drug problem, and

WHEREAS, many students find easy access to illegal drugs, particularly marijuana, and

WHEREAS, Alaska statutes present a mixed message by currently allowing the use and possession of marijuana in the home, and

WHEREAS, current research and medical opinion concerning marijuana indicates that marijuana is harmful and does present a serious health problem, and

WHEREAS, the utilization of marijuana possession in Alaska sends the message to outside suppliers that Alaska is an open state which condones the "personal use" of marijuana, and

WHEREAS, a show of community resolve against the legal possession and use of marijuana sends a message to the state legislature and the governor's office,

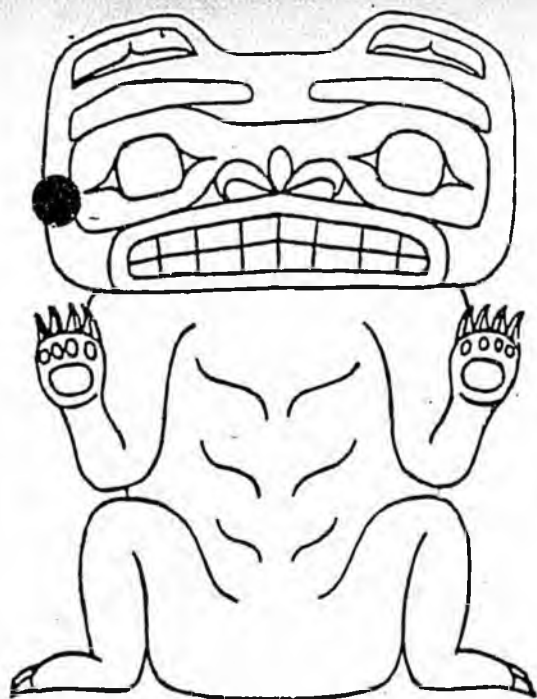
THEREFORE BE IT RESOLVED by the Ketchikan Gateway Borough School District that:

1. The School District encourages and supports the reenactment of statutes which will recriminalize the possession of marijuana.
2. The School District makes this position one of public record so that all in the community, in other school districts, and across the state will understand our position that the present statutes in Alaska governing marijuana are not in the best interest of its citizens.
3. The School District requests our legislators, locally and across the state, to give the recriminalization of marijuana immediate attention during the 1st session of the 15th legislature so that effective July 1, 1987 the possession and use of marijuana will be illegal and carry consequences.

PASSED, APPROVED, AND ADOPTED BY THE BOARD OF EDUCATION OF THE KETCHIKAN GATEWAY BOROUGH SCHOOL DISTRICT OF KETCHIKAN, ALASKA THIS _____ DAY OF _____, 1987.

President of the Board

Clerk-Treasurer of the Board



City of Saxman

Rt. 2, Box 1
Saxman, Alaska 99901
907-225-4166

CITY OF SAXMAN

RESOLUTION NO. 87-01-030

A RESOLUTION OF THE CITY OF SAXMAN, ALASKA, SUPPORTING REPEAL OF A.S. 11.71.070 AND AMENDMENT OF A.S. 11.71.060(a) TO MAKE MARIJUANA ILLEGAL AND ESTABLISHING AN EFFECTIVE DATE.

- WHEREAS, Alaska is the only state in the union with a permissive statute for personal possession of marijuana; and
- WHEREAS, findings of local, state and federal authorities conclude that marijuana is detrimental to the health, welfare and public safety of all people and of all ages; and
- WHEREAS, the Supreme Courts of other states and the U.S. Supreme Court have upheld state statutes prohibiting the use and possession of marijuana; and
- WHEREAS, current Alaska state statutes are not in conformity with federal drug enforcement laws controlling drug abuse; and
- WHEREAS, the conflict between federal and state law pertaining to marijuana causes unnecessary barriers for local police and Alaska State Troopers in protecting the public from drug abusers; and
- WHEREAS, Ketchikan Youth Service, Families in Action and other concerned local citizens have expressed concern over the drug abuse problem in the community; and
- WHEREAS, representatives of sixty (60) Alaska high schools at the Alaska Association of School Governments' Annual Fall Conference held on October 18, 1986, unanimously passed a resolution to repeal the current marijuana law and make the drug in all its forms illegal in Alaska.



**BOYS & GIRLS CLUBS
OF ALASKA**

Administrative Offices
2300 W. 36th Avenue
Anchorage, Alaska 99517
(907) 248-0088

Officers
David G. Kolesky
President
Caroline Dowling
President-Elect
Michael P. Chudecka
V.P. - Property Management
Mary Bath Finley
V.P. - Programs
Bill Woodland
V.P. - Athletics
Cynthia Miles
Treasurer
LaJuana Strelli
Secretary

March 27, 1987

Representative Terry Martin
P.O. Box V
Juneau, AK 99811

Dear Terry:

On behalf of Boys & Girls Clubs of Alaska and its Board of Directors, I urge your continued support for House Bill 55. As you are aware, substance abuse among Alaska's young continues to prevail in alarming numbers. The recriminalization of marijuana is an important step the State must take to bring those numbers down.

Boys & Girls Clubs have addressed the drug and alcohol problem with today's youth and are developing programs aimed at education and service of needs related to substance abuse. The State of Alaska's recriminalization of marijuana will not only boost our efforts, but also the work of many other agencies, schools and private businesses throughout Alaska. Your participation is appreciated.

Sincerely,

David Choquette
David Choquette
Board Member

cc: David G. Kolesky, President

Board of Directors

Peter S. Aadland
Elaine Andrews
Bob Baer
Dave Baumeister
Karen L. Beck
Tom Behan
*Carl Brady, Jr.
David Choquette
William Doss
Bobbi Enloe
Michael A. Flaa
Mike Gordon
Jack Good
Carroll Grant
*Gerald Grilly
Carolyn Guess
Rick Hagen
William J. Hofer
Robert D. Jackson
George Kallas
Hans Kruger
Dave Kuta
Fritz Ledbetter
Eins Lorange
Ken Lythgoe
Jay Dee Martin
Kathy Moores
Fred Moseley
Murphy O'Brien
Ski Olsonoski
Bill Parks
*Don Patterson
Andrew A. Reimer
Rick Short
Paul K. Skogland
Barbara Steckel
Gene Zerke

Honorary Board of Trustees

Ken Brady
*Richard Collins
Don Ellis
*J. Chester Gordon
Walter J. Hickle
Ben Humphries
George N. Nelson
George Petrovich
Edward Rasmuson
George Sullivan
Ike Waldrop
Leo Walsh

Alaska Heritage Club
Standard Alaska Production Co.
Anchorage Daily News

Executive Director
Richard L. Hanlin

*Past Presidents



Alaska State Legislature

SENATOR PAUL FISCHER, Chairman
SENATOR JOE JOSEPHSON, Vice Chairman
SENATOR LLOYD JONES
SENATOR JAY KERTULLA
SENATOR RICK HALFORD



P. O. BOX V
ROOM 508
STATE CAPITOL
(907) 465-3762

Senate Committee on Health, Education and Social Services

April 9, 1987

To: Senator Jay Kerttula, Chairman &
Members of Senate Judiciary Committee

From: Senator Paul Fischer

Subject: SB 32, Recriminalizing Marijuana

The Senate Health Education and Social Services Committee has held extensive hearings on the marijuana issue. The Committee held 4 public hearings including 2 statewide teleconferences. A total of 85 people testified of which 50 testified for recriminalization and 29 against. Six people gave us their undecided philosophical reflections. The written testimony and POMs have been overwhelming in favor of recriminalization.

Throughout the course of our hearings, it became apparent that the first section of the bill, "Legislative Findings", was going to be the emphasis and heart of the bill. We must draft a law that is capable of persuading the Courts that the detrimental effects of marijuana override the Constitution's questions to the right to privacy laid out in the *Ravin* decision. We do not have a right to privacy with respect to cocaine, LSD, or heroin for obvious reasons. The Senate HESS Committee found, that some of these same reasons now apply to marijuana based upon new scientific evidence that was not previously available during the *Ravin* decision. The conclusions of this new evidence is listed in the first section of the bill entitled "Legislative Findings". Further information substantiating these findings can be found in an accompanying memo and reference materials in my office.

The CS offered by the Senate HESS Committee incorporates these new findings in a convincing and compelling format that will both aid in the bill's passage and State's defense in court if the new law should be challenged.

Attached please find the minutes of our Committee hearings.

STATE OF ALASKA THE LEGISLATURE

POUCH Y - STATE CAPITOL
JUNEAU, ALASKA 99811
907-465-3100

LEGISLATIVE AFFAIRS AGENCY LEGISLATIVE REFERENCE LIBRARY

Copies of minutes listed below were originally included in this file. The minutes are available on the STAIRS database CMPR. In order to save space copies of minutes have not been left in the files.

Mary Van Nimwegen

S. HESS	Feb. 18, 1987	7:10 pm
S. HESS	Feb. 25, 1987.	7:07 pm
S. HESS	Feb. 27, 1987	3:30 pm

mentioned in previous
S. HESS committee
minutes Feb. 1987

LIST OF DOCUMENTS

1. Institute of Medicine, Division of Health Sciences
Policy. Marijuana and Health. 1982.

2. State Troopers and Public Health Department. Annual
Drug Report to the Alaska Legislature. 1984.

3. Anchorage Crime Commission. Marijuana Study. 1985.

Harold Heinze, Chairman of the Anchorage Crime Commis-
sion. Letter dated 2/25/87.

4. Robert A. Harrington, Chief of Galena Police Depart-
ment. Letter dated 2/24/87.

Brent C. Moody, Village Public Safety Officer. Letter
to Senator Paul Fischer.

Central Council, Tlingit and Haida Indian Tribes of
Alaska. Letter dated 2/23/87.

D. A. Anslinger, III, Chief of Ketchikan Police Depart-
ment. Letter dated 2/24/87.

5. Municipality of Anchorage, Anchorage Assembly. Resolu-
tion.
6. Dalterio, Dr. Susan L. "Marijuana and the Unborn."
Listen, a Journal of Better Living. 1984.
7. Spence, W.R., M.D. Marijuana and Its Effects. March,
1985.
8. Secretary of the Department of Health and Human Servic-
es. Drug Abuse and Drug Abuse Research: The First in a
Series of Triennial Reports to Congress. 1984.
9. McCoy, Kathleen. "Scared Straight." We Alaskans.
February, 1987.
10. Secretary of Health and Human Services. Marijuana and
Health: Eighth Annual Report to the U.S. Congress. 1980.
11. Secretary of Health and Human Services. Marijuana and
Health: Ninth Annual Report to the U.S. Congress. 1982.
12. National Institute on Drug Abuse, Department of Health
and Human Services. For Parents Only: What you need to
know about marijuana. 1981.

13. National Institute on Drug Abuse, Department of Health and Human Services. Marijuana: Just Say No.

14. National Institute on Drug Abuse, Department of Health and Human Services. For Kids Only: What you should know about marijuana.

15. Mann, Peggy. "Marijuana Alert III: The Devastation of Personality." Readers Digest. December, 1981.

16. Bromwell, Susan. "How I got my Daughter to Stop Smoking Pot." Good Housekeeping. March, 1979.

17. "Drugs: Use and Abuse in the Southern Panhandle." New Alaskan. September, 1983.

"Drugs: Use and Abuse in the Southern Panhandle." New Alaskan. January and February, 1982.

18. Editorial from Ketchikan Daily News. Anchorage Times.

Konet, Bob. Letter to the Editor. Ketchikan Daily News. 2/6/84.

19. Kiwanis Club of Anchorage. Resolution.

20. Reagan, President. The White House. Office of the Press Secretary. Remarks by the President. 8/4/86.
21. The War on Drug Abuse
22. Continuation of Fiscal Note Analysis for HB 55.
23. Alaska Court of Appeals. Marijuana is a controlled substance: State v. Resek.
24. Jennings, Mary. Effects of the Decriminalization of Marijuana. March, 1986.
25. FBI National Academy Associates, Alaska Chapter. Letter to Representative Martin from Pat Wellington, President. 2/9/87.
26. Congressional Delegation Request.
27. City of Saxon. City of Wrangell. City of Ketchikan. City of Valdez. Ketchikan Gateway Borough School District. Galena City School District. Alaska Association of School Governments.
28. National Institute on Drug Abuse, Department of Health and Human Services. Research 31: Marijuana Research Findings. June, 1980.

Others:

National Institute of Justice, U.S. Department of Justice.
Drug Use and Pretrial Crime in the District of Columbia.
October, 1984.

Konet, Bob. Letter to Walt Furnace. Ward Cove. 2/18/85.

Smith, Carol, Dr. "Retarding Reproduction: How marijuana users impair their sexuality and fertility." Listen. February, 1983.

Committees of Correspondence. "Nipping marijuana in the bud: A comparison of paraquat, the herbicide, with Cannabis, nature's toxic plant." Drug Abuse Newsletter.

Adams, Robert. Letter to all House members. 4/30/84.

Burrell, Sharon. Letter to Joe Hayes. 4/16/84.

Committees of Correspondence. "A Straight Pitch about Marijuana." Junior League of Dallas. 1982.

Committees of Correspondence. "What Parents Must Learn about Marijuana."

Mann, Peggy. "Death on the Highways: Driving on Drink and Pot." Published in Families, a Reader's Digest Publication condensed from The Saturday Evening Post. 1981.

Alaska State Legislature

SENATOR PAUL FISCHER, Chairman
SENATOR JOE JOSEPHSON, Vice Chairman
SENATOR LLOYD JONES
SENATOR JAY KERTULLA
SENATOR RICK HALFORD



P. O. BOX V
ROOM 508
STATE CAPITOL
(907) 465-3762

Senate Committee on Health, Education and Social Services

REFERENCES FOR LEGISLATIVE FINDINGS TO CS SB 32 (HESS)

Subsection (a)

1. Marijuana and Health, Institute of Medicine, National Academy Press, 1982. Page 10
2. Institute, page 20.
3. Institute, page 26
4. original (*original bill finding, see House Research Report #87.158*)
5. original
6. Institute, page 16. Also, conversation with officials at state crime lab.
7. Conversation with crime lab officials.
8. original
9. original
10. original
11. original
12. original
13. original
14. 21 U.S.C. 812.

Subsection (b)

1. Essentially a conclusion
2. "Patterns of Drug Use: Community Survey", Center for Alcohol and Addiction Studies, UAA; Benard Segal, Ph.D., editor; 1983. Also "Patterns of Drug Use: School Survey", same publisher and editor.

3. Same as 2.

4. Conversation with Teresa Johnson, Anchorage School District, March 1987. Includes elements of a legislative conclusion and finding.

5. Conclusion.

6. A conclusion

Consult the attached House Research Agency report dated February 27, 1987 for those items marked as being from the original bill.



ALASKA STATE LEGISLATURE
HOUSE OF REPRESENTATIVES
RESEARCH AGENCY

P.O. Box Y, State Capitol
Juneau, Alaska 99811-3100
Mail Stop 3100
(907) 465-3991

February 27, 1987

MEMORANDUM

TO: Representative Terry Martin

ATTN: John Manley

FROM: Penelope Weyhrauch
Legislative Analyst

RE: Findings on Marijuana (House Bill 55)
Research Request 87.158

You asked us to substantiate the findings on marijuana included in House Bill 55. I have addressed each of the findings included in the bill with the most applicable research available to me. Wherever possible, I have presented the research without paraphrasing it. For this reason, the memorandum may not read smoothly. As you requested, I have not included any research which disputes the findings set out in the bill.

1. Delta-9-tetrahydrocannabinol (THC), the mind-altering ingredient in marijuana, is not soluble in water, but goes into the fatty tissues of the brain, testicles, ovaries, and other internal organs, and takes 30 days to be eliminated from the body.

According to Dr. W.D.M. Paton, Professor of Pharmacology at Oxford University, "the various cannabinoid substances are highly soluble in fat, but have a low solubility in water".¹ Other research shows that "THC--the principal psychoactive ingredient of marijuana...tends to accumulate in the brain and gonads and other fatty tissues."²

¹George K. Russell, "Marihuana Today--A Compilation of Medical Findings for the Layman," p. 45.

²Senator Eastland, Chairman of the Internal Security Subcommittee of the United States Senate, May 1974, summarizing testimony given before the Subcommittee. Quoted in "Marihuana Today", p. 14.

Research completed by the National Institute on Drug Abuse shows that THC tends to remain for long periods of time in fatty tissues. Five days after a single injection of THC, 20 percent of the THC remains stored in body fats. Complete elimination of a single dose can take 30 days.³

2. 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, initiative, as well as moodiness and depression.

Studies indicate that a tolerance to THC can develop, when increasing doses of a drug are required to produce the same effect.⁴ "It appears now, both in animals and in humans, that tolerance develops quite rapidly to many of the effects of THC. The more frequent the administration and the higher the dose the more rapidly it develops, but even subjects smoking as little as one marijuana cigarette per day in a laboratory experiment demonstrate tolerance on some behavioral and physiologic dimensions."⁵

To maintain constant blood levels of THC, healthy subjects were given doses of the oral equivalent of several marijuana cigarettes a day. Within hours after the last dose of THC, subjects showed "irritability, restlessness, decreased appetite, sleep disturbances, sweating, tremor, nausea, vomiting and diarrhea."⁶

3. 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.

"We have found that...behaviors are linked behaviors, so that the consumption of any substance, licit or illicit, is positively correlated with an increased consumption of all other substances."⁷ "Taking the total of animal and human research, simultaneous use of both alcohol and marijuana

³"Marijuana Research Findings: 1980," Research Monograph Series 31, National Institute on Drug Abuse, U.S. Department of Health and Human Services, p. 57.

⁴"Marijuana Today," pp. 73 - 74.

⁵"Marijuana Research Findings: 1980," p. 74.

⁶"Marijuana Research Findings: 1980," p. 75. See also "Marijuana and Health," Report of a Study by a Committee of the Institute of Medicine, Division of Health Sciences Policy, 1982, p. 27.

⁷R.L. DuPont, testimony before the Senate Subcommittee on Internal Security, May 1975, ref. 90, pp. 461-471. Quoted in "Marijuana Today," p. 16.

typically has more profound effect than the use of either alone."⁸ "From the evidence it can be said that these two psychochemicals add to the effects of each other. This is common 'street' knowledge, and it is confirmed in the laboratory. The degree of intoxication is increased, and it lasts longer. This means that behavior and psychomotor functioning are more impaired."⁹

4. The THC content of a marijuana cigarette 10 years ago was one percent, but it is as high as 10 percent per cigarette today.

"The marijuana used today is many times--five to ten times--stronger than in the 60s. At the beginning of the drug movement, marijuana with THC content as low as .02 to .5 percent was commonly available and marijuana with two percent THC was considered 'real good grass.' Now confiscated marijuana analyzed in government laboratories has been found to have THC content as high as 14 percent."¹⁰

"'Street' marijuana has increased markedly in potency over the past five years. Confiscated materials in 1975 rarely exceeded one percent THC content. By 1979, samples as high as five percent THC content were common. 'Hash oil,' a marijuana extract unavailable a decade ago, has been found to have a THC content as high as 28 percent, with more typical samples analyzed by University of Mississippi chemists ranging from 15 to 20 percent THC."¹¹

5. Marijuana causes 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.

"The acute anxiety reaction that may occur during marijuana intoxication can include paranoid delusions,... a full blown acute toxic psychosis with loss of contact with reality, delusions, hallucinations... These acute reactions seem to occur most frequently in individuals who are under stress, depressed, or have a history of schizophrenia."¹²

⁸"Marijuana Research Findings: 1980," pp. 38, and 170.

⁹Sidney Cohen, M.D., and Phyllis J. Lessin, "Marijuana and Alcohol," American Council for Drug Education, 1982, p. 21.

¹⁰Helen C. Jones, "On Marijuana Reconsidered," Executive Health, Volume 10, Number 5, February, 1984.

¹¹"Marijuana Research Findings: 1980," p. 2.

¹²"Marijuana Research Findings: 1980," pp. 71-72. See also "Marijuana and Health," p. 126.

One researcher described a higher dose-related phase of cannabis intoxication as "...the appearance of delusions, labile emotions, particularly anxiety, decreased impulse control and, at the highest doses, profound sensory illusions and hallucinations."¹³ Dr. Harris Isbell, with the University of Kentucky Medical Center, confirmed these findings, stating that "...the data in our experiments definitely indicate that the psychotomimetic (capable of inducing altered states of consciousness) effects of THC are dependent on dosage and that sufficiently high doses can cause psychotic reactions in any individual." Dr. Isbell classified cannabis among the hallucinogens.¹⁴

One report stated that "...acute psychotic behavior resembling schizophrenic psychosis..." had been reported.¹⁵ Another said that "Sufficient clinical information is available to recommend abstinence for schizophrenics in remission, because of the danger of relapse."¹⁶

6. 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.

"Recent clinical evidence and findings from several research laboratories demonstrate that cannabis inhalation may have seriously damaging effects on human lung tissue... The damage is described as 'pre-cancerous.' The caustic and irritating effects of cannabis smoke are well known to users, and recent work has shown that 'like tar from tobacco cigarettes, reefer tar is carcinogenic when painted onto mouse skin.' Benzopyrene, a potent carcinogenic agent, is 50 percent more concentrated in the smoke of marijuana than smoke from varieties of high tar Kentucky tobacco."¹⁷

Dr. Cecile Leuchtenberger of the Swiss Institute for Experimental Cancer Research exposed small portions of excised mouse lung tissue to standardized puffs of marijuana. She summarized her work by stating: "The observations that marijuana cigarette smoke stimulates irregular growth in the respiratory system which resembles closely precancerous lesions would indicate that long-term inhalation of marijuana cigarette smoke may either directly evoke lung cancer or may at least contribute to the development of lung cancer."¹⁸

¹³"Marijuana Research Findings: 1980," p. 62.

¹⁴"Marijuana Today," p. 24.

¹⁵Robert G. Heath, M.D., "Marijuana and the Brain," The American Council on Marijuana and Other Psychoactive Drugs, 1981, p. 6.

¹⁶"Drug Abuse and Drug Abuse Research," The first in a Series of Triennial Reports to Congress, Department of Health and Human Services, 1984, p. 77.

¹⁷"Marijuana Today," pp. 54 - 55.

¹⁸"Marijuana Today," pp. 55 - 56.

"According to researchers at the American Health Foundation, marijuana smoke contains 50 percent more cancer-producing hydrocarbons than tobacco smoke."¹⁹ Further, "...abnormalities suggestive of cancerous lesions have been recorded."²⁰

7. THC affects eggs, sperm, sexual hormones, and the development of a fetus, and marijuana use may result in deformed or undersized offspring.

"Studies have shown that THC accumulates in the ovaries of the female, where it will kill and injure eggs" and that a "...significant decrease in sperm concentration and total sperm count occurs."²¹ "This effect is apparently accompanied by a decline in sperm motility and an increase in abnormal sperm forms."²²

"Studies with laboratory animals clearly show that the crude drug marijuana and THC...inhibit secretion of the pituitary hormones, luteinizing hormone and follicle stimulating hormone as well as prolactin. These changes in pituitary hormone levels produce decreases in sex steroid hormones and cause disruption of ovulation and spermatogenesis. With chronic drug use, disruption of sex accessory organs (e.g., uterus and vagina in the female; prostate gland and seminal vesicles in the male) has also been observed."²³

Other studies show that "...the risks of pregnancy loss and other adverse effects on the fetus are increased by marijuana use...significant changes consistent with retardation of fetal growth and development have been observed."²⁴

"Low maternal weight gain during pregnancy, maternal illnesses during pregnancy, and cigarette and marijuana smoking during pregnancy were consistently related to adverse fetal development. Women who used marijuana during pregnancy delivered infants with significantly smaller

¹⁹"On Marijuana Reconsidered," p. 2.

²⁰"Marijuana and Health," p. 63. See also "Effects of Long Term Marijuana Use", p. 156, and, "Marijuana and Health," pp. 3, and 62.

²¹"Marijuana," Narcotic Information Bulletin, No.1-80, p. 2.

²²Carol Grace Smith, Ph.D. and Ricardo H. Asch, M.D., "Marijuana and Reproduction," the American Council for Drug Education, 1982; pp. 16, 17.

²³"Marijuana and Reproduction," p. 7.

²⁴"Marijuana and Reproduction", p. 8.

birth weight, body length and head circumference, as well as infants who were five times more likely to have features compatible with the fetal alcohol syndrome."²⁵

"In males, marijuana has been found temporarily to lower testosterone, the principal male sex hormone, decrease sperm count, cause abnormalities in the sperm...In women, a study of marijuana users done at the Masters and Johnson Institute found that the drug disrupted the menstrual cycle...At the University of California, Davis, Dr. Ethel Sassenrath, on exposing pregnant rhesus monkeys (who have a reproductive system similar to humans), to THC in doses equal to one or two marijuana cigarettes a day for humans, found significantly lower weight gains during pregnancy and 40 percent of the conceptions ending in miscarriages, fetal deaths, stillbirths, or infant deaths shortly after birth."

8. Other physical reactions to marijuana include irreversible changes in the brain, sinusitis, pharyngitis, bronchitis, emphysema, increased heart rate, and decreased blood circulation.

One study stated that "The findings reported here indicate that exposure to ...THC...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."²⁶

Testimony on this subject before the Senate Subcommittee on Internal Security was summarized by finding that: "1) Chronic cannabis smoking can produce sinusitis, pharyngitis, bronchitis, emphysema and other respiratory difficulties in a year or less, as opposed to ten or twenty years of cigarette smoking to produce similar complications; and 2) Cannabis smoke, or cannabis smoke mixed with (tobacco) cigarette smoke, is far more damaging to lung tissue than tobacco smoke alone."²⁷

"There is good evidence to show that marijuana increases the work of the heart, usually by raising heart rate and in some persons, by raising blood pressure."²⁸

²⁵"Marijuana and Reproduction," p. 16, 17.

²⁶Robert G. Heath, M.D., "Marijuana and the Brain," The American Council on Marijuana and Other Psychoactive Drugs, Inc., 1981, p. 10.

²⁷"Marijuana Today," p. 14. See also "Marijuana and Health," p. 60.

²⁸"Marijuana and Health," p. 3.

9. Other psychological reactions to marijuana include loss of memory, impairment in thinking, reading comprehension, and verbal and arithmetic problem solving; impairment of perception of distance and time; and anxiety, panic, paranoia, psychosis, and psychological dependence.

Dr. Ronald C. Bloodworth, Clinical Director at the Psychiatric Institute of Atlanta, reported that "...Many heavy users suffer from distorted emotional responses, disordered thinking, and loss of memory and motivation." Dr. Bloodworth also reported that there is enough evidence to confirm that psychologic dependence is common among marijuana users and that physical dependence can also occur.²⁹

Other studies concur with Dr. Bloodworth's findings: "...cannabis intoxication...impairs judgments of distance and time, memory for recent events, ability to learn new information, and physical coordination,"³⁰ and, "...several studies have shown that marijuana intoxication impairs driving, flying and other complex skilled activities. Many elements of effective psychomotor performance are worsened by the drug because of decrements in recent memory, tracking performance, glare recovery, motor coordination, depth perception, time sense, and peripheral vision."³¹

"Under the influence of moderate doses of the drug, most investigators report that subjects consistently overestimate the amount of time that has elapsed. Thus, under the influence of marijuana, a given event is reported to last longer than it actually does last."³²

"Marijuana's popularity notwithstanding, a surprisingly high proportion of users report reactions that they regard as unpleasant or undesirable. For example, 33 percent of regular users reported that while intoxicated they occasionally experienced such symptoms as acute panic, paranoid reaction, hallucinations, and unpleasant distortions in body image."³³

Another study reported that "16 percent of regular users reported anxiety, fearfulness, confusion, dependency, or aggressive urges as a usual occurrence. Acute paranoid reactions under controlled conditions has also been reported."³⁴

²⁹-----
²⁹"On Marijuana Reconsidered," p. 4.

³⁰"Marijuana Research Findings: 1980," page 67.

³¹"Marijuana Research Findings: 1980," p.71.

³²"Marijuana and Health," p. 116.

³³"Marijuana and Health," p. 121.

³⁴"Marijuana and Health," pp. 122 to 123.

Representative Martin
February 27, 1987
Page 8

"Cannabis psychosis refers to a chronic psychotic condition (out of contact with reality) reportedly seen in heavy marijuana users, but extending beyond the period of acute intoxication. Some authors have described a schizophrenia-like picture with delusions and hallucinations."³⁶

"Although infrequent..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 reaction."³⁷

* * *

I hope this information is useful to you. If you would like excerpts from the articles cited in this memorandum, please contact our agency.

³⁶"Marijuana and Health," p. 124.

³⁷"Effects of Long Term Marijuana Use," p. 158.

THE PRECEDING PAGES WERE TREATED AS
A UNIT IN THE ORIGINAL FILE.

MARIJUANA AND HEALTH

EIGHTH ANNUAL REPORT
TO THE
U.S. CONGRESS
From the
Secretary of
Health and
Human Services
1980



MARIJUANA AND HEALTH

**Eighth Annual Report
to the U.S. Congress
From the Secretary of
Health and Human Services
1980**

**National Institute on Drug Abuse
5600 Fishers Lane
Rockville, Maryland 20857**



ACKNOWLEDGMENTS

Preparation of the Eighth Marijuana and Health Report has been made possible by the generous contribution of preliminary reports and other information by members of the scientific community. Their assistance is gratefully acknowledged.

Several researchers provided technical reviews on which this Report is based. They include:

- Dr. Sidney Cohen -- Therapeutic Aspects
- Dr. Douglas P. Ferraro -- Acute Effects of Marijuana on
Human Memory and Cognition
- Dr. Jack Harclerode -- The Effect of Marijuana on Reproduction
and Development
- Dr. Reese Jones -- Human Effects: An Overview
- Dr. Albert J. Siemens -- Effects of Cannabis in Combination
with Ethanol and Other Drugs
- Dr. Carol Grace Smith -- Effects of Marijuana on Neuroendo-
crine Function
- Dr. Carlton E. Turner -- Chemistry and Metabolism

Members of the National Institute on Drug Abuse staff who reviewed the Report and offered many helpful suggestions included: Drs. Monique Braude, Meyer Glantz, Tom Glynn, Dan Lettieri, William Pollin, Stephen Szara, and Robert Willette.

Dr. Robert C. Petersen of the NIDA staff wrote the Report and had primary responsibility for its overall preparation.

TABLE OF CONTENTS

Executive Summary	v
Introduction	1
Nature and Extent of Marijuana Use in the United States	2
Summary--Nature and Extent of Marijuana Use	5
Current Attitudes and Beliefs About Marijuana	5
Human Effects	7
Chemistry and Metabolism of Cannabis	7
Acute Effects of Marijuana	10
Acute Marijuana Intoxication and Complex Psychomotor Performance in Driving and Flying	11
Pulmonary Effects	12
Reproductive Effects of Marijuana	15
Cardiovascular Effects	17
Marijuana and the Immune Response	18
Chromosome Abnormalities	18
Alterations in Cell Metabolism	19
Brain Damage Research	19
Psychopathology	21
Effects of Chronic Use on Intellectual Functioning	24
Tolerance and Dependence	26
Therapeutic Aspects	28
Control of Nausea in Cancer Chemotherapy	28
Glaucoma	29
Other Therapeutic Uses	30
Effects of Marijuana in Combination with Alcohol and Other Drugs	32
The Hazards of Marijuana Versus Other Recreational Drugs	35
Future Directions	35
References	38

EXECUTIVE SUMMARY

In this eighth edition of the Marijuana and Health Report several areas of recent developments in marijuana research are highlighted together with a summary of the scientific research accumulated through the end of 1979 concerning the drug's possible health implications.

Nature and Extent of Use

By contrast with a decade ago, marijuana use now often begins at a much earlier age and is more likely to be frequent rather than experimental use. The most significant increases noted in the 1977 National Survey of drug use were in marijuana use by 12-to-17-year-olds. Other, more recent sources of data are generally consistent. Among high school seniors, for example, daily use nearly doubled from the Class of 1975 to those of 1978 and 1979 (from 5.8 percent to 10.7 and 10.3 percent for each of these classes). Moreover the percentage of each of these senior classes which began use in the ninth grade or earlier has also nearly doubled (from 16.9 percent of the Class of 1975 to 30.4 percent of the 1979 class). Despite these increases in use, most members of all age groups surveyed continue to disapprove of regular marijuana use and to advocate continued prohibition.

Chemistry

"Street" marijuana has increased markedly in potency over the past five years. Confiscated materials in 1975 rarely exceeded one percent THC content. By 1979 samples as high as five percent THC content were common. "Hash oil," a marijuana extract unavailable a decade ago, has been found to have a THC content as high as 28 percent, with more typical samples analyzed by University of Mississippi chemists ranging from fifteen to twenty percent THC.

Considerable progress has been made in developing simpler laboratory techniques for detecting marijuana use by examining body fluids. Methods are now being field tested which will probably be commercially available by mid 1980 which can be used for such purposes as detection of driving under the influence of marijuana.

Acute Effects

A review of marijuana's acute effects on intellectual functioning done for this year's report indicates the data is generally consistent: marijuana intoxication interferes with immediate memory

and a wide range of intellectual tasks in a manner that might be expected to impair classroom learning among student users. There is also good evidence that marijuana interferes with driving skills and is a significant factor in erratic driving.

Long Term Effects

While much remains to be learned about the chronic effects of marijuana, there are converging lines of evidence with respect to its pulmonary effects. Both animal and human experiments suggest that marijuana impairs lung function to a greater extent than tobacco cigarettes do. While there is as yet no direct evidence that it can play a causal role in lung cancer, it is known that, like tobacco smoke residuals, the "tar" from marijuana is tumor-producing when applied to the skin of test animals. One known cancer-producing chemical, benzopyrene, has been reported to be 70 percent more abundant in marijuana smoke than in tobacco smoke. Following exposure to marijuana smoke the lung's defense systems against bacterial invasion have been shown to be impaired.

Although the evidence is by no means definitive, several kinds of animal and human research have suggested that heavy marijuana use may impair reproductive functioning. Such impairment may include diminished sperm count and motility in males and possible interference with fertility in females. Such preliminary findings may have greater significance for the marginally fertile. Given the many unknowns concerning the effects of marijuana on fetal development, the use of marijuana during pregnancy should continue to be strongly discouraged.

Other questions of possible marijuana effects continue to be unresolved. Evidence concerning an effect on the body's principal defense against disease, the immune response, remains contradictory. While some human studies have found laboratory evidence of impairment, others have not, and the clinical significance of such findings is still in doubt. There have been no large-scale epidemiological studies to determine whether or not chronic marijuana users suffer from infections and other diseases to a greater extent than do nonusers of similar life style. Evidence concerning possible effects on chromosomes is also contradictory and its clinical significance questionable.

Psychopathological Effects

There have been few new developments in this area. An acute panic anxiety reaction is the most common adverse psychological reaction to use, especially when unexpectedly strong material is consumed. A number of clinicians have cautioned against use of marijuana by those with a history of serious psychological problems or who have previously had drug-precipitated emotional disturbances (so-called "bad trips"). While more serious psychiatric problems such as a cannabis-related psychosis have been reported in countries with a long tradition of use, such reactions

e
do not appear common here. Concern has been expressed that availability of much stronger varieties of cannabis may result in more serious problems than in the past.

o
t
While there have been a number of overseas studies of the impact of chronic marijuana use on intellectual functioning, most of which have reported some impairment, the quality of such studies is highly variable and the question also remains in doubt. Studies of American users have not generally reported such impairment, although the American experience has been limited to relatively highly motivated college populations using smaller amounts of cannabis for shorter periods of time. Since user populations in the United States are generally younger than those overseas, the question of possible impact on younger users is an important one which remains to be studied.

e.
Therapeutic Uses

f
se
a
Overall, marijuana, THC and related drugs have shown definite promise in treating the nausea and vomiting which often accompany cancer chemotherapy. While thus far they have not proven to be invariably superior to other medication, they may be enduringly useful with patients for whom other drugs are relatively ineffective.

y
a-
A second therapeutic application which has received wide publicity is the use of THC or marijuana in reducing the vision-destroying intraocular pressure in open-angle glaucoma. Initial trials with oral THC found the drug to be of variable success, although when used with other standard drugs better results were achieved. An eye drop preparation has been developed which in initial human trials produced eye irritation and was not consistently effective. Additional studies are in progress.

f
ch
na
ent
It should once again be emphasized that although marijuana, THC and related drugs have shown some therapeutic promise, much work remains to be done and that any pharmaceuticals developed will be chemically related but not identical to the constituents of the natural material. Such compounds would be chosen to minimize undesirable side effects and to provide a better-focused therapeutic effect. Like any other new medication, chemically related materials must be carefully tested for toxicity and for therapeutic effectiveness.



INTRODUCTION

This edition of Marijuana and Health represents the eighth in a series of annual reports from the Secretary of Health, Education, and Welfare to the Congress and the American people as required by Title V of Public Law 91-296. The seventh edition dated 1977, which included research findings available to the end of 1977, was released last year. This edition has been dated 1980 so as to reduce the confusion concerning the date of actual release. In order to make it as current as possible, research reports have been included virtually to the end of 1979. Although it is not yet possible to be definitive in our answers to many of the health questions that marijuana use raises, the report once again tries to answer the central question as it can best be answered at this time: "What are the health implications of marijuana use for Americans?"

While all of us would wish for greater certainty in this area, such certainty is not yet possible. The American marijuana experience has been of brief duration. It is comparatively recently that significant numbers of individuals have been using the more potent cannabis now available on a daily basis. As our experience with tobacco and alcohol demonstrates, it frequently requires many years of use by large numbers for long range effects of a drug to become apparent. While there are cultures in which cannabis use has been traditional for many years, the drug is often used differently, and traditional users rarely include women or the very young. Perhaps the most disquieting development in our society has been the rapid increase in younger users, under age eighteen. Use is beginning earlier and earlier and is often on a daily basis. Even those who regard occasional use by well integrated, healthy adults as unlikely to pose serious public health problems agree that use, especially frequent use, by children and adolescents can be seriously disruptive.

Research developments since issuance of the seventh report last year include additional information on the possible effects on reproduction and pulmonary function. Despite our increasing knowledge, much remains to be learned about the effects of chronic use. Unfortunately, our present limited knowledge is often interpreted as indicating that marijuana is "safe." More accurately, there are many areas in which we simply do not know the parameters of risk. We do know that even acute use poses hazards in driving and other complex behavior and definitely interferes with memory and intellectual functioning while "high." As use comes to involve both younger and older persons it becomes increasingly important that we be able to specify more precisely the kinds and degree of public health risk which present and anticipated levels of cannabis use pose. This report summarizing our present knowledge is another step in achieving a better understanding of marijuana's public health implications.

NATURE AND EXTENT OF MARIJUANA USE IN THE UNITED STATES

Although a comprehensive updated picture of national trends in marijuana use since the last 1977 National Survey on Drug Abuse will not be available until the 1979 Survey results have been tabulated and analyzed in mid-1980, a review of previous years and of more limited recent findings indicates a generally consistent upward trend in use.* There are indicators that the increase is greatest among younger users (under 18). For example, the most notable changes in the 1977 National Survey from its predecessor in 1976 were a 25 percent increase in the total of those between ages 12 and 17 who had ever used marijuana and a nearly 30 percent increase in the number of that age group who were currently using marijuana (i.e., who had used it in the month preceding the Survey). By contrast, current use in the over-18 population did not increase significantly. Nearly three out of ten (28.2 percent) of 12-to 17-year-olds in 1977 reported having tried marijuana at some point in their lives; nearly one in six (16.1 percent) were current users (1).

Young adulthood--from age 18 to 25--represents the peak period for marijuana use. Three out of five in that age group reported having ever used marijuana in the most recent National Survey; over one in four (27.7 percent) 18-to 25-year-olds was currently using in 1977. Use continues to be correlated with age. This is true whether we are talking about those who have ever used the drug or about current use. For example, among children between ages 12 and 13, eight percent have had some experience with marijuana, a figure which climbs to 29 percent for 14-and 15-year-olds and to 47 percent for those ages 16 and 17. The 22-to 25-year-old group reports the peak level of use--with 62 percent indicating ever having done so. The percentage who have used is 44 percent in the 26-34-year-old group and only 7 percent of those over 35 report any past use. Similar trends are to be found in current use (i.e., use in the month preceding the Survey). While 4 percent of the 12-and 13-year-olds report current use, the peak years for such use are between 18 and 21. Three out of ten (31 percent) of those between 18 and 21 were current users in the 1977 Survey (1).

Although the percentages of females who had either tried marijuana or were currently using it have generally increased in the course of the five national surveys to date, female use has tended to lag behind that of males. Interestingly enough, among 12-to 17-year-olds, the percentage of girls and boys who had ever used remained nearly equal in the three Surveys conducted in 1971, 1972, and 1974. However, by 1976 the percentage of males who had used in this age group was significantly greater than that of females (26 percent for males and 19 percent for females). In 1977, a still greater difference in cannabis use by the two sexes developed in the 12 to 17 age group (33 percent of males had used at some point compared with 23 percent for females). While boys' use in the 12 to 17 group increased significantly between 1976 and 1977, use by girls did not. Among those over 18, by contrast, prevalence of male use

*see ADDENDUM, pages 37-38

in all five survey years has been consistently higher, about twice that of females up until the 1977 survey in which the gap narrowed. This survey indicates 30 percent of males over 18 had ever used marijuana as compared with 19 percent of females. However, the percentage of females over 18 who had ever used increased statistically significantly between 1976 and 1977 while that of males did not. When one examines current use, generally similar trends are present--male use predominates by a ratio of about two to one among those over 18, while in the 12 to 17 age group the difference is smaller. Half again more boys than girls ages 12 to 17 were currently using in 1977, unchanged from the 1976 findings (1).

Racial differences are of some interest although the broad statistical breakdown into "white" and "other races" categories precludes more detailed analysis. Among the 12 to 17 age group, white use for most survey years has slightly exceeded that of other races whether we are talking about those who have ever used or about those currently using. In 1977, use by whites 12 to 17 significantly increased both in the "ever used" and "current use" categories (from 22 percent to 29 percent ever having used and from 12 percent to 17 percent for current use). Among those over 18 the percentages of whites and of other races who have ever tried marijuana were nearly equal in 1977 (24 percent of whites had used compared to 27 percent of other races) in contrast to previous years in which "other races" use by the over-18 group tended to be greater than that of whites. Among current users in the 12-to 17-year age group, whites consistently predominate over "other races" for all survey years. Among those over 18, current use by whites and other races was approximately equal for all survey years including that of 1977 (eight percent of each group in the current survey).

In earlier national surveys adults with college training were considerably more likely to have used marijuana than were adults who had not gone beyond high school graduation. These differences have narrowed in recent years. For example, the percentage of college graduates who had ever used marijuana at the time of the 1977 Survey was 28 percent, compared to 26 percent of the high school graduates.

In terms of the four geographical regions into which the National Survey results are divided (Northeast, Northcentral, South, and West), the only area to note a statistically significant increase in marijuana use between 1976 and 1977 was the Northeast. There a significant increase was found in the number of 12- to 17-year-olds who reported having used marijuana. By contrast with previous survey years, marijuana use in 1977 in the Northeast approximately equalled that in the West. This was true both for lifetime prevalence and for current use. Other areas of the country had lower levels of use.

If one takes the percentages of cannabis users noted in the 1977 Survey and extrapolates to the general population, 43 million

Americans had tried marijuana as of spring 1977, and about 16 million were currently using the drug (i.e., had smoked it in the month previous to the 1977 Survey).

Although more recent national statistics for the general population are not yet available, there are some additional data on the drug attitudes and behavior of American youth who are at a pivotal point of transition to adult life--their senior year in high school. Since 1975, a representative nationwide sample of high school seniors has been queried. Because of the large sample involved, this survey is a particularly reliable source of information on drug using trends, sensitive to even small changes. It is also a source of information on student attitudes and beliefs about drugs, which may be useful in anticipating future drug trends. While statistically significant increases (i.e., increases likely to reflect actual behavior changes rather than survey artifacts) in marijuana use were noted in each of the years through 1978, data for the senior class of 1979 indicate a leveling off of marijuana use, although at fairly high levels. The percentage of each of the five senior classes from 1975 to 1979 who had tried marijuana steadily increased from 47.3 percent in 1975 to 60.4 percent of the Class of 1979. Indeed, the percentage of 1979 high school seniors with marijuana experience is equal to that of the National Survey's peak-using group, the 18- to 25-year-olds. The increase in use between the classes of 1978 and 1979 was the smallest annual increment to date, less than one percent (2,3).

Daily use rates which rose from six percent in 1975 to 9.1 percent in 1977, reaching a peak level of 10.7 percent in the Class of 1978, were 10.3 percent in 1979. While use within the 30 days prior to each of the surveys rose from a little over a quarter of the seniors of the Class of 1975 to 37.1 percent of the Class of 1978, it leveled off at 36.5 percent in the 1979 senior class. Thus, this study suggests that the proportion of high school seniors using marijuana has remained stable over the past two years (2,3).

A disturbing trend continues to be the tendency toward initial marijuana use at younger ages. For example, 16.9 percent of the Class of 1975 had used the drug prior to the tenth grade, but the corresponding percentages in the 1976, 1977, and 1978 classes were 22.3, 25.2, and 28.2 percent. In the most recent senior high school class studied, the 1979 group, 30.4 percent had used prior to the tenth grade. Thus, the percentage of seniors who first used in the ninth grade or earlier has nearly doubled over the past five years (2,3).

Although overall the use of alcohol and tobacco continues to exceed that of marijuana, daily use of marijuana among high school seniors in the Class of 1978, for example, (10.7 percent) was nearly double that for alcohol (5.7 percent daily use) and exceeded only by daily cigarette smoking (27.5 percent). Daily use of marijuana has been about twice as frequent among males as females. However, at less

frequent levels of marijuana use, the sexes do not differ markedly in the percentages using (2,3).

Nationwide statistics may obscure considerable local variation. For example, in Maryland and Maine, where drug surveys were conducted in 1978, higher levels of daily or nearly daily use of marijuana were found than among high school seniors nationwide (10.7 percent of seniors nationally). In Maryland, use "daily or several times a week" was reported by a quarter (25.3 percent) of the twelfth graders (4). In Maine, nearly one in six high school students reported daily marijuana use, four times as many as used alcohol daily (four percent) (5).

Summary--Nature and Extent of Marijuana Use

Although national data representative of the general population subsequent to 1977 are not available at this time, several trends are noteworthy. Among high school seniors use may be plateauing, although at fairly high levels--over a third of the seniors in recent years--report use in the month preceding the surveys. About one in ten reported daily use in the 1979 senior class. The percentages of seniors using marijuana prior to the tenth grade has steadily increased since 1975, nearly doubling in that five year period.

Current Attitudes and Beliefs About Marijuana

Both the National Survey and the high school senior survey include questions dealing with respondents' attitudes and beliefs about drugs in addition to asking about actual behavior. Such attitudes and beliefs are, of course, subject to change in response to new information and do not necessarily reflect objective reality. Nevertheless, they are of considerable interest in enabling us to better understand user assumptions and present behavior, and they may be to some extent predictive of future behavior.

Despite the general assumption of widespread acceptance of marijuana in our society it is noteworthy that youth (12-17), young adults (18-25), and older adult groups (26+) all contain substantial proportions advocating either that marijuana continue to be illegal or our present laws be made still stricter. Seventy-four percent of youth and 79 percent of older adults take this tack. Even among the peak-using 18-25 year-old group, 40 percent support in about equal proportions the position that marijuana continue to be illegal (20 percent) or that ideally the laws be made still stricter (also 20 percent of the group). Similarly two-thirds of high school seniors disapprove of regular use.

Respondents in the National Survey were also asked to indicate which of a list of drugs each regarded as "addictive," ("that is, anybody who uses it regularly becomes physically and psychologically dependent on it and can't get along without it"). Alcohol and heroin were classified as "addictive" by four out of five or more respondents

in the 12- to 17-, the 18- to 25-, and the over-26 age groups. Tobacco was also typically classified as "addictive," with the percentage so designating it increasing with age (youth: 62.4 percent; young adults: 78.6 percent, and older adults: 83.1 percent). Marijuana, by contrast, was seen as "addictive" by less than half of youth and young adults (47.3 percent and 43.7 percent respectively), but was so classified by over three out of five (63.6 percent) older (26+) adults.

The percentage of high school seniors who disapprove of regular marijuana use has remained fairly constant at just over two-thirds in senior classes from 1975 to 1978 (1975 = 71.9 percent; 1976 = 69.5 percent; 1977 = 65.5 percent; and 1978 = 67.5 percent). A similar percentage to those disapproving of regular marijuana use objects to taking one or two alcoholic drinks each day and to smoking one or more packs of cigarettes daily. A little less than half of the classes of 1976 to 1978 disapproved of occasional marijuana use; about a third objected to even trying it. Although nearly half (or more) of the seniors disapproved of even occasional marijuana use, they did not associate "great risk" with use. The percentage who believe there is great risk of some form of harm even from regular use of marijuana has steadily decreased. While 43.3 percent of the Class of 1975 placed regular use in the "great risk" category, the percentage of those in the 1978 Class who so described it had decreased to 34.9 percent. Only 15 percent in the Class of 1975 saw "great risk" in trying marijuana once or twice, and that has decreased to nearly half (8.1 percent) in the Class of 1978. While three out of five seniors in the Classes from 1975 to 1978 continued to feel people should be legally prohibited from smoking marijuana in public, the percentage who believe that use in private should be legally prohibited has steadily decreased (from a third of the Class of 1975 to a quarter of the Class of 1978). While two out of five 1977 and 1978 seniors believe that cigarette smoking should be legally prohibited in public, only a quarter believe that marijuana smoking should be illegal in private.

F
C
A
i
t
t
t
4
t
c
s
t
F
a
c
A
t
s
t
t
m
a
o
e
t
t
r
r
w
c
o
f
f
o
i
A
m
t
h
a
s
o
c
i
s
c
a
o
s

HUMAN EFFECTS

Chemistry and Metabolism of Cannabis

Although the chemistry and metabolism of marijuana (i.e., the ways in which the drug is broken down and chemically transformed in the body) are technical topics not easily translated into everyday language, they are important. For example, contrary to popular belief, the plant material is quite complex, containing at least 421 individual compounds. Sixty-one of the chemicals which have been identified in the plant--the cannabinoids--are specific to cannabis. Ten are now routinely quantified in identifying cannabis samples. When smoked, some of the chemicals contained are further transformed by burning (pyrolysis) into still other compounds (6).

Plant material differs widely in the amount of the principal psychoactive ingredient--delta-9-tetrahydrocannabinol (THC, for short)--contained, as well as in the proportions of other chemicals. Although the effects of cannabinoids other than delta-9-THC have been studied, much remains to be learned about their effects, both singly and in interaction with one another. While, for many practical purposes, the percentage of delta-9-THC is a useful guide to the psychoactivity of a drug sample, other chemical ingredients may ultimately prove to be important in modifying THC's effects as well as because of their own impact on the body. A good deal of valuable basic research has been done on THC, but it should be emphasized that it is only one ingredient of the natural material. Thus, some of the research on THC may be only partially relevant to the effects of the plant material itself. In addition, the ratios of the different cannabinoids found in cannabis change in response to the passage of time and storage conditions. Plants which have been specifically cultivated for their psychoactivity contain much more delta-9-THC than do those grown for fiber. Most of the cannabis growing wild in the United States derives from plants which were originally cultivated for their fiber, rather than drug content, so that they could be used in making rope and other nondrug products. Thus the THC content of this wild cannabis in the United States rarely exceeds one percent THC.

Although there has been no representative random sampling of illicit marijuana that can provide an accurate indication of changes over time, there is evidence that material now sold is significantly higher in THC content than was true only a few years ago. Chemists at the University of Mississippi who have been analyzing confiscated samples of cannabis for several years have found increases on the order of ten times in potency since 1974. Mexican "brick" (i.e., compressed kilogram quantities of marijuana) samples studied in 1974 averaged about a fifth of one percent delta-9-THC. Mexican samples analyzed thus far in 1979 have averaged nearly two percent. Other cannabis samples, probably of Colombian origin, which were analyzed in 1979 have averaged over four percent THC content. Hash oil, a concentrated liquid marijuana extract not available on the street up until a few years ago has been found to have THC levels

ranging from nearly eleven percent to twenty-eight percent. Such stronger materials are more likely to lead to higher levels of intoxication and to possibly adverse consequences.

As knowledge of cannabis chemistry and metabolism has increased and the role of various metabolites becomes more important, there has been a corresponding need to synthesize supplies of these substances. Research availability of these materials enables us to tease out their effects from those of other constituents. In the past year several improved methods for synthesizing metabolites have been developed. The ability to synthesize marijuana components and metabolites in research quantities has accelerated work on the detection of marijuana in body fluids, as well as permitted studying the drug's metabolism. By radioactively labelling the substance involved, it is possible to trace their passage through the body.

The chemistry of marijuana smoke has commanded considerable attention in recent years. Some 150 compounds have been identified in the smoke itself (7). One of them, benzopyrene, known to be carcinogenic, is 70 percent more abundant in marijuana smoke than in tobacco smoke (7). There is also evidence that more "tar" is found in marijuana cigarettes than in high tar tobacco cigarettes (8).

The metabolism of marijuana is only partially understood. Over 35 metabolites of delta-9-THC have thus far been identified along with several dozen metabolites of other marijuana constituents. Ability to identify and trace the pathways of these chemicals in the body provides vital information concerning how they are stored and eventually eliminated. Such information is useful in helping determine the possible sites of action for long term effects of marijuana.

Detection and quantification of cannabinoids and their metabolites in body fluids continues to be an important problem. Sophisticated laboratory techniques are available for the precise measurement of cannabinoid levels in blood and other biological samples. More routine and simpler techniques have also been developed recently and are currently undergoing field testing. When this is completed and the techniques become generally available (probably by mid 1980), they will be useful for such purposes as the routine laboratory detection of marijuana-intoxicated automobile drivers, screening individuals for current marijuana use in treatment programs, etc. The earlier, more elaborate techniques have been important for research purposes as well as to provide the necessary standards by which the results of more rapid and convenient techniques can be evaluated.

A good beginning has been made in understanding marijuana chemistry and metabolism. It has enabled researchers to demonstrate that marijuana constituents cross the placental barrier and as a result may affect fetal development (9). The presence of cannabinoids in mother's milk also raises the question of possible impact on the

infant of the marijuana-using mother (10). Greater understanding of the chemistry of marijuana has also raised the possibility (cf., Therapeutic Aspects) that one or more of the synthesized components of cannabis in its original or chemically modified form may come to have therapeutic usefulness. Finally, our increased awareness of marijuana's chemical complexity and the ways in which components other than delta-9-THC modify the drug's effects may shed light on the common street belief that different types of marijuana have different effects not wholly related to their THC content.

Acute Effects of Marijuana

Although much recent interest has been focused on the possible long term, chronic effects of marijuana, it is important to recognize that some of the drug's acute effects on intellectual and psychomotor performance have definite practical significance. This includes the likelihood of impaired learning ability when marijuana is used by students during the school day, as well as adverse effects on driving and other complex psychomotor performance.

Effects of the marijuana "high" on various aspects of psychological performance were systematically observed as early as the 1930s and, of course, more subjective accounts of marijuana's effects exist that long antedate scientific description (11, 12). These earlier clinical descriptions have generally been verified by more systematic research investigation.

A wide range of impairment of intellectual performance was initially found. It included such tasks as digit symbol substitution (a timed task in which the individual substitutes a series of symbols for numbers) (13), choice-reaction time (a reaction-time task in which the response depends on rapidly discriminating between choices) (14), the ability to repeat in forward and backward order a succession of digits (15), and to mentally make a succession of repeated subtractions (16). Many other task performances, including concept formation (17), reading comprehension (18), and speech have also been found to be impaired to a greater or lesser extent (19).

Generally, such impairment has been found to be related to several kinds of variables, including the dose of drug, the level of motivation, the individual's tolerance to marijuana, and the complexity and familiarity of the task being performed. More familiar, less demanding tasks are less interfered with than those involving new material and more difficult task requirements. A common denominator to impairment of functioning is the effects of marijuana on short term memory. Marijuana appears to interfere with the transfer of material from immediate to longer term memory storage.(20)

When marijuana is smoked, the ability to recall material learned while "high" is typically impaired. This impairment occurs with a wide variety of verbal, as well as graphic, material. The body of research evidence accumulated to date indicates that marijuana intoxication has a detrimental effect on memory functioning, in that material learned while "high" is significantly less well recalled than that learned in a nondrugged state. This is especially true when the task involves recalling the learned material rather than simply its recognition.

There are now dozens of experimental studies which have been conducted, all of which are generally consistent. While marijuana's acute effects on memory and cognition vary with the task and amounts used, they are almost invariably detrimental.

Although there have been no studies directly assessing the impact of marijuana intoxication on classroom learning the similarities with laboratory experiments which have been done make it virtually certain that the drug interferes with classroom performance as well. Since there is now evidence that substantial numbers of high school students are using marijuana during the course of the school day, it is likely that its use is having a detrimental effect on their classroom functioning and knowledge acquisition.

Acute Marijuana Intoxication and Complex Psychomotor Performance in Driving and Flying

There is good evidence that marijuana use at typical social levels definitely impairs driving ability and related skills. Studies indicating impairment of driving skills include: laboratory assessment of driving-related skills (22), driver-simulator studies (23), test-course performance (24), actual street-driver performance (25) and, as previously reported, a study conducted for the National Highway Traffic Safety Administration of drivers involved in fatal accidents (26).

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. In limited surveys, from 60 percent to 80 percent of marijuana users questioned indicated that they sometimes drive while high.

Marijuana use in combination with alcohol is also quite common and the risk of the two drugs in combination may well be greater than that posed by either substance alone.

A study of drivers involved in fatal accidents in the greater Boston area was conducted by the Boston University Accident Investigation Team. They found that marijuana smokers were over-represented in fatal highway accidents as compared to a control group of nonusers of similar age and sex (26).

A more recent study, conducted by the California State Department of Justice, found that of nearly 1,800 blood samples taken from drivers arrested for driving while intoxicated, sixteen percent were positive for marijuana. Where no alcohol was present in the blood sample (about ten percent of the samples) the incidence of marijuana detected rose to twenty-four percent (27). Additional studies of motorist impairment related to marijuana use are being conducted.

There are, therefore, several converging lines of evidence that driving performance is impaired when under the influence of marijuana, viz.: users' subjective assessments of their driving skills while high, measures of driving-related performance, a limited study of actual highway fatalities and a study of individuals arrested for driving while intoxicated.

The parameters of impairment for the average driver under various dosages of marijuana cannot yet be adequately specified. It is important to develop reliable standards for what constitutes driving under the influence of cannabis so as to discourage potentially dangerous driving. At present it is clearly desirable to discourage driving while "high" and to make drivers aware that it is a significant risk.

While there have been no recent studies, previous research findings indicate that experienced pilots undergo marked deterioration in performance under flight simulator test conditions while "high"(28). Thus, flying while marijuana-intoxicated is clearly dangerous.

A continuing danger common to both driving and flying is that some of the perceptual or other performance decrements resulting from marijuana use may persist for some time (possibly several hours) beyond the period of subjective intoxication. Under such circumstances, the individual may attempt to fly or drive without realizing that his or her ability to do so is still impaired although he or she no longer feels "high."

Pulmonary Effects

Because marijuana is typically smoked, its possible adverse effects on the lung and pulmonary function have long been of concern both here and abroad. It is noteworthy that one of the earliest attempts to assess the health and social implications of cannabis use, the Report of the Indian Hemp Drugs Commission of 1893-94, includes observations about its pulmonary effects that are surprisingly similar to more contemporary observations. For example, this report mentions a possible value in the treatment of asthma because of the drug's "pulmonary sedative" qualities. However, it goes on to say that "long continued smoking...doubtless results in the deposition of finely divided carbonaceous matter in the lung tissues, and the presence of other irritating substances in the smoke ultimately causes local irritation of the bronchial mucous membrane, leading to increased secretion, and resulting in the condition which is described as chronic bronchitis in ganja smokers." ("Ganja" is the Indian term for a type of smoked cannabis preparation intermediate in potency between that of marijuana and hashish.) The report makes still another observation strikingly descriptive of present day marijuana use, viz.: "In ganja smoking...the

inspiratory act is far greater and more prolonged, a larger volume of smoke entering the lungs than in cigarette smoking "(29). Such deep inhalation of marijuana may well offset the typically smaller amounts smoked as compared to cigarette smoking. One indication of this is to be found in a study comparing marijuana and cigarette smokers which found that smoking less than one "joint" per day decreases vital capacity--the amount of air the lungs can expel following a deep breath--as much as smoking sixteen cigarettes per day (30). Although the ratio found needs to be confirmed by more extensive research, it suggests that the mode of marijuana inhalation and the way in which it is consumed may result in disproportionately adverse pulmonary effects as compared to modern cigarettes. Part of this difference may be accounted for by the fact that present day cigarettes are filtered and have significantly lower levels of "tar" than was true in the past. Marijuana "joints" are unfiltered and virtually entirely consumed. Moreover, under conditions of ready availability there is some evidence that the number of "joints" consumed may approach that of tobacco cigarettes (as high as ten per day) (31).

Thus far there is no direct evidence that smoking marijuana is correlated with lung cancer. The American experience has been too brief for this to be a likely outcome. Nevertheless, there is good reason for concern about the possibility of pulmonary cancer resulting from extended use over several decades. Like tobacco smoke residuals--so-called "tar"--cannabis residuals when applied to the skin of experimental animals have been shown to be tumor-producing (32). Analysis of marijuana smoke has also found evidence that it contains larger amounts of cancer-producing hydrocarbons. For example, benzopyrene, a known cancer-producing chemical found in tobacco smoke, has been reported to be 70 percent more abundant in marijuana smoke (33).

Cilia which assist in moving inhaled dust and other small foreign particles from the lungs have been found to be adversely affected by marijuana smoke. Following exposure to marijuana smoke, anti-bacterial defense systems in the lung have been shown to be less effective against staphylococcus aureus, a bacterium causing a serious form of pneumonia (34).

While similar effects have not yet been demonstrated in humans, it would be surprising if they did not occur and they may be expected to be dose related. The greater the amount and frequency of use, the greater the likelihood of adverse pulmonary (and other) consequences.

Serious effects on the lungs have been found in rats exposed to marijuana smoke in quantities producing blood cannabinoid levels similar to those of human daily users. The animals were made to inhale smoke in a specially constructed apparatus at daily

intervals for periods corresponding to an eighth to one-half their normal life span. Extensive lung inflammation and degenerative changes were found, similar to but more severe than those produced by exposure to tobacco smoke. The authors conclude that in addition to the irritating effects of smoke, the cannabinoids, chemicals specific to marijuana, "may have a direct undesirable effect on pulmonary function "(35).

There have been several clinical studies of human users which have reported such symptoms as laryngitis, cough, hoarseness, bronchitis, and cellular change in chronic marijuana and hashish smokers which resemble those of heavy tobacco smokers (36,37,38). In one of these, a study of American soldiers stationed in Europe, these symptoms were serious enough for the chronic hashish users involved to seek medical treatment (38). While studies of small numbers of chronic cannabis users in Jamaica, Greece, and Costa Rica did not find evidence of lung pathology, this may have been because traditional users in those countries do not inhale cannabis smoke as deeply and retain it in their lungs as do American users (39,40,41).

From the total body of clinical and experimental evidence accumulated to date, it appears likely that daily use of marijuana leads to lung damage similar to that resulting from heavy cigarette smoking. Since marijuana users often smoke both tobacco and marijuana, the effects of the combination require additional study.

Reproductive Effects of Marijuana

Effects on reproduction have been attributed to marijuana as far back as the earliest cannabis commission's scientific report, that of the Indian Hemp Drugs Commission of 1894. While commenting on a sexual "stimulant" effect similar to that of alcohol, the Report also describes cannabis as "used by ascetics in this country (i.e., India) with the ostensible object of destroying sexual appetite" (42). Quite apart from the drug's psychologically related reproductive effects, there have been numerous experiments with animals detailing effects on organs, processes, and hormone levels related to reproduction. At doses generally much higher than those used by humans, 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. Some more recent studies have examined the effects in animals of drug doses more clearly comparable to heavy use in humans. There have also been a few experiments in which researchers have attempted to study human reproductive effects directly.

With respect to human males, some have found a decrease in levels of serum testosterone correlated with heavy marijuana use, although several others have not. One explanation for this apparent discrepancy in experimental findings is that after smoking marijuana the temporarily depressed levels of testosterone may rapidly return to more usual levels. Depending on the time schedule in which sampling is done, the effect may be missed. Even when testosterone decreases have been found, the levels have been within normal limits. Whether more persistent chronic use of marijuana might result in permanently depressed levels of serum testosterone is not known at this time.

Two studies of the semen of male chronic users have found abnormalities in sperm count, motility and in the structural characteristics of the sperm examined (44,45). In one of these, the semen of 16 healthy young males smoking marijuana under controlled conditions was studied (44). The levels of use while "high"--eight to twenty "joints" per day--were comparable to those of other very heavy users in the general population. Decreases in sperm count and motility were found, together with evidences of structural abnormality in the user's sperm. A second study of Greek chronic users also found structural abnormalities in sperm that were associated with heavy use (45). While the clinical implications of these animal and human findings are by no means certain, decreased fertility might well result, especially in those of already marginal fertility. In the more controlled laboratory study there was an apparent gradual return to normal functioning when marijuana use was discontinued (44). To date (late 1979), there have been no published reports of abnormal offspring of fathers which have been related to their marijuana use. Whether or not alterations in reproductive function might have greater

significance for the developing child or adolescent is not known at this time, although this is a concern since the younger user is probably more vulnerable.

When we turn to the question of marijuana's effects on the female reproductive system, there is some recent animal experimentation with doses comparable to those in actual societal use that suggests possible adverse consequences. Results to date are, however, far from definitive. One study, using THC at levels which the authors describe as "equivalent to moderately heavy marijuana usage in the United States," found that the rate of "reproductive loss" in THC-treated female rhesus monkeys was about four times greater than that in drug-free controls. The majority of these losses represented deaths, abortions, or resorptions of the fetus. No clear pattern of fetal abnormality was evident. The authors conclude that their experimental results "raise the possibility that exposure of the human female to marijuana in amounts in relatively common use may be associated with an increased risk of reproductive loss " (46).

A study of female "street users"--women using marijuana on their own and of unknown potency--has also raised questions about the possible reproductive effects of cannabis on women. In this research 26 women in their twenties who used marijuana three times a week or more for six months or more were compared to a nonusing group of women of similar age. The experimental group had a significantly higher frequency of abnormal menstrual cycles in which they failed to ovulate (i.e., produce a ripened egg) or showed possible evidence of a shortened period of potential fertility--shortened luteal phase of the menstrual cycle. Lowered prolactin levels--a hormone important after childbirth in producing adequate mother's milk--were also found, suggesting that nursing might be impaired in marijuana-using women following childbirth (47). While such findings are of considerable interest, they must be regarded as preliminary. The drug-using women also used larger amounts of alcohol than did the controls, which may have contributed to the result, and there may have been other differences in lifestyle which contributed to the experimental outcome. Nevertheless, both animal and human data raise the distinct possibility that fertility may be impaired in heavy marijuana users as a result of their use. Studies which have been done in countries of more traditional cannabis use are of little value in clarifying this question since male use overwhelmingly predominates among traditional users.

Experiments with radioactively labelled THC (enabling its progress through the body to be traced) clearly indicate that the drug appears in the milk of nursing monkey mothers and in their offspring when the drug is administered to the mothers (48). There is also good evidence that THC and other cannabinoids pass through the placental barrier, reaching the fetus during uterine development where they tend to concentrate in the fetus' fatty tissue

(including the brain) (49). While pre- and postnatal changes related to maternal use have usually only been found with larger doses in animals and have not been reported in humans, the distinct possibility that marijuana use during pregnancy might result in abnormal fetal development makes its use during pregnancy very unwise.

While much remains to be learned about the possible effects of marijuana on reproduction, several points are reasonably clear. Marijuana at higher doses has a range of effects relevant to reproduction in animals. These appear to result from a variety of mechanisms, including the drug's effects on adrenal function and hormone production in testes and ovaries. More recently, at dose levels that might be encountered in the heavy, regular user, possible adverse consequences for fertility in both males and females have been identified. Such effects may be of greater importance for the marginally fertile or the developing adolescent than for the mature, healthy adult. Finally, given the many unknowns concerning possible effects on the human fetus, use of marijuana during pregnancy should be especially discouraged.

Cardiovascular Effects

Although cardiovascular effects of marijuana have been investigated extensively, such research in humans has been largely restricted to healthy young male volunteers in whom the effects appear to be limited in duration and generally benign. One such study examined the short range effects of smoking one to three marijuana cigarettes on 21 male experienced smokers participating in a 94-day in-hospital study of heavy marijuana smoking. They found, as have others, a significant increase in heart rate after smoking although not as clearly dose related as previous findings. They attribute the lack of a clear dose relation to tolerance that developed for the cardiovascular effects of the drug as a result of chronic use. The changes they found in heart functioning were secondary to temporarily increased heart rate and appeared to be free of adverse consequences (50). As previous editions of this report emphasize, however, there is evidence that in patients with already impaired heart function use of marijuana may precipitate chest pain (angina pectoris) more rapidly and following less effort than tobacco cigarettes (51). This possible difference in the response to marijuana in heart disease patients may prove to be of considerable practical significance if use expands to include older populations or if presently young adult users continue to use cannabis as they progress through middle life. Despite the limited evidence to date, a warning to heart patients and others who may have impaired cardiac function not to use marijuana, continues to be justified.

Marijuana and the Immune Response

Because of the importance of the body's natural defenses against illness, principally the immune response, in preserving the health of the individual, reports of impairment of this vital function must continue to be carefully considered. There have been contradictory reports of impairment of this response in humans (52, 53,54,55,56). The animal data, using generally higher doses, have consistently indicated a definite suppression of the test animals' immune responses (51,58). In humans, even when there have been indications of a diminished response, it has not been found in all users and the clinical implications are in doubt. As yet, there has been no epidemiological research undertaken to determine whether marijuana smokers suffer from infections and other diseases to a greater extent than others of similar lifestyle who do not use the drug. For the present, this important question must be regarded as unresolved and the evidence far from clear cut.

Chromosome Abnormalities

There is no new evidence in this area. While there were early reports of increases in chromosomal breaks and abnormalities in human cell cultures, more recent results have been inconclusive. The three positive studies in humans that have been reported have decided limitations (50,60,61). All were retrospective--i.e., studies of those already using marijuana who were compared to nonusers. Such variables as differences in lifestyle, exposure to viral infections and possible use of other drugs, all known to affect chromosome integrity, could not be reliably assessed. In two of the studies, the aberrations observed were found only in a minority of the users.

Three other studies done prospectively (i.e., before and after use) have been reported (62,63,64). All are negative, but the results could have been influenced by the fact that all the subjects had at least some prior experience with marijuana. It is possible that the baseline levels of chromosome deficits may have been elevated by earlier casual marijuana use, thus masking a drug-related effect.

A team investigating the effect of marijuana smoke on human lung cells in laboratory culture has found an increase in the number of cells containing an abnormal number of chromosomes (65). Another investigator who previously reported a high proportion of cells in marijuana smokers with reduced numbers of chromosomes has more recently reported that the addition of delta-9-THC (the principal psychoactive ingredient of marijuana) to human white blood cell cultures also resulted in an increased frequency of cells with abnormally low chromosome numbers (66). The implications of these findings continue to be uncertain.

Overall, there continues to be no convincing evidence that marijuana use causes clinically significant chromosome damage. However, it should be emphasized this year as last that the limitations of the research to date preclude definitive conclusions.

Alterations in Cell Metabolism

The implications of laboratory findings on the inhibition of DNA, RNA, and protein synthesis (all of which are basically related to cellular reproduction and metabolism) are still unknown. Adding delta-9-THC to various types of human and animal cell cultures has been found to inhibit DNA, RNA, and protein synthesis. No effect on DNA repair synthesis was found although the uptake of the chemical precursors within the cells was reduced by half (67).

The possibility that cannabis, or one or more of its chemical ingredients, differentially affects the cell metabolism and reproduction of cancer cells in animals was raised by earlier reported research. One aspect of the mechanism by which this may occur is an inhibition of DNA metabolism in abnormal cells but not in normal cells.

If this preferential inhibition of DNA synthesis in animal tumors also occurs in humans, marijuana might prove of value as an anti-cancer drug. It should, however, once again be stressed that there is no evidence to date that cannabis or any of its synthesized or naturally occurring constituents is of value in inhibiting human cancer growth. If animal findings of a depressed cell immunity response which is also related to cell metabolism are substantiated in humans, cannabis, its synthesized components or chemically related drugs might prove useful in preventing organ rejection in human organ transplant surgery.

Brain Damage Research

A British research report, which originally appeared in 1971, attributed brain atrophy to cannabis use in a group of young male users. In the original study, 10 patients, with histories of from 3-11 years of marijuana use, were examined by air encephalography, a neurological technique used to detect gross brain changes. The authors concluded that their findings suggested that regular use of cannabis may produce brain atrophy (68). This research was faulted on several grounds: all of the patients had used other drugs, making the causal connection with marijuana use questionable; and the appropriateness of the comparison group and diagnostic technique was questionable. The potential seriousness of the original observations justifies a brief review of several subsequent studies bearing on the original British observations.

In a study of chronic Greek users, a different technique (echo-encephalography) was employed to determine whether brain atrophy

might be present in heavy users. The findings from the Greek study were negative; that is, users were not found to differ from nonusers in evidence of gross brain pathology (69).

Two studies were subsequently conducted in Missouri and Massachusetts (70,71). They examined two samples of young men with histories of heavy cannabis smoking using computerized transaxial tomography (CTT), a brain scanning technique for visualizing the anatomy of the brain. In both studies, the resulting brain scans were read by experienced neuroradiologists independent of the drug histories. In neither was there any evidence of cerebral atrophy. As was emphasized last year, however, several additional points should be stressed. Neither study rules out the possibility that more subtle and lasting changes of brain function may occur as a result of heavy and continued marijuana smoking. It is entirely possible to have impairment of brain function from toxic or other causes that is not apparent on gross examination of the brain in the living organism. Nevertheless, virtually all studies completed to date (late 1979) show no evidence of chronically impaired neuropsychologic test performance in humans at dose levels experimentally studied.

A researcher who used electrodes implanted deep within the brains of monkeys instead of more conventional scalp recording techniques has found persistent changes related to chronic use (72). 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 (73). While both 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 are 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 (74,75).

Psychopathology

Although this has been discussed in previous editions of this report, and there is little new evidence since the seventh edition, a reiteration of what is known may be useful to those unfamiliar with the area. The most common adverse psychological reaction of marijuana use represents an exaggeration of the more usual marijuana response in which the individual loses perspective (i.e., the realization that what she or he is experiencing is a transient drug-induced distortion of reality) and becomes acutely anxious. This reaction appears to be more common in relatively inexperienced users although unexpectedly higher doses of the drug (e.g., a higher potency variety of marijuana) can cause such a response even in the more experienced user. The symptoms generally respond to authoritative assurance and diminish in a few hours as the immediate effects of acute intoxication recede.

Transient mild paranoid feelings are common in users and it has been suggested that those who are characterized by more paranoid defense mechanisms are less likely to experience other acute adverse reactions. It has been repeatedly emphasized that reactions of users are very much influenced by the set and setting of use. Set refers to the pre-existing expectations the individual has regarding use; by setting is meant the physical environment during use. It is generally conceded that anxiety and mild paranoid reactions are more likely if the user is initially anxious about the experience and/or the circumstances of use are anxiety producing. Additional research support for this clinical impression is found in a field survey which used a questionnaire to measure acute adverse drug reaction. Preliminary work has found that, in a college population, those who are more hypochondriacal, and who feel less in control of their own lives and more at the mercy of external events are more likely to have adverse reactions to marijuana and other psychoactive drugs (79).

An acute brain syndrome associated with cannabis intoxication including such features as clouding of mental processes, disorientation, confusion, and marked memory impairment has been reported (80). It is thought to be dose-related (much more likely at unusually high doses) and to be determined more by the size of the dose than by pre-existing personality. This set of acute symptoms has not been frequently reported in the United States, possibly because until recently very strong cannabis materials were less readily available here than in some overseas locations. Acute brain syndrome also diminishes as the toxic effects of the drug wear off.

Descriptions of a specific cannabis psychosis are to be found principally in the Eastern literature from cultures where use

is typically more frequent and at much higher doses than those generally consumed in the United States (81). It continues to be difficult to interpret such reports because the diagnosis of mental illness is partly dependent upon sociocultural factors. In addition, the diagnostic picture is frequently complicated by use of other drugs and earlier evidence of psychopathology not necessarily associated with drug use. While the overseas studies conducted under United States auspices in Jamaica, Greece, and Costa Rica did not find such adverse consequences, the small size of the user samples studied, together with the probable rarity of the disorder, would have made its detection unlikely.

One clinical study in India has contrasted the features of a paranoid psychosis arising in the course of long term cannabis use with that of paranoid schizophrenia. Twenty-five consecutive patients admitted with each diagnosis were compared. The cannabis users, reportedly, had used the drug for 5 or more years in amounts up to several grams per day in gradually increasing quantities. Those diagnosed as having a cannabis psychosis were characterized by the authors as showing more bizarre behavior, more violence and panic, an absence of schizophrenic thinking and greater insight into their illness. Patients with the cannabis-related disorder recovered rapidly upon being hospitalized and being treated with a major tranquilizer (82).

In this and other clinical studies, it is often difficult to distinguish the role of cannabis from that of pre-existing psychological problems or other environmental precipitants in marijuana-related psychological difficulties. Frequently, heavy marijuana users are also those who have had emotional problems prior to use.

Some further indication of this is to be found in a paper reporting on four cases of well documented schizophrenia in which the use of marijuana is believed to have led to an exacerbation of psychotic symptoms in patients whose psychoses were in at least partial remission prior to use. The author concludes that "While marijuana can perhaps be safely used by many persons, this is not so with the schizophrenic." He urges that schizophrenics be alerted to the special hazards he feels marijuana poses for them in the same way other patients would routinely be alerted to possible hazardous interactions between their illness and substances they might use (83).

In a detailed review of the relationship between cannabis and violence the author concludes that while marijuana probably does not precipitate violent behavior in the majority of users, nevertheless there may be some individuals with a prior history of poor impulse control or special circumstances of stress which combine with pre-existing personality may make use inadvisable.

It is not clear, however, he points out, whether it is specifically marijuana which might have the undesirable effect of releasing violence or any of a variety of other drugs including alcohol (84).

Based on his experience with some five thousand drug-related psychoses encountered while medical director of many youth festivals, one author has summarized his clinical experience including that with marijuana users. In his experience, serious adverse reactions to marijuana are rare, but he offers several sources of concern about its widespread and indiscriminate use. Specifically, he feels that the possibly unexpectedly high potency of some of the cannabis preparations may pose a hazard for those used to weaker materials. Although he believes it to be very rare, he thinks that it is possible to have a psychotic reaction to marijuana. He also believes that persistent psychiatric symptoms after psychotic drug experiences are more common than is generally believed, as many as 5 to 10 percent of those cases which he was able to follow up. While some patients reporting "flashbacks" had their initial "bad trip" on drugs other than marijuana, the flashback recreation of the disturbing aspects of the original experience frequently occurred following alcohol or marijuana use. He concludes by advising that "Those with a history of emotional disturbances and especially 'bad trips' (i.e., previous drug precipitated emotional disturbances) should avoid intoxicants including alcohol and marijuana." Finally, this author advises that present emergency room and psychiatric hospital procedures should be altered to make the situation less judgmental, less frightening and coercive, more compassionate and more acceptable to youth, with more homelike and reassuring surroundings (85).

Marijuana flashbacks--spontaneous recurrences of feelings and perceptions similar to those produced by the drug itself--have been reported. A survey of United States Army users found that flashbacks occurred in both frequent and infrequent users and were not necessarily related to a history of LSD use. Such occurrences may range from the quite vivid recreation of a drug-related experience to a mild evocation of a previous incident. The origin of such experiences is uncertain but those who have had them typically appear to require little or no treatment (86).

One source of information about possible adverse reaction to drugs, including marijuana, is the federally sponsored Drug Abuse Warning Network (DAWN). This is a nationwide reporting system which provides information about the frequency with which various drugs in common use are implicated in patient contacts with such facilities as hospital emergency rooms.

During a 1-year period beginning in May 1976 and ending in April 1977, marijuana ranked thirteenth among the drugs mentioned in drug-related emergency room contacts. But during the year 1978, the most recent year for which complete data are available, marijuana had risen to sixth place. While such figures are not always easy to interpret, they do suggest that marijuana is not an uncommon factor in causing individuals to seek help and that its importance may be rising, possibly because of an increase in the number using the drug or because of the increased availability of stronger materials more likely to precipitate adverse reactions.

Effects of Chronic Use on Intellectual Functioning

The question of whether or not enduring effects on memory and other aspects of intellectual functioning occur as a result of chronic use is a difficult one to answer. While three more carefully controlled studies of heavy users in Jamaica, Greece, and Costa Rica failed to find evidence of this, several caveats should be mentioned. The numbers studied were small, the testing procedures with the populations studied may have been insensitive to drug-induced decrements, if any, and even the mode of drug use may have differed from American use. Overall, the majority of studies have suggested impairment does occur. Unfortunately, the quality of studies in this area leaves much to be desired. Thus the issue still remains in significant doubt, especially with reference to American users.

A retrospective study of an Egyptian prison population of cannabis users compared 850 chronic users with 839 noncannabis-using controls, using a number of tests of psychological functioning. Users were reported to be slower in their psychomotor performance and to show impaired visual coordination and memory for designs. These performance deficiencies were found to be more common in younger, better educated users from urban backgrounds than in older, illiterate users from rural areas (87,88). This study has been sharply criticized for alleged sampling and psychometric deficiencies and equally sharply defended by its author (89,90). Despite the apparent disagreement on many points, there was agreement on the desirability of replicating the work and possibly doing further analysis of the original data. The large samples employed, despite some of the methodological deficiencies, might well make the original Egyptian study more sensitive to modest differences between smoker and nonsmoker groups which smaller studies may well have missed. At present the information available does not permit a conclusive judgment of the adequacy of the study's findings particularly if the data were subjected to more elaborate analysis designed to take some of the criticisms leveled against the study into account.

ty
ns.

A study of chronic cannabis users in Northern India has been published based primarily on a comparison of 11 male users (out of a larger sample of 23, in turn chosen from 139 long term cannabis users) with 11 male nonusers who were matched in terms of age, occupation, and marital status. Users had all used cannabis equivalent to about 50 mg THC per day (about the equivalent of 5 to 10 "joints" of typical 1 to 2 percent THC content marijuana) for 5 years or more. They were given physical examinations including various laboratory tests of blood and urine as well as chest X-rays, electrocardiogram (EKG), and electroencephalogram (EEG). Subjects were also given a range of psychological tests of intelligence, memory, and other intellectual functions sometimes impaired in the brain-damaged.

The physical examinations including all but one of the laboratory tests (for uric acid blood levels which were found to be somewhat elevated in users) were normal for both users and controls. On the psychological tests, however, users did significantly less well than did nonusers on: two measures of intelligence (9 to 11 I.Q. points lower for users), a measure of memory, a task requiring reproduction from memory of geometric figures, a test of combined cognitive psychomotor speed, and a test of time perception (91).

Unfortunately, several questions of methodology which might have had an influence on these findings are not clear from the report. Twenty-three users more carefully examined were selected from a larger sample of 139 long-term heavy cannabis users and of these only 11 were then matched with 11 nonusers. It is not clear whether the basis for selection of the initial 23 was random or whether some non-random criteria were used such as ready availability, willingness to be further tested, need for possible inducements to participate, etc. The authors themselves raise the question whether the impairments found in user functioning were caused by drug use or if the impairments detected existed prior to such use. They argue for the desirability of doing a prospective study if the question of cannabis-related impairment of function is ultimately to be resolved. The possibility that other aspects of lifestyle such as inadequate diet might have played a role cannot be dismissed as a factor in the poorer performance of the users. Since users were from among the poorer groups in the society, the cost of their cannabis might well significantly reduce the amounts available for food purchases. At present, the results must be regarded as provocative and should be more carefully explored.

American studies comparing college student users with nonusers have found little in the way of evidence of intellectual performance decrement associated with cannabis use at least as such performance is measured by college grades. As was pointed out in previous reports, the higher levels of motivation of students

A study of chronic cannabis users in Northern India has been published based primarily on a comparison of 11 male users (out of a larger sample of 23, in turn chosen from 139 long term cannabis users) with 11 male nonusers who were matched in terms of age, occupation, and marital status. Users had all used cannabis equivalent to about 50 mg THC per day (about the equivalent of 5 to 10 "joints" of typical 1 to 2 percent THC content marijuana) for 5 years or more. They were given physical examinations including various laboratory tests of blood and urine as well as chest X-rays, electrocardiogram (EKG), and electroencephalogram (EEG). Subjects were also given a range of psychological tests of intelligence, memory, and other intellectual functions sometimes impaired in the brain-damaged.

The physical examinations including all but one of the laboratory tests (for uric acid blood levels which were found to be somewhat elevated in users) were normal for both users and controls. On the psychological tests, however, users did significantly less well than did nonusers on: two measures of intelligence (9 to 11 I.Q. points lower for users), a measure of memory, a task requiring reproduction from memory of geometric figures, a test of combined cognitive psychomotor speed, and a test of time perception (91).

Unfortunately, several questions of methodology which might have had an influence on these findings are not clear from the report. Twenty-three users more carefully examined were selected from a larger sample of 139 long-term heavy cannabis users and of these only 11 were then matched with 11 nonusers. It is not clear whether the basis for selection of the initial 23 was random or whether some non-random criteria were used such as ready availability, willingness to be further tested, need for possible inducements to participate, etc. The authors themselves raise the question whether the impairments found in user functioning were caused by drug use or if the impairments detected existed prior to such use. They argue for the desirability of doing a prospective study if the question of cannabis-related impairment of function is ultimately to be resolved. The possibility that other aspects of lifestyle such as inadequate diet might have played a role cannot be dismissed as a factor in the poorer performance of the users. Since users were from among the poorer groups in the society, the cost of their cannabis might well significantly reduce the amounts available for food purchases. At present, the results must be regarded as provocative and should be more carefully explored.

American studies comparing college student users with nonusers have found little in the way of evidence of intellectual performance decrement associated with cannabis use at least as such performance is measured by college grades. As was pointed out in previous reports, the higher levels of motivation of students

in the schools studied, the rather modest levels of use compared with that overseas and the possibility that those whose performance was impaired by marijuana use had dropped out earlier, all limit broader interpretation of these more limited findings.

Tolerance and Dependence

Tolerance to cannabis--i.e., a diminished response to a given repeated drug dose--is now well substantiated. Tolerance development was originally suspected because experienced overseas users were able to use large quantities of the drug that would have been toxic to United States users accustomed to smaller amounts of the drug. Carefully conducted studies with known doses of marijuana or THC leave little question that tolerance develops with prolonged use.

Several more detailed reviews of tolerance development to the behavioral and physiological effects of marijuana in both animals and humans have been published (92,93,94). A report detailing tolerance development of 30 young adult subjects in a 94-day closed experimental ward environment has also been published which stresses tolerance to both the effects on heart rate and the subjective "high" (95). The practical implications of this work are that experienced, frequent users of marijuana experience less pronounced physiological and psychological changes at a constant level of use than would less experienced users. This is in some contrast with the original impression that users had a "reverse tolerance"--i.e., a greater sensitivity to marijuana upon repeated use. The latter impression probably derived from the relatively low dose, infrequent use that characterized some of the earlier observations. Under those conditions neophyte users may have become more aware of marijuana's subjective effects with repeated use partly as a result of social learning of what was to be expected from the experience and thus subjectively believed that its effects were enhanced. Since marijuana's metabolites (the transformation products which result as marijuana is metabolized) are also persistent in body fat, it is also possible that repeated low dosage use released some of the previously stored material, enhancing the effects. Whatever the ultimate explanation of these earlier impressions, under conditions of heavier, more regular use, tolerance now appears to be well established.

When one turns to the question of "cannabis dependence" the term has often been used in an imprecise way with meanings ranging from a vague desire to continue use, if available, to the manifestation of physical withdrawal symptoms following its discontinuance. If "dependence" is defined as experiencing definite physical symptoms following withdrawal of the drug, there is now experimental evidence that such symptoms can occur at least under conditions of extremely heavy research ward administration that

red
s.
seas
d
doses
lops
nals
which
sub-
are
ant
ome
se
re-
the
may
re-
to
d
s
ible
e
erm
i-
i-
e
ow
nder
it

are atypical of social marijuana use in the United States. The changes noted after drug withdrawal under these experimental conditions include one or more of the following symptoms: irritability, restlessness, decreased appetite, sleep disturbance, sweating, tremor, nausea, vomiting, and diarrhea (96,97). Some of these symptoms were experienced in a similar research study by users who selected their own smoked marijuana doses (98). Such a "withdrawal syndrome" has thus far been reported clinically in only one formal research report.

THERAPEUTIC ASPECTS

A "fringe benefit" of the past decade's marijuana research has been a renewed interest in its potential as a therapeutic agent. As earlier editions of these reports have indicated, cannabis has a very ancient history of use for the treatment of an unusually wide range of human ills. Almost from the dawn of history, cannabis has been used in many parts of the world as a pharmaceutical preparation. As recently as 1937, tinctures of cannabis were still listed in the United States Pharmacopoeia and presumably used therapeutically in the United States. One limitation of these earlier preparations was the extreme variability of drug potency--ranging from inert or nearly so to unexpectedly potent.

Renewed interest in the potential usefulness of cannabis or of some synthetically related drug has led to experimentation with these drugs for a wide range of symptoms and disorders. Although several of these applications have shown promise, much remains to be learned about even the most promising applications.

Control of Nausea in Cancer Chemotherapy

Use of marijuana, THC, or related drugs for the treatment of the extreme nausea and vomiting which often accompany cancer chemotherapy is probably the single most promising application of these drugs. While by no means invariably effective, they are sometimes valuable when other standard anti-nausea drugs are not. One of the earlier studies done in 1970 found that THC-treated cancer chemotherapy patients showed improved appetite and diminished weight loss (99). A subsequent study done in Boston found that when compared with a placebo--that is, an inert substance--in a double-blind study in which neither patients nor physicians knew which drug was being administered, THC had an antiemetic effect in seven out of ten patients. The placebo-treated patients showed no improvement (100). In one recent study of 15 patients receiving methotrexate for their bone cancer, THC or placebo was randomly assigned. Fourteen of the 15 patients showed improvement following the use of THC. The amount of reduction in nausea and vomiting was closely related to the dose of THC given. At the highest THC dose employed, in 6 percent of the treatment sessions, patients experienced nausea and/or vomiting, compared to 44 percent when half the dosage was used. Such adverse symptoms were found in 72 percent of the sessions in which the pharmacologically inert placebo was employed. In a second phase of the same experiment, four patients who had shown excellent therapeutic response in the first phase were again treated with THC, but this time much less favorable results were achieved. The reasons for this are unclear, although the authors suggest the possibility that these patients developed a tolerance to the effect during the first phase of the experiment (101). Other studies have attempted to compare marijuana-related drugs to other standard anti-nausea medication to determine their relative effectiveness. Nabilone, a drug chemically related to marijuana constituents, was compared to

prochlorperazine, a standard anti-nausea drug, in a series of 113 patients receiving cancer chemotherapy. Eighty percent responded to nabilone, compared to 32 percent who responded to prochlorperazine (102). Use of this experimental drug has, however, since been suspended because of toxic effects observed in dogs.

A partial analysis of the response of the first 66 patients of a series of 200 receiving prochlorperazine and THC in an experimental design in which each patient received trials of both found that equal numbers--25--preferred each, 12 had no preference, and four patients did not respond to the question. Sleepiness was the most common side effect of both drugs (103).

Overall, marijuana, THC, and related drugs show promise for treating the nausea and vomiting which are common side effects of chemotherapy. Although thus far, THC and marijuana do not appear to be invariably superior to other medication, they may be useful with patients for whom other drugs are relatively ineffective.

Glaucoma

A second treatment application which has received wide publicity in the mass media is to reduce the vision-destroying intraocular pressure which occurs in open-angle glaucoma. This use is based on the original observation, both in normal young men and in test animals, that such pressure reductions occur (104). Initial trials with oral THC alone found the drug to be of variable success. When used as a supplemental drug with other standard intraocular-pressure-reducing drugs, greater success was achieved. Because of the desirability of developing a more convenient dosage form with fewer side effects, an eye-drop preparation has been tried. Although it showed initial promise in reducing intraocular pressure in rabbits, it produced eye irritation and was ineffective in humans in one trial. Additional human testing is planned.

A recent study employing smoked marijuana with 16 glaucoma patients, eight of whom were hypertensive and eight of whom were not, found that the hypertensive patients showed a significantly greater drop in eye pressure than did those with normal blood pressure (105).

At present, marijuana-related drugs have been shown capable of reducing intraocular pressure in people with glaucoma, alone and in combination with more conventional anti-glaucoma medications. However, the long-term safety and efficacy of marijuana-related drugs administered chronically to glaucoma patients has not been established, nor is there any data from long-term controlled studies to demonstrate whether these preparations can actually preserve visual function in such individuals.

As with other clinical applications, a synthesized drug with fewer of the side effects found with the natural material may ultimately be more useful. Continued clinical trials to determine the most useful combinations with other drugs could be desirable.

Other Therapeutic Uses

A variety of other clinical uses of marijuana have been suggested or experimentally employed. While marijuana's ability to dilate the lung's air passages (bronchodilation) has been thought to have promise in treating asthmatics, the drug's lung-irritating properties seem to have offset this potential benefit. Aerosol preparations for inhalation have shown some promise, but have produced lung irritation and may not be commercially feasible (106). Despite these problems, a marijuana-related drug may still prove to be of limited usefulness since its different mechanism of action from that of conventional drugs may make it useful with some patients with whom other drugs are ineffective.

The paradox that THC and marijuana have both convulsant and anti-convulsant properties has led both to concern about the implications of marijuana use by epileptics and to speculation about its possible value in controlling seizures. In animal experimentation, these drugs have reduced as well as increased seizure activity, depending on how the experiment was conducted. As in the treatment of glaucoma, the possibility that one or more of marijuana's constituents may be useful in combination with other standard antiseizure medication exists, although its usefulness, if any, appears limited at this time. Although a small survey of youthful epileptics did not disclose any particular effect of cannabis use upon their seizure patterns, our present limited knowledge and the possibility that marijuana might adversely affect these patients suggests that caution be exercised in use (107).

While there have been some clinical reports of marijuana reducing muscular spasticity in paraplegics and patients with multiple sclerosis, such work is still in an early stage, and a definite usefulness has not yet been found on a more systematic basis (108).

Still other applications of marijuana in the treatment of depression, pain, and of alcoholism and drug dependence have been variously considered. Although these applications have not been adequately explored, there is little evidence that they are likely to prove useful at this time.

While marijuana and/or its synthesized constituents have shown some promise as therapeutic agents, it should again be emphasized that additional work is necessary before such agents become generally approved as standard medications, even for limited purposes.

If consistently useful medical applications for marijuana are found, it is quite likely that the product or products resulting will be chemically related to but not identical to the natural material's constituents.

gested
ilate
to have
proper-
repara-
iced
Despite
be of
from
ients

Whether or not cannabis, one of its synthesized constituents, or a chemically related compound once again finds a place in modern medicine depends on several considerations. One problem is that pharmaceutically desirable effects may not be persistently useful for the chronic disorders. Tolerance undoubtedly develops for a number of the effects of the natural material. This may also be true for new chemically related compounds. Like any other new medication, chemically related materials must be carefully tested for toxicity and for therapeutic effectiveness. This process is time-consuming and many new pharmaceuticals showing initial promise are ultimately discarded as unanticipated drawbacks and limitations to their use arise.

anti-
lications
possible
these
depending
f glau-
ituents
e medi-
ited at
did not
eizure
that
at

lucing
le
rite
s (108).

epression,
usly con-
ely
prove

own some
d that
rally

re found,
ill be
cial's

EFFECTS OF MARIJUANA IN COMBINATION WITH ALCOHOL AND OTHER DRUGS

Since marijuana is so commonly used in combination with alcohol and other drugs, the combined effects of these drugs has potentially important implications. Given the extremely wide range of possible doses and interactions, it is not surprising that our present knowledge is still quite limited. This is true even of the most commonly used combination, alcohol and marijuana.

A related issue is the extent to which marijuana use might displace alcohol use were both drugs equally available. Although some marijuana users in the 1960s were ideologically opposed to alcohol, it now appears that use of both has generally increased. While it is not possible to be certain what would occur under conditions of equal availability, there is no indication that increased marijuana use among teenagers and young adults has resulted in a decrease in alcohol use. In fact, several researchers have noted a positive correlation between heavy marijuana use and that of alcohol; that is, those using marijuana heavily were more likely to use alcohol than those who either did not use it or used it less frequently. One large scale longitudinal study of children from elementary school to high school age has found that the early use of alcohol (and tobacco) is more common in those who also begin marijuana use early or use it more regularly and heavily (109). In one study of marijuana use in young men conducted in a closed experimental ward setting, marijuana smoking increased regardless of the availability of alcohol, although, conversely, alcohol use decreased when marijuana was available (110). Thus the larger question of what would happen in American culture were marijuana more freely available cannot readily be answered. It might well depend on the kinds of informal social attitudes and controls which developed among users.

Animal studies of the behavioral effects of the alcohol-cannabis (or THC-alcohol) combination have generally found that the combined effect is greater than that of either alone (111). For example, the duration of alcohol-induced sleep increased as much as three-fold when rats or mice also received a marijuana extract or THC prior to being given alcohol (112, 113, 114, 116). Animals receiving THC in doses that ordinarily did not interfere with their ability to remain on a moving belt showed increased alcohol-related impairment of their performance (117). When animals have been simultaneously administered both drugs, conditioned avoidance (i.e., a learned avoidance of a noxious stimulus), general activity level, heart rate, and body temperature have been more affected than when either was used alone (118).

The limited human research to date is generally consistent with the results of animal research. Experiments at alcohol levels within the range commonly used socially showed that performance reductions from combined use are greater than those from the use

of either alone. Such decrements have been detected in reasoning, manual dexterity, and standing steadiness (119,120). Although the effects after 40 minutes were greater than either drug separately, 2 hours and 40 minutes later some of the changes were less than those of THC alone. This apparently antagonistic action under some circumstances may result from the different rate at which the two drugs are metabolized. In more recent experiments, when alcohol was given one hour after THC, the effects of the drugs were clearly additive. Combined use reduced reaction time, cognitive performance, standing steadiness, and psychomotor coordination more than that of either alone (121).

In measuring glare recovery--the time it takes for light adaptation after exposure to bright light--it was only slightly greater for the combination than for either alone (122).

The authors of a research paper dealing with the side effects of alcohol and marijuana caution that the use of the two simultaneously may be dangerous for those with cardiac disorders. In a study of seven healthy male volunteers aged 20 to 29, they found that four of the seven developed intense nausea and vomiting when they smoked a marijuana cigarette after drinking a moderate amount of alcohol. The doses of alcohol involved (1 gm ethanol/kg. of body weight or about 57 cc. of pure alcohol for an average man weighing 154 lbs.) represented about the equivalent of three drinks containing one and a half ounces each of 90 proof liquor. All four men were markedly incapacitated during the height of the adverse effects, although they recovered in three to four hours. The fact that not all seven subjects were equally affected illustrates large individual differences in response. One subject, for example, experienced a marked drop in heart rate under the influence of the drugs--from 150 to 36 beats per minute. When the experiment was repeated with half the amount of alcohol originally used, no adverse effects occurred. The volunteers acknowledged that similar adverse consequences had sometimes occurred when they had used the drug recreationally (123).

Taking the total of animal and human research simultaneous use of both alcohol and marijuana typically has more profound effects than the use of either alone. However, the magnitude and duration of the effect may vary depending on the dosages of the two drugs involved, the type of effect measured, and the time intervals involved in administering the drugs. As with either drug alone, there are also undoubtedly individual differences in response to the drugs in combination.

Animal research has raised the question of a possible cross tolerance between alcohol and marijuana. By this is meant regular administration of one drug may result in a decreased response to another drug, even though the other has not been given. A recent experiment has found that when both alcohol and THC were administered to rats, they developed tolerance to alcohol much more quickly than when

they received only alcohol (124). In humans the question of cross tolerance has not yet been resolved. While there is some evidence that the performance of male heavy marijuana users is less affected by drinking four to five ounces of 100 proof alcohol than is that of nonusers, a later study of performance under similar conditions found the trend to be statistically insignificant (that is, the difference found may well have been the result of chance rather than due to prior marijuana use) (125).

There have been few human studies of the interactive effects of marijuana with drugs other than alcohol. However, limited evidence suggests that such interactions may be significant. A study in which high doses of THC were given to young adult males indicates that chronic marijuana use may affect the persistence of barbiturates in the body as well as their rate of absorption (126). Only limited studies of combined use of amphetamines and marijuana in humans have thus far been done. One study found that simultaneous use resulted in an increase in the intensity and duration of the subjective "high" greater than use of either alone produced (127).

The possibility that absorption, distribution, and the metabolism of therapeutic drugs might be modified by marijuana use has been raised. In rats, aspirin has been found to decrease the rate of disappearance of THC in their blood as well as to increase the THC brain levels (128). Since there are many therapeutic drugs in widespread use which are used in many different forms and dosages, much work remains to be done.

THE HAZARDS OF MARIJUANA VERSUS OTHER RECREATIONAL DRUGS

A question that frequently arises is how hazardous is marijuana as compared to alcohol and tobacco. As appealing as such a comparison is, it is also misleading on several grounds. Any comparison of alcohol and tobacco use and that of marijuana compares drugs with great differences in social acceptability, period of use, and degree of availability. The hazards of alcohol and tobacco are reasonably well known and the social and public health costs quite high. For example, fully 10 percent of alcohol users have been described as having an alcohol problem, and alcohol has been implicated in half the automotive fatalities in the United States. The health costs of alcohol in terms of cirrhosis, mental illness, crime, and industrial accidents can also be documented. A similar analysis can be done for tobacco. By contrast, marijuana has only recently become a popular substance; it remains illegal and most use is not habitual at present. Moreover, unlike cigarettes and alcohol, for which the health hazards can be reasonably well specified, much less is known about the implications of marijuana use.

Any consideration of the hazard a drug poses must take into account not only its present use, but also use that might be reasonably expected in the future. At present, this involves many imponderables such as the parameters of risk for various groups in our society at different levels of use, the likely circumstances of use, effects on user functioning and motivation of heavier use patterns, degree of use restriction possible, combined use with other drugs--to name but a few. As the history of the introduction of alcohol demonstrates, it is very difficult to anticipate the problems which will arise in a given society in advance. 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.

FUTURE DIRECTIONS

The past decade's priority emphasis on Federal marijuana research has brought about an impressive increase in our knowledge concerning cannabis and its effects. Our understanding of the basic chemistry of marijuana, its mode of action in the body, and some of the acute and chronic effects of the drug have all expanded rapidly. Nevertheless, there are still many areas in which our knowledge continues to be modest. For example, we know little about the implications of use by girls and women both for their own health and for possible offspring. Since nearly half of the

American users are females of childbearing age, this is an important area for further research.

As marijuana use has come to include much younger ages--a decade ago use was largely restricted to young adults, now significant numbers use it in their early teens--the need to understand the implications of use by this group has also become imperative. Unfortunately, teasing out the effects of marijuana from that of both other drugs and other aspects of lifestyle is not always easy. Heavier users of marijuana at any age are more likely than nonusers or light users to take other drugs as well. As we have seen, "street" marijuana can also vary in potency from inert or nearly so to material with high THC content, which is very psychoactive.

While carefully controlled animal experimentation in which factors as disparate as genetic and learning history can be specified is very useful, there are important differences between animals and humans. While marijuana, for example, slows heart action in most animals, in humans it accelerates it. And, while significant progress has been made through special apparatus to induce animals to smoke the material, it is not easy to replicate typical conditions of human use.

The National Institute on Drug Abuse (NIDA), the agency within the Department of Health, Education and Welfare* which has principal responsibility for marijuana research, makes repeated use of non-government scientists serving as consultants to assist in determining new directions for research. One of the central questions that has been considered is the desirability of conducting large-scale, long-term epidemiological studies analogous to those which were done to determine the effects of cigarette smoking. Because the level of marijuana use for most of the population has been modest and because the potency of the material has been so variable, this approach is unlikely to produce results in proportion to its high cost. Instead, the Institute has elected to support a large variety of smaller studies focusing on some of the already identified specific effects as well as exploring implications of use in high risk groups.

Following the recommendations of its consultants, NIDA is particularly concerned with studying the implications of use during periods of likely maximum sensitivity. These include childhood, adolescence, and prenatal development. The study of groups receiving standardized health care is being investigated to determine cost-effective means of doing larger scale studies likely to detect effects in children, adolescents, and young adults. Development of standardized data collection methods which will enable researchers to effectively pool data from several sources is also being pursued. This enables us to detect use implications employing samples larger than are available in any single study. Such standardized methods also make it possible to compare data from different sources.

* Now the Department of Health and Human Services (1980)

Because of the increasing importance of multiple drug use patterns, the implications of that type of use are also being studied. While simultaneous use of alcohol and marijuana is the most common pattern, many users use the drug with other licit and illicit drugs. Such patterns of use and their implications must be explored.

It is unlikely that any single approach will be sufficient. Methods as diversified as the study of the impact of marijuana's constituents on cell membrane metabolism to psychosocial research on changing patterns of use are all essential to developing a well-rounded picture of the implications of marijuana use. It is also unlikely that any single piece of research will provide the definitive answers to our concerns about marijuana's effects. As with other drugs, it is probable that our understanding will increase gradually and that the effects of the drug will not be uniform, but will vary significantly depending upon the age, mental and physical health of the user, and the individual differences in vulnerability to the drug's effects.

Finally, given the marked increase in use by children and adolescents, it is important that we develop more effective means of discouraging use. While some progress has been made in this area, much more needs to be learned about individuals and groups at high risk of becoming seriously involved with marijuana use. Through an improved understanding of the factors which play a role in individual vulnerability we may ultimately be better able to "target" prevention efforts toward those most likely to suffer serious adverse consequences rather than at a more general population.

An important step in the ongoing process of exploring the implications of cannabis use and the best ways of coping with it is an independent review of the marijuana area being sponsored by the Department to be conducted in 1980. This review will provide a fresh look at our present knowledge and possible future directions of effort. It will encompass research into the physiological effects of marijuana use as well as behavioral research into such use-related problems as intervention strategies to help adolescents resist peer pressure. A report is expected to be produced in about one year.

ADDENDUM

The 1979 National Survey--A Marijuana Use Update

At the time of completion of the Eighth Marijuana and Health Report (late 1979), the 1979 National Household Survey had not yet been completed. The following addendum is a brief summary of this most recent National Survey, which was released on June 20, 1980.

As has been consistently true since the National Survey was first conducted in 1972, marijuana use is highly correlated with age. This past year (1979), 8 percent of 12- and 13-year-olds reported some experience with the drug, but by ages 14 and 15 the percentage who had used it increased to 32 percent. A simple majority--51 percent--had used it by ages 16 and 17. Peak use was found among 18- to 25-year-olds, a group in which over two-thirds (68 percent) had tried the drug at some time in their lives. Taking the 12- to 17-year-old group as a whole, the percentage that had ever used marijuana had more than doubled since 1972--from 14 percent to 31 percent. Among young adults (18- to 25-year-olds) the increase was smaller--from 48 percent in 1972 to 68 percent in 1979 (a significant increase from 60 percent in 1977).

Current use--defined as use within the month preceding the survey--is also markedly age related. For youth (12 to 17) and young adults (18 to 25), about half as many currently use marijuana as have ever used. Thus 16.7 percent of youth currently use marijuana, figure unchanged from the 1977 survey, but also more than double the 7 percent of this age group that reported current use in 1972. Thirty-five percent of young adults are currently using by late 1979, a figure nearly a third larger than that of 1977. Until this past year's survey, current use was consistently between 25 and 28 percent for all survey years from 1972 to 1977.

For older age groups, that is, those over 26, both lifetime prevalence and current use are markedly lower than for younger persons. Nearly 20 percent (19.6 percent) of older adults had ever used marijuana by 1979, compared to the 7.4 percent who had had marijuana experience in 1972. Current use by this age group has risen from 2.5 percent in 1972 to 6.0 percent this past year (1979). The percentage of older adults reporting current use has nearly doubled since 1977 (from 3.3 to 6 percent).

As the figures indicate, while there have been marked changes in all age groups since 1972, statistically significant changes (i.e., changes not likely to be the result of chance) between 1977 and 1979 were confined to the young adult and older age groups. Youthful use was unchanged from 1977.

This year's survey, for the first time, included questions about perceived hazards of marijuana use. It is noteworthy that only 5 percent of the peak-using 18- to 25-year-old group saw the drug as having "no bad effects." Perceived adverse consequences range from performance and health impairment to possible psychological effects and the increased likelihood of using stronger drugs. Nearly three quarters (72.2 percent) of young adults believed that being high causes impaired driving performance. One in eight young adults felt it would not. These observations on perceived hazards should serve as a useful baseline for future comparisons.

REFERENCES

1. Abelson, H.I., Fishburne, P.M., and Cisin, I. National Survey on Drug Abuse: 1977. National Institute on Drug Abuse, 1977.
2. Johnston, L.D., Bachman, J.G., and O'Malley, P.M. Drugs and the Class of '78: Behaviors Attitudes, and Recent National Trends. Rockville, Md: National Institute on Drug Abuse, 1979.
3. Johnston, L.D. Personal communication. 1979.
4. Maryland Department of Health and Mental Hygiene Drug Abuse Administration. 1978 Survey of Drug Abuse Among Adolescents - General Report. Annapolis, Maryland. March 23, 1979.
5. State of Maine, Department of Human Services, Office of Alcoholism and Drug Abuse Prevention. An Evaluation of the Decriminalization of Marijuana in Maine - 1978. Augusta, Maine. January 5, 1979.
6. Turner, C.E. Chemistry and metabolism of marijuana. In: Petersen, R.C. (ed.). Marijuana Research Findings: 1980. Washington, D.C.: U.S. Government Printing Office, in press.
7. Lee, M.L., Novotny, M., and Bartle, K.D. Gas chromatography/mass spectrometric and nuclear magnetic resonance spectrometric studies on carcinogenic polynuclear aromatic hydrocarbons in tobacco and marijuana smoke condensate. Anal Chem, 48(2): 405-416, 1976.
8. Turner, C.E. See reference 6.
9. Vardaris, R.M.; Weisz, D.J.; Fazel, A.; and Rawitch, A.B. Chronic administration of delta-9-tetrahydrocannabinol to pregnant rats: studies of pup behavior and placental transfer. Pharmacol Biochem Behav, 4:249-254, 1976.
10. Chao, F.-C.; Green, D.E.; Forrest, I.S.; Kaplan, J.N.; Winship-Ball, A.; and Braude, M. The passage of ^{14}C -delta⁹-tetrahydrocannabinol into the milk of lactating squirrel monkeys. Res Commun Chem Pathol Pharmacol, 15(2):303-317, 1976.
11. Bromberg, W. Marijuana intoxication. Am J Psychiatry, 91: 303-330, 1934.
12. Gautier, T. The hashish-eaters' club (1844). In: Haining, P. (ed.). The Hashish Club - An Anthology of Drug Literature. London: Peter Owen, Ltd., 1975.

13. Weil, A.T., Zinberg, N.E., and Nelsen, J.M. Clinical and psychological effects of marijuana in man. Science, 162: 1234-1242, 1968.
14. Clark, L.D. and Naskashima, E.N. Experimental studies of marijuana. Am J Psychiatry, 125:379-384, 1968.
15. Melges, F.T.; Tinklenberg, J.R.; Hollister, L.E.; and Gillespie, H.K. Marijuana and the temporal span of awareness. Arch Gen Psychiatry, 24:564-567, 1971.
16. Manno, J.; Kiplinger, G.F.; Haine, S.E.; Bennett, I.F.; and Forney, R.B. Comparative effects of smoking marijuana or placebo on human motor and mental performance. Clin Pharmacol Ther, 11:808-815, 1970.
17. Klonoff, H., Low, M., and Marcus, A. Neuropsychological effects of marijuana. Can Med Assoc J, 108:150-156, 1973.
18. Clark, L.D., Hughes, R., and Nakashima, E.N. Behavioral effects of marijuana: Experimental studies. Arch Gen Psych, 23:193-198, 1970.
19. Tart, C.T. On Being Stoned, A Psychological Study of Marijuana Intoxication. Palo Alto: Science and Behavior Books, 1971.
20. Tinklenberg, J.R. and Darley, C.F. Psychological and cognitive effects of cannabis. In: Cornell, P.H. and Dorn, N. (eds.). Cannabis and Man. New York: Churchill Livingstone, 1975.
21. Ferraro, D.P. Acute effects of marijuana on human memory and cognition. In: Petersen, R.C. (ed.). Marijuana Research Findings: 1980. Washington, D.C.: U.S. Government Printing Office, in press.
22. Moskowitz, H., McGlothlin, W., and Hulbert, S. The effects of marijuana dosage on driver performance. Contract No. DOT-HS-150-2-236; University of California; Los Angeles, California; 1973.
23. Moskowitz, H. Marijuana and driving. Accident Analysis and Prevention, 8(1):21-26, 1976.
24. Klonoff, H. Effects of marijuana on driving in a restricted area and on city streets: Driving performance and physiological changes. In: Miller, L.L. (ed.). Marijuana: Effects on Human Behavior. New York: Academic Press, 1974. pp. 359-397.
25. Klonoff, H. Marijuana and driving in real-life situations. Science, 186:317-324, 1974.
26. Sterling-Smith, R.S. A special study of drivers most responsible in fatal accidents. Summary for Management Report; Contract No. DOT-HS-310-3-595; April, 1976.

d
:
f mari-
llespie,
1 Gen

and
r pla-
col
effects

effects
:193-

rijuana
971.

gnitive
ds.).

y and
ch
nting

cts of
T-HS-
rnia;

and

cted
ologi-
cts on
359-397.

ns.

spon-
; Con-

27. Reeve, V.C. Incidence of marijuana in a California impaired driver population. State of California; Department of Justice, Division of Law Enforcement Investigative Services Branch; Sacramento; 1979.
28. Janowsky, D.S.; Meacham, M.P.; Blaine, J.D.; Schorr, M.; and Bozzetti, L.P. Marijuana effects on simulated flying ability. Am J Psychiatry, 133(4):383-388, 1976.
29. Marijuana. Report of the Indian Hemp Drug Commission, 1893-1894. (Reprinted by Thomas Jefferson Publishing Co., Silver Spring, Md., 1969.)
30. Tashkin, D.P., Calvarese, B., and Simmons, M. Respiratory status of 75 chronic marijuana smokers: Comparison with matched controls. UCLA School of Medicine, Los Angeles, California. Abstract in: Am Rev Resp Dis, 117:(4-Part 2)261, 1978.
31. Cohen, S.; Lessin, P.J.; Hahn, P.M.; and Tyrrell, E.D. A 94-day cannabis study. In: Braude, M.C. and Szara, S. (eds.). Pharmacology of Medicine. New York: Raven Press, 1976. pp. 621-626.
32. Hoffmann, D.; Brunnemann, K.D.; Gori, G.B.; and Wynder, E.L. On the carcinogenicity of marihuana smoke. Res Adv Phytochem, 9:63-81, 1975.
33. Novotny, M., Lee, M.C., and Bartle, K.D. A possible chemical basis for the higher mutagenicity of marihuana smoke as compared to tobacco smoke. Experientia, 32(3):280-282, 1976.
34. Huber, G.L.; Simmons, G.A.; McCarthy, C.R.; Cutting, M.B.; Laguarda, R.; and Pereira, W. Depressant effect of marihuana smoke on antibactericidal activity of pulmonary alveolar macrophages. Chest, 68:769-773, 1975.
35. Rosenkrantz, H. and Fleischman, R.W. Effects of cannabis on lungs. In: Nahas, G.G. and Paton, W.D.M. (eds.). Marihuana: Biological Effects. New York: Pergamon Press, 1979. pp. 279-300.
36. Chopra, G.S. Studies on psycho-clinical aspects of long-term marihuana use in 124 cases. Int J Addict, 8:1015-1026, 1973.
37. Henderson, R.L., Tennant, F.S., and Guerry, R. Respiratory manifestations of hashish smoking. Arch Otolaryng, 95:248-251, 1972.
38. Tennant, F.S.; Preble, M.; Prendergast, T.J.; and Ventry, P. Medical manifestations associated with Hashish. J Amer Med Assoc, 216:1965-1969, 1971.
39. Coggins, W.J. Costa Rica Cannabis Project: An interim report on the medical aspects. In: Braude, M.C. and Szara, S. (eds.). Pharmacology of Marihuana. New York: Raven Press, 1976. pp. 667-670.

40. Rubin, V. and Comitas, L. Ganja in Jamaica: The Effects of Marihuana. New York: Anchor/Doubleday, 1976.
41. Stefanis, C., Boulougouris, J., and Liakos, A. Clinical and psychophysiological effects of cannabis on long-term users. In: Braude, M.C. and Szara, S. (eds.). Pharmacology of Marihuana. New York: Raven Press, 1976. pp. 659-665.
42. Marijuana. Report of the Indian Hemp Commission. See reference 29.
43. Harclerode, J. The effect of marijuana on reproduction and development. In: Petersen, R.C. (ed.). Marijuana Research Findings: 1980. Washington, D.C.: U.S. Government Printing Office, in press.
44. Hembree, W.C., Nahas, G.G., and Huang, H.F.S. Changes in human spermatozoa associated with high dose marihuana smoking. In: Nahas, G.G. and Paton, W.D.M. (eds.). Marihuana: Biological Effects. New York: Pergamon Press, 1979. pp. 429-439.
45. Issidorides, M.R. Observations in chronic hashish users: nuclear aberrations in blood and sperm and abnormal acrosomes in spermatozoa. In: Nahas, G.G. and Paton, W.D.M. (eds.). Marihuana: Biological Effects. New York: Pergamon Press, 1979. pp. 377-388.
46. Sassenrath, E.N., Chapman, L.F., and Goo, G.P. Reproduction in Rhesus monkeys chronically exposed to delta-9-THC. In: Nahas, G.G. and Paton, W.D.M. (eds.). Marihuana: Biological Effects. New York: Pergamon Press, 1979. pp. 501-512.
47. Bauman, J.E.; Kolodny, R.L.; Dornbush, R.L.; and Webster, S.K. Endocrine effects of human female chronic marihuana use. In press.
48. Chao, R.-C.; Green, D.E.; Forrest, I.S.; Kaplan, J.N.; Winship-Ball, A.; and Braude, M. The passage of ^{14}C -delta⁹-tetrahydrocannabinol into the milk of lactating squirrel monkeys. Res Commun Chem Pathol Pharmacol, 15(2):303-317, 1976.
49. Vardaris, R.M.; Weisz, D.J.; Fazel, A.; and Rawitch, A.B. Chronic administration of delta-9-tetrahydrocannabinol to pregnant rats: studies of pup behavior and placental transfer. Pharmacol Biochem Behav, 4:249-254, 1976.
50. Nowlan, R. and Cohen, S. Tolerance to marihuana: heart rate and subjective "high." Clin Pharmacol Ther, 22(5):550-555, 1977.
51. Prakash, R. and Aronow, W.S. Effects of marihuana in coronary disease. Reply. Clin Pharmacol Ther, 19(1):94-95, 1976.
52. Nahas, G.G.; Suci-Foca, N.; Armand, J.P.; and Morishima, A. Inhibition of cellular mediated immunity in marihuana smokers. Science, 183:419-420, 1974.

ts of
l and
ars.
f Mari-
reference
and de-
rch Find-
ng Office,
in human
. In:
ogical
s: nuc-
nes in
. Mari-
1979.
ction
In:
ogical
r, S.K.
. In
vinship-
rahydro-
Res
3. Chron-
agnant
Pharma-
t rate
555, 1977.
ronary
5.
a, A.
okers.

53. Gupta, S., Grieco, M., and Cushman, P. Impairment of rosette-forming T-lymphocytes in chronic marihuana smokers. N Eng J Med, 291:874-877, 1974.

54. Silverstein, M.D. and Lessin, P.J. Normal skin test response in chronic marijuana users. Science, 186:740-742, 1974.

55. Petersen, B.H., Graham, J., and Lemberger, L. Marijuana, tetrahydrocannabinol and T-cell function. Life Sciences, 19:395-400, 1976.

56. Cushman, P. and Khurana, R. A controlled cycle of tetrahydrocannabinol smoking: T and B cell rosette formation. Life Sciences, 20:971-980, 1977.

57. Rosenkrantz, H. The immune response and marijuana. In: Nahas, G.G. (ed.). Marihuana: Chemistry, Biochemistry and Cellular Effects. New York: Springer-Verlag, 1976.

58. Zimmerman, S.; Zimmerman, A.M.; Cameron, I.L.; Laurence, H.L. Delta-9-tetrahydrocannabinol, cannabidiol, and cannabinol effects on the immune response of mice. Pharmacology, 15:10-23, 1977.

59. Herha, J. and Obe, G. Chromosomal damage in chronic users of cannabis. Pharmakopsychiatric, 7:328-337, 1974.

60. Kumar, S. and Kunwar, K.B. Chromosome abnormalities in cannabis addicts. J Assoc Physicians India, 19:193-195, 1972.

61. Stenchever, M.A., Kunysz, T.J., and Allen, M.A. Chromosome breakage in users of marijuana. Am J Obstet Gynecol, 118:106-113, 1974.

62. Matsuyama, S.S.; Jarvik, L.F.; Fu, T.K.; and Yen, F.S. Chromosome studies before and after supervised marijuana smoking. In: Braude, M.C. and Szara, S. (eds.). Pharmacology of Marijuana. New York: Raven Press, 1976. pp. 723-729.

63. Matsuyama, S.S.; Yen, F.S.; Jarvik, L.F.; Sparkes, R.S.; Fu, T.K.; Fisher, H.; Reccius, N.; and Frank, I.M. In vivo marijuana exposure and human lymphocyte chromosomes. Mutation Research, 1977.

64. Nichols, W.W.; Miller, R.C.; Heneen, W.; Bradt, C.; Hollister, L.; and Kanter, S. Cytogenetic studies on human subjects receiving marijuana and delta-9-tetrahydrocannabinol. Mutation Research, 26:413-417, 1974.

65. Leuchtenberger, C. and Leuchtenberger, R. Correlated cytological and cytochemical studies of the effects of fresh smoke from marijuana cigarettes on growth and DNA metabolism of animal and human lung cultures. In: Braude, M.C. and Szara, S. (eds.). Pharmacology of Marijuana. New York: Raven Press, 1976. pp. 595-612.

66. Morishima, A.; Henrich, R.T.; Jayaraman, J.; and Nahas, G.G. Hypoploid metaphases in cultured lymphocytes of marihuana smokers. In: Nahas, G.G. and Paton, W.D.M. (eds.). Marihuana: Biological Effects. New York: Pergamon Press, 1979. pp. 371-376.
67. Blevins, R.D. and Regan, J.D. Delta-9-tetrahydrocannabinol: Effect on macromolecular synthesis in human and other mammalian cells. Archives of Toxicology, 35:127-135, 1976.
68. Campbell, A.M.G.; Evans, M.; Thompson, J.L.G.; and Williams, M.R. Cerebral atrophy in young cannabis smokers. Lancet, 1219, 1971.
69. Fink, M.; Volavka, J.; Panagiotopoulos, C.P.; and Stefanis, C. Quantitative EEG studies of marihuana, delta-9-THC, and hashish in man. In: Braude, M.C. and Szara, S. (eds.). Pharmacology of Marihuana. New York: Raven Press, 1976. pp. 383-392.
70. Co, B.T.; Goodwin, D.W.; Gado, M.; Mikhael, M.; and Hill, S.Y. Absence of cerebral atrophy in chronic cannabis users. J A M A, 237(12):1229-1230, 1977.
71. Kuehnle, J.; Mendelson, J.H.; Davis, D.R.; and New, P.F.J. Computed tomographic examination of heavy marihuana smokers. J A M A, 237(12):1231-1232, 1977.
72. Heath, R.G. Marihuana and delta-9-tetrahydrocannabinol: Acute and chronic effects on brain function of monkeys. In: Braude, M.C. and Szara, S. (eds.). Pharmacology of Marihuana. New York: Raven Press, 1976. pp. 345-356.
73. Heath, R.G.; Fitzjarrell, A.T.; Garey, R.E.; and Myers, W.A. Chronic marihuana smoking: Its effect on function and structure of the primate brain. In: Nahas, G.G. and Paton, W.D.M. (eds.). Marihuana: Biological Effects. New York: Pergamon Press, 1979. pp. 713-730.
74. Fink, M.; Volavka, J.; Panagiotopoulos, C.P.; and Stefanis, C. Quantitative EEG studies of marihuana, delta-9-THC, and hashish in man. In: Braude, M.C. and Szara, S. (eds.). Pharmacology of Marihuana. New York: Raven Press, 1976. pp. 383-392.
75. Klonoff, H. and Low, M.D. Psychological and neurophysiological effects of marihuana in man: An interaction model. In: Miller, L.L. (ed.). Marihuana: Effects on Human Behavior. New York: Academic Press, 1974. pp. 359-397.
76. Halikas, J.A. Marihuana use and psychiatric illness. In: Miller, L.L. (ed.). Marihuana: Effects on Human Behavior. New York: Academic Press, 1974. pp. 265-302.

77. Meyer, R.E. Psychiatric consequences of marihuana use: The state of the evidence. In: Tinklenberg, J.R. (ed.). Marihuana and Health Hazards: Methodologic Issues in Current Research. New York: Academic Press, 1975. pp. 133-152.
78. Naditch, M.P. Acute adverse reactions to psychoactive drugs, drug usage and psychopathology. J Abnorm Psychol, 83(4): 394-403, 1974.
79. Naditch, M.P. Progress Report to NIDA, 1976.
80. Meyer, R.E. Psychiatric consequences of marihuana use: The state of the evidence. In: Tinklenberg, J.R. (ed.). Marihuana and Health Hazards: Methodologic Issues in Current Research. New York: Academic Press, 1975. pp. 133-152.
81. Halikas, J.A. Marihuana use and psychiatric illness. In: Miller, L.L. (ed.). Marihuana: Effects on Human Behavior. New York: Academic Press, 1974. pp. 265-302.
82. Thacore, V.R. and Shukla, S.R.P. Cannabis psychosis and paranoid schizophrenia. Arch Gen Psych, 33(3):383-386, 1976.
83. Treffert, D.A. Marihuana use in schizophrenia: a clear hazard. Amer J Psych, 135:10, October 10, 1978.
84. Abel, E.L. The relationship between cannabis and violence: a review. Psychol Bull, 84:193-211, 1977.
85. Abruzzi, W. Drug-induced psychosis. Int J Addict, 12(1): 183-193, 1977.
86. Stanton, M.D., Mintz, J., and Franklin, R.M. Drug flashbacks, II. Some additional findings. Int J Addict, 11(1):53-69, 1976.
87. Soueif, M.I. Chronic cannabis users: Further analysis of objective test results. Bull Narc, 27(4):1-26, 1975.
88. Soueif, M.I. Some determinants of psychological deficits associated with chronic cannabis consumption. Bull Narc, 28(1): 25-42, 1976.
89. Fletcher, J.M. and Satz, P. A methodological commentary on the Egyptian study of chronic hashish use. Bull Narc, 29(2): 29-34, 1977.
90. Soueif, M.I. The Egyptian study of chronic cannabis use: a reply to Fletcher and Satz. Bull Narc, 29(2):35-43, 1977.
91. Wig, N.N. and Varma, V.K. Patterns of long-term heavy cannabis use in North India and its effects on cognitive functions: a preliminary report. Drug and Alcohol Dependence, 2:211-219, 1977.

92. Fried, P.A. Behavioral and electroencephalographic correlates of the chronic use of marihuana - a review. Bull Narc, 29(2): 29-34, 1977.
93. Jones, R.T. and Benowitz, N. The 30-day trip--Clinical studies of cannabis tolerance and dependence. In: Braude, M.C. and Szara, S. (eds.). Pharmacology of Marihuana. New York: Raven Press, 1976. pp. 627-642.
94. Karler, R. Toxicological and pharmacological effects (of marihuana). In: Petersen, R.C. (ed.). NIDA Research Monograph 14, Marihuana Research Findings: 1976. Washington, D.C.: U.S. Government Printing Office, Stock No. 017-024-00622-0, 1977. pp. 55-66.
95. Nowlan, R. and Cohen, S. Tolerance to marihuana: heart rate and subjective "high." Clin Pharmacol Ther, 22(5):550-556, 1977.
96. Jones, R. Human effects. In: Petersen, R.C. (ed.). NIDA Research Monograph 14, Marihuana Research Findings: 1976. Washington, D.C.: U.S. Government Printing Office, Stock No. 017-024 00622-0, 1977. pp. 128-178.
97. Jones, R.T. and Benowitz, N. The 30-day trip--Clinical studies of cannabis tolerance and dependence. In: Braude, M.C. and Szara, S. (eds.). Pharmacology of Marihuana. New York: Raven Press, 1976. pp. 627-642.
98. Mendelson, J.H., Rossi, A.M., and Meyer, R.E. (eds.). The Use of Marihuana, a Psychological and Physiological Inquiry. New York: Plenum Press, 1974.
99. Regelson, W.; Butler, J.R.; Schultz, J.; Kirk, T.; Peck, L.; Green, M.L.; and Zakis, O. Delta-9-THC as an effective anti-depressant and appetite stimulating agent in advanced cancer patients. In: Braude, M.C. and Szara, S. (eds.). Pharmacology of Marijuana. New York: Raven Press, 1976.
100. Sallan, S.E., Zinberg, N.E., and Frei, E. Antiemetic effect of delta-9-THC in patients receiving cancer chemotherapy. New Eng J Med, 293:795-797, 1975.
101. Chang, A.E.; Shiling, D.J.; Stillman, R.C.; Goldberg, N.H.; Seipp, C.A.; Barofsky, I.; Simmon, R.M.; and Rosenberg, S.A. Evaluation of antiemetic effects of delta-9-THC during adjuvant chemotherapy in patients receiving high dose therapy. Annals of Int Med, to be published, 1979.
102. Herman, T.S.; Einhorn, L.H.; Jones, S.E.; Nagy, C.; Chester, A.B.; Dean, J.C.; Furnas, B.; Williams, S.D.; Leigh, S.A.; Dorr, R.T.; and Moon, T.E. Superiority of nabilone over pro-

elates
29(2):

chlorperazine as an antiemetic in patients receiving cancer chemotherapy. New Eng J Med, 300:1295-1297, 1979.

studies
and

103. Ungerleider, J.T. and Andrysiak, T. Effect of inhaled delta-9-THC in reduction of nausea and vomiting associated with bone marrow transplant and chemotherapy. Personal communication, 1979.

f
ono-
n, D.C.:
-0,

104. Hepler, R.S. and Frank, I.M. Marihuana smoking and intraocular pressure. J A M A, 217:1392, 1971.

rate
56,

105. Crawford, W.J. and Merritt, J.C. Effects of tetrahydrocannabinol on arterial and intraocular hypertension. Int J Clin Pharmacol & Biopharm, 17:191-196, 1979.

IDA
6.
k

106. Tashkin, D.P.; Calverese, B.M.; Simmons, M.S.; and Shapiro, B.J. Respiratory status of 74 habitual marijuana smokers. Presented at the annual meeting of the American Thoracic Society, Boston, 1978.

studies
and
Raven

107. Feeney, D.M., Spiker, M., and Weiss, G.K. Marihuana and epilepsy: Activation of symptoms by delta-9-THC. In: Cohen, S. and Stillman, R.C. (eds.). The Therapeutic Potential of Marijuana. New York: Plenum Press, 1976.

The
jury.

108. Petro, D.J. and Ellenberger, C. Marijuana (cannabis sativa) as a therapeutic agent in patients with muscle spasms or spasticity: Case reports and literature review. Presented at the American Academy of Neurology Meeting, Chicago, 1979.

, L.;
anti-
ancer
armacolo-

109. Smith, G.M. and Fogg, C.P. High school performance and behavior before and after initiation of illicit drug use. Fed Proc, 35(3):564, 1976.

ffect of
New Eng

110. Mello, N.K.; Mendelson, J.H.; Kuehnle, J.C.; and Sellers, M.L. Human polydrug use: marijuana and alcohol. J Pharmacol Exp Ther, 207:922-934, 1978.

.H.;
S.A.
adju-
py.

111. Siemens, A.J. Effects of cannabis in combination with ethanol and other drugs. In: Petersen, R.C. (ed.). Marijuana Research Findings: 1980. Washington, D.C.: U.S. Government Printing Office, in press.

ster,
A.;
r pro-

112. Siemens, A.J.; Kalant, H.; Khanna, J.M.; Marshman, J.; and Ho, G. Effect of cannabis on pentobarbital-induced sleeping time and pentobarbital metabolism in the rat. Biochem Pharmacol, 23:477-488, 1974.

114. Phillips, R.N.; Neel, M.A.; Brown, D.J.; and Forney, R.B. Enhancement of caffeine or methamphetamine stimulation in mice with aqueous-suspended delta-9-tetrahydrocannabinol. Pharmacologist, 13:297, 1971.

115. Sofia, R.D. and Knobloch, L.C. The interaction of delta-9-tetrahydrocannabinol pretreatment with various sedative-hypnotic drugs. Psychopharmacologia (Berl), 30:185-194, 1973.
116. Siemens, A.J. and Khanna, J.M. Acute metabolic interactions between ethanol and cannabis. Alcoholism. Clin Exp Res, 1: 343-348, 1977.
117. Kalant, H. and LeBlanc, A.E. Effect of acute and chronic pretreatment with delta-1-tetrahydrocannabinol on motor impairment by ethanol in the rat. Can J Physiol Pharmacol, 52: 291-297, 1974.
118. Pryor, G.T.; Larsen, F.F.; Carr, J.D.; Braude, M.C. Interactions of delta-9-tetrahydrocannabinol with phenobarbital, ethanol and chlordiazepoxide. Pharmacol Biochem Behav, 7: 331-345, 1977.
119. Chesher, G.B.; Franks, H.M.; Hensley, V.R.; Hensley, W.J.; Jackson, D.M.; Starmer, G.A.; and Teo, R.K.C. The interaction of ethanol and delta-9-tetrahydrocannabinol in man. Effects on perceptual, cognitive and motor functions. Med J Aust, 2: 159-163, 1976.
120. Chesher, G.B.; Franks, H.M.; Jackson, D.M.; Starmer, G.A.; and Teo, R.K.C. Ethanol and delta-9-tetrahydrocannabinol. Interactive effects on human perceptual, cognitive and motor functions. Med J Aust, 1:478-481, 1977.
121. Belgrave, B.E.; Bird, K.D.; Chesher, G.B.; Jackson, D.M.; Lubbe, K.E.; Starmer, G.A.; and Teo, R.K.C. The effect of (-) trans-delta-9-tetrahydrocannabinol, alone and in combination with ethanol, on human performance. Psychopharmacology, 62: 53-60, 1979.
122. Brown, B.; Adams, A.J.; Haegerstrom-Portnoy, G.; Jones, R.T.; and Flom, M.C. Pupil size after use of marijuana and alcohol. Am J Ophthalmol, 83:350-354, 1977.
123. Sulkowski, A. and Vachon, L. Side effects of simultaneous alcohol and marijuana use. Amer J Psych, 134(6):691-692, 1977.
124. Siemens, A.J., George, P., and McConnell, J.E. Influence of non-psychoactive drugs on delta-9-tetrahydrocannabinol disposition. Fed Proc, 38:591, 1979.
125. Jones, R.T. and Stone, G.C. Psychological studies of marijuana and alcohol in man. Psychopharmacologia (Berl), 18:108-117, 1970.
126. Benowitz, N.L. and Jones, R.T. Effects of delta-9-tetrahydrocannabinol on drug distribution and metabolism. Clin Pharmacol Ther, 22:259-268, 1977.

127. Evans, M.A.; Harbison, P.D.; Brown, D.J.; and Forney, R.B. Stimulant actions of delta-9-tetrahydrocannabinol in mice. Psychopharmacology, 50:245-250, 1976.

128. Siemens, A.J., George, P., and McConnell, J.E. Influence of non-psychoactive drugs on delta-9-tetrahydrocannabinol disposition. Fed Proc, 38:591, 1979.

373.

ns
l:

pre-
r-

ac-

tion
ts
2:

or

Lub-
)
on
2:

.T.;
chol.

of
;posi-

ij ana
i,

dro-
armacol

☆ U.S. GOVERNMENT PRINTING OFFICE: 1981-341-166/6373

MARIJUANA: THE MYTH OF HARMLESSNESS GOES UP IN SMOKE

by Peggy Mann



Reprinted by the Medical Education and Research Foundation