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Marijuana . . .

infectious disease or cancer. If there were significant damage, we might expect to find a higher rate of these diseases among young people beginning in the 1960s, when marijuana first became popular. There is no evidence of that.

The effects of marijuana on the reproductive system are a more complicated issue. In men, a single dose of THC lowers sperm count and the level of testosterone and other hormones. Tolerance to this effect apparently develops; in the Costa Rican study, marijuana smokers and controls had the same testosterone levels. Although the smokers in that study began using marijuana at an average age of 15, it had not affected their masculine development. There is no evidence that the changes in sperm count and testosterone produced by marijuana affect sexual performance or fertility.

In animal experiments THC has also been reported to lower levels of female hormones and disturb the menstrual cycle. When monkeys, rats, and mice are exposed during pregnancy to amounts of THC equivalent to a heavy human smoker's dose, stillbirths and decreased birth weight are sometimes reported in their offspring. There are also reports of low birth weight, prematurity, and even a condition resembling the fetal alcohol syndrome in some children of women who smoke marijuana heavily during pregnancy. The significance of these reports is unclear because controls are lacking and other circumstances make it hard to attribute causes. To be safe, pregnant and nursing women should follow the standard conservative recommendation to avoid all drugs, including cannabis, that are not absolutely necessary.

A well-confirmed danger of long-term heavy marijuana use is its effect on the lungs. Smoking narrows and inflames air passages and reduces breathing capacity; damage to bronchial cells has been observed in hashish smokers. Possible harmful effects include bronchitis, emphysema, and lung cancer. Marijuana smoke contains the same carcinogens as tobacco smoke, usually in somewhat higher concentrations. Marijuana is also inhaled more deeply and held in the lungs longer, which increases the danger. On the other hand, almost no one smokes 20 marijuana cigarettes a day. Higher THC content in marijuana may reduce the danger of respiratory damage, because less smoking is required for the desired effect. This is true only as long as no significant tolerance develops, and as long as users do not try to get a proportionately more intense effect from a stronger form of the drug.

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Assessing Allegations of Child Sexual Abuse

By Diane H. Schetky, MD and Elissa P. Benedek, MD

Heightened public and professional concern has led to overreporting of suspected child sexual abuse. According to the American Humane Association, 60 percent of such reports are unsubstantiated. Some of these are probably valid cases dropped for lack of evidence or because a child is too young to testify. Since sexual abuse of very young children usually does not involve penetration of orifices, physical evidence is often lacking, and it may also be difficult for a young child to describe such experiences accurately and repeatedly. Other cases are not prosecuted because the law chooses to disregard evidence obtained by highly coercive or suggestive techniques. In perhaps 5 to 30 percent of cases, however, unsubstantiated allegations occur because malicious or well-meaning persons have misinterpreted physical symptoms or behavior that has other causes.

Types of Unfounded Allegations

1. Charges of abuse sometimes arise in divorce cases when there are disputes about custody or visitation rights. The mother may anxiously misinterpret things the father has done while physically caring for their child. Less often a mother vindictively fabricates allegations to punish her former husband or exclude him from the child's life. Children who hear such charges repeated often enough may come to believe them and doubt their own perceptions.

2. A child occasionally makes a false allegation. In rare cases a child's fantasizing about sexual rela-

constantly thinking about the drug, or intoxicated, or recovering from its effects. The habit impairs their mental and physical health and hurts their work, family life, and friendships. They often know that they are using too much and repeatedly make unsuccessful attempts to cut down or stop. These problems seem to afflict proportionately fewer marijuana smokers than users of alcohol, tobacco, heroin, or cocaine. Even heavy users in places like Jamaica and Costa Rica do not seem to be dependent in this damaging sense.

Cause or Effect

It is often difficult to distinguish between drug use as a cause of problems and drug use as an effect; this is especially true in the case of marijuana. Most people who develop a dependency on marijuana would also be likely to develop other dependencies because of anxiety, depression, or feelings of inadequacy. The original condition is likely to matter more than the attempt to relieve it by means of the drug. The troubled teenager who smokes cannabis throughout the school day certainly has a problem, and excessive use of marijuana may be one of its symptoms.

The idea has persisted that in the long run smoking marijuana causes some sort of mental or emotional deterioration. In three major studies conducted in Jamaica, Costa Rica, and Greece, researchers have compared heavy long-term cannabis users with non-users and found no evidence of intellectual or neurological damage, no changes in personality, and no loss of the will to work or participate in society. The Costa Rican study showed no difference between heavy users (seven or more marijuana cigarettes a day) and lighter users (six or fewer cigarettes a day). Experiments in the United States show no effects of fairly heavy marijuana use on learning, perception, or motivation over periods as long as a year.

On the other side are clinical reports of a personality change called the amotivational syndrome. Its symptoms are said to be passivity, aimlessness, apathy, uncommunicativeness, and lack of ambition. Some proposed explanations are hormone changes, brain damage, sedation, and depression. Since the amotivational syndrome does not seem to occur in Greek or Caribbean farm laborers, some writers suggest that it affects only skilled and educated people who need to do more complex thinking.

...m of distinguishing causes from symp- ...s particularly acute here. Heavy drug users in our society are often bored, depressed, and listless, or alienated, cynical, and rebellious. Sometimes the drugs cause these states of mind and sometimes they result from personality characteristics that lead to drug abuse. Drug abuse can be an excuse for failure or a form of self-medication. Because of these complications and ... sence of confirmation from controlled studi... existence of an amotivational syndrome caused by cannabis use has to be regarded as unproven.

Stepping Stone Hypothesis

Much attention has also been devoted to the idea that marijuana smoking leads to the use of opiates and other illicit drugs: the stepping stone hypothesis. In this country, almost everyone who uses any other illicit drug has smoked marijuana first, just as almost everyone who smokes marijuana has drunk alcohol first. Anyone who uses any given drug is more likely to be interested in others, for some of the same reasons. People who use illicit drugs, in particular, are somewhat more likely to find themselves in company where other illicit drugs are available. None of this proves that using one drug leads to or causes the use of another. Most marijuana smokers do not use heroin or cocaine, just as most alcohol drinkers do not use marijuana. The metaphor of a stepping stone suggests that if no one smoked marijuana it would be more difficult for anyone to develop an interest in opiates or cocaine. There is no convincing evidence for or against this. What is clear is that at many times and places marijuana has been used without these drugs, or these drugs have been used without marijuana.

It is hard to generalize about abuse or define specific treatments, because the problems associated with marijuana are so vague, and cause and effect so hard to determine. Marijuana smokers may be using the drug to demonstrate rebelliousness, cope with anxiety, or medicate themselves for early symptoms of mental illness. People with serious problems who have been smoking marijuana heavily should be persuaded to stop so that their problems can be more effectively dealt with by psychotherapy or other means.

Health Hazards

Most recent research on the health hazards of marijuana concerns its long-term effects on the body. Studies have examined the brain, the immune system, the reproductive system, and the lungs. Suggestions of long-term damage come almost exclusively from animal experiments and other laboratory work. Observations of marijuana users and the Caribbean, Greek, and other studies reveal little disease or organic pathology associated with the drug.

For example, there are several reports of damaged brain cells and changes in brain-wave readings in monkeys smoking marijuana, but neurological and neuropsychological tests in Greece, Jamaica, and Costa Rica found no evidence of functional brain damage. Damage to white blood cells has also been observed in the laboratory, but again, its practical importance is unclear. Whatever temporary changes marijuana may produce in the immune system, they have not been found to increase the danger of

Continued on next page

Marijuana . . .

could be a problem for people with cardiovascular disease, dangerous physical reactions to marijuana are almost unknown. Like many other drugs, it produces a toxic delirium when taken at very high doses, especially by mouth. The symptoms are confusion, agitation, disorientation, loss of coordination, and often hallucinations; the delirium ends when the drug passes out of the body. No human being is known to have died of an overdose. By extrapolation from animal experiments, the ratio of lethal to effective (intoxicating) dose is estimated to be on the order of thousands to one.

Anxiety Reactions

The most common disturbing reaction to marijuana is acute anxiety, sometimes accompanied by paranoid thoughts. The user becomes fearful of dying or going insane, and may read hostility or ridicule into the gestures and words of companions. Mounting anxiety may lead to panic. The most likely victim of this reaction is an inexperienced user inadvertently taking a high dose in an unpleasant or unfamiliar setting. The best way to handle the anxiety and paranoia is calming support and reassurance. The reaction is not a psychosis; there are no hallucinations, and reassurance would not be effective without an ability to test the reality of thoughts and perceptions. Some authorities also refer to a cannabis delusional disorder with feelings of persecution or jealousy. Whether or not this is distinguishable from the anxiety reaction, the treatment is the same—reassurance and waiting for the drug effect to fade.

The anxiety reaction or delusional disorder is a milder version of the frightening LSD experience known as a bad trip. A truly nightmarish experience is rare under the influence of cannabis, because it is less potent than hallucinogenic or psychedelic drugs and the user is better able to control its effects. Use of LSD and other psychedelic drugs is often followed by flashbacks—the recurrence of emotions and perceptions originally experienced under the influence of the drug. They usually last only a few seconds and are not necessarily disturbing, but sometimes they become a persistent problem, which has been labelled post-hallucinogen perception disorder. Marijuana smoking may precipitate flashbacks in psychedelic drug users; a few reports suggest that marijuana flashbacks also occur without the previous use of psychedelic drugs.

Some observers, mainly in India and North Africa, have reported a cannabis psychosis caused mainly by long-term heavy use of the drug. It is described as a prolonged psychotic reaction with symptoms that include delusions, hallucinations, inappropriate emotions, and disordered thinking. In the descriptions, this psychosis is usually difficult to distinguish from acute schizophrenia, manic states, panic reactions, and other conditions. The reaction is rarely reported in the United States. Given the many millions of marijuana smokers in this country, the evidence for it would probably be less equivocal if it occurred with any regularity. Some people may suffer a psychotic reaction to cannabis because they are vulnerable to psychosis under any stress or after any change in consciousness or body image. For example, marijuana smoking probably increases the danger of relapse in schizophrenic patients (although any effect of this kind must be distinguished from a desperate attempt at self-medication because symptoms of schizophrenia are already returning).

Long-Term Effects

In recent years the psychological and physical effects of long-term use have caused the most concern. Studies are often conflicting and permit various views of marijuana's possible harmfulness. This complicates the task of presenting an objective statement about the issue.

One of the first questions asked about any drug is whether it is addictive or produces dependence. This question is hard to answer because the terms 'addiction' and 'dependence' have no agreed-upon definitions. Two recognized signs of addiction are tolerance and withdrawal symptoms; these are rarely a serious problem for marijuana users. In the early stages, they actually become more sensitive to the desired effects. After continued heavy use, some tolerance to both physiological and psychological effects develops, although it seems to vary considerably among individuals. Almost no one reports an urgent need to increase the dose to recapture the original sensation. What is called behavioral tolerance may be partly a matter of learning to compensate for the effects of high doses, and may explain why farm workers in some Third World countries are able to do heavy physical labor while smoking a great deal of marijuana.

A mild withdrawal reaction also occurs in animal experiments and apparently in some human beings who take high doses for a long time. The symptoms are anxiety, insomnia, tremors, and chills, lasting for a day or two. It is unclear how common this reaction is; in a Jamaican study, heavy ganja (marijuana) users did not report abstinence symptoms when withdrawn from the drug. In any case, there is little evidence that the withdrawal reaction ordinarily presents serious problems to marijuana users or causes them to go on taking the drug.

In a more important sense, dependence means an unhealthy and often unwanted preoccupation with a drug to the exclusion of most other things. People suffering from drug dependence find that they are

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Marijuana

The present generation of young people cannot remember when marijuana was an exotic weed with an aura of mythical power and mysterious danger. Although still illegal, it has become a commonplace part of the American social scene, used regularly by millions and occasionally by millions more. A realistic view of this drug is now both more important and easier to achieve.

The use of marijuana reached a high point in the late 1970s and early 1980s, and has been declining ever since. In a 1978 survey, 37 percent of high school seniors said they had smoked marijuana in the last 30 days, and 11 percent said they used it daily. By 1986 the number who said they had smoked it in the last 30 days had fallen to 23 percent—lower than in 1975—and the proportion of daily users had dropped steadily to 4 percent. The trend among people aged 18 to 25 is similar. On the other hand, more people over 25 may be using marijuana occasionally, and young people are still experimenting with it. In 1969, 20 percent of high school seniors had used marijuana at least once; in 1979, 60 percent had; and in 1985, 54 percent. The attitudes expressed in surveys show why habitual marijuana use is in decline. In 1978, 65 percent of high school students said they disapproved of it; in 1985, 85 percent disapproved. In 1978, 35 percent said it was very risky, and in 1985, 70 percent said it was.

The main active ingredient of marijuana is delta-9-tetrahydrocannabinol (THC), one of more than 60 related chemicals found in the resin that covers the flowers and top leaves of the cannabis (hemp) plant. The leaves and flowers can be ground up in drinks or food, but more often they are dried and smoked in a cigarette or pipe. The pure resin, known as hashish, can also be smoked, eaten, or drunk. New breeding and cultivation techniques have raised the THC content of marijuana smoked in the United States as much as ten times over the last 20 years, from an average of 0.4 percent to 4 percent. Some varieties now contain as much as 10 percent.

The effects last two to four hours when marijuana is smoked and five to twelve hours when it is taken by mouth. Although the intoxication varies with psychological set and social setting, the most common response is a calm, mildly euphoric state in which time slows and sensitivity to sights, sounds, and touch is enhanced. The smoker may feel exhilaration or hilarity and notice a rapid flow of ideas with a reduction in short-term memory. Images sometimes appear before closed eyes; visual perception and body image may undergo subtle changes. It is dangerous to operate complex machinery, including automobiles, under the influence of marijuana, because it slows reaction time and impairs attention and coordination. This impairment persists for at least several hours after the feeling of intoxication has passed.

The main physiological effects of cannabis are increased appetite, a faster heartbeat, and slightly bloodshot eyes. Although the increased heart rate

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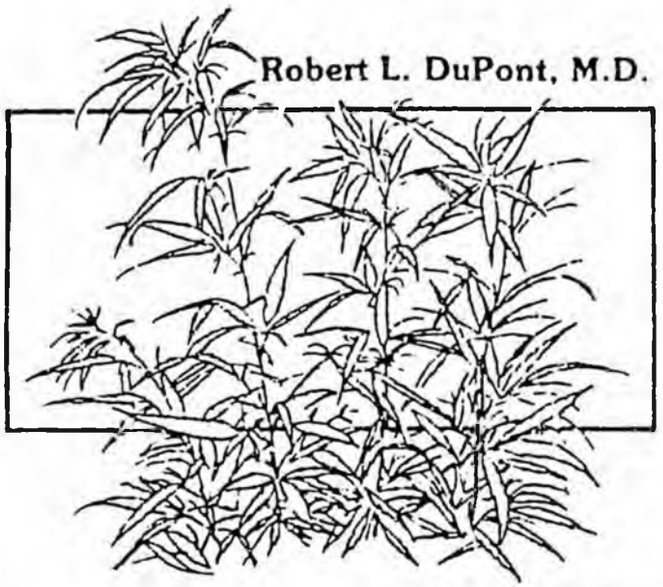
MARIJUANA SMOKING— A NATIONAL EPIDEMIC

Robert L. DuPont, M.D.



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MARIJUANA SMOKING constitutes the greatest single new threat to the health of our lungs in the United States. In the next ten years, the potential exists for an enormous worsening of the respiratory health of Americans, unless we do something about it now.

Marijuana is a new problem in American society. Twenty years ago, virtually no one used it. As recently as 1962, only 1% of American youth aged 12 to 17 and 4% of Americans aged 18 to 25 had ever tried marijuana. By 1979, these figures had risen to 31% and 68%.

A national epidemic

Today, marijuana smoking is a national epidemic. Fifty-five million Americans have smoked it at least once. Twenty-three million Americans are currently regular smokers of the weed. Four million young people of 17 years and under are at present smokers. Among the nation's ninth graders, the percentage of students who have smoked it jumped from 16% in 1975 to over 32% in 1979. Among high school seniors, slightly less than 11% smoke it every day, and the average number of joints smoked by those seniors is 3½% a day.

Substances used most commonly on a daily basis by high school seniors are tobacco, marijuana, and alcohol. Among high school seniors, 29% use tobacco daily, roughly 11% use marijuana every day, and 6% use alcohol daily. Those percentages of daily tobacco and alcohol users have remained the same since 1975, while the proportion of daily marijuana users has doubled in that period. There is certainly no other illegal drug that compares with marijuana in terms of frequence of usage.

The extent of marijuana usage in the United States comes more clearly into focus when you compare it with the experience of other countries with the habit. Most people are aware that marijuana has been smoked around the world for a long time. However, you may not know that American young people are literally the only population in the history of the world in which large numbers of an entire generation have smoked marijuana; experience with the cannabis product (it comes from the cannabis sativa plant) is restricted in other parts of the world. The use of marijuana in other countries does not involve an entire society; generally, its use is limited to either religious groups or social classes that are relatively isolated and generally looked down on in the society.

How we got into the mess

Something new and dramatic has happened that may affect the growing acceptance of marijuana in the United States: Scientists have identified some of the hazardous effects of marijuana smoke on the body.

Before I discuss those new findings, let me talk about how we got into the mess we are in with marijuana; it will reveal some of the challenges that we must meet

The first thing to realize about the drug is that it does work — it produces powerful effects. The major psychoactive agent is THC (delta-9-tetrahydrocannabinol). Ten years ago, the average THC content in a marijuana cigarette was 2/10 of a percent. Today, it's more like 4% or 5%. That's an increase of 20 to 25 times in the last six or seven years.

The second point is that marijuana is unique in that it has been a potent symbol. It has been a symbol of youth, a symbol of anti-authority positions, a symbol of modernity.

There has also been a unique tendency to trivialize the marijuana experience, and this is truly frightening to people who are aware of the effects of marijuana on the body. As one high school student said to me a year or so ago, "Marijuana is not a drug. It's part of the scene, like blue jeans." This remark represents the evolution of an attitude from the days ten years ago when marijuana was a meaningful symbol to its present status as "part of the scene."

Reasons why it has been accepted

Now, one might ask why there are 23 million people regularly smoking a new substance which society would ordinarily resist. I want to outline some of the reasons for this. First, there is a history of exaggerations in the past about the harmfulness of marijuana, based on little or no data. This has been captured by pro-marijuana lobbyists with a 1930's film called "Reefer Madness." The message is putdown for anyone who has anything bad to say about marijuana.

Second, the decriminalization of marijuana use has led to greater acceptance. Over half of the public attention devoted to the issue in recent years has focused on the criminal sanctions for possession. Much of the debate is symbolic: If you are for decriminalization, you are for marijuana. If you're against decriminalization, you're against marijuana use.

The reality is that virtually no one in the United States is sent to jail for possession of the product any more. There are still about 400,000 arrests for marijuana possession a year, but the offenders are rarely prosecuted. The concept that we need to reform our laws to deal with the marijuana possessor is unreasonable when viewed against the realities of the present enforcement attitude.

The third reason why marijuana has been accepted lies in the charge of parental or adult hypocrisy. The idea is that, because adults smoke cigarettes or drink alcohol, kids ought to be able to smoke marijuana. Therefore, if adults condemn marijuana smoking, they are being hypocritical.

The answers to the parental or adult hypocrisy charge is that decisions about the use of a psychoactive substance — whether it be marijuana, alcohol or tobacco — should be made by adults and not by children. Even Keith Stroup of the national marijuana lobbying organization opposes the use of cannabis, as well as tobacco and alcohol, by people under the age of 18.

The therapeutic use argument, another red herring

The fourth red herring that has been drawn across the path of anyone trying to do something about the marijuana epidemic is the therapeutic-use argument. Twenty state legislatures in the past year have been bamboozled into passing laws to legalize the use of marijuana as a medicine. The legislation is unnecessary, there are federal statutes that make marijuana available as a medication, if it were ever to pass muster as a clinically effective agent for any specific ailment. In my opinion, that possibility is extremely unlikely.

Marijuana is not a chemical; it is a vegetable plant product. It contains over 400 separate chemicals, 60 of them unique to the cannabis sativa plant and known as cannabinoids. When marijuana is smoked, it emits more than 4,000 separate, identifiable chemical substances. The idea of treating any disease with something so complex is unmedical and unscientific. It is a little like saying, "We'll have people eat bread mold to treat pneumococcal pneumonia instead of using penicillin."

At the same time, some of the components of marijuana — and particulary THC — may have some therapeutic use. I certainly favor the investigation of those components, but we do not need any new laws for that. My point is that if marijuana is treated as a helpful medicine, it will gain acceptability in terms of public perception. That is why marijuana lobbyists are so vigorously promoting the use of marijuana for glaucoma sufferers and those who are undergoing chemotherapy for cancer. They don't want doctors to use purified chemicals such as THC, because they lose their symbolic argument.

Marijuana and the lungs

So much for the past. Let me review quickly some of the basic outlines of the case against marijuana in relation to the lungs. Marijuana smoke is much like tobacco smoke, with two exceptions: It has THC in it, and it does not contain nicotine. If you switch those two compounds, putting nicotine in the marijuana and THC in the tobacco, they are similar in their biological effects and their chemical constituents. Although nicotine is clearly a toxic substance, the effects of THC are possibly even more devastating because of the intoxicating qualities of cannabis.

Another aspect of marijuana is that it is at least as serious a respiratory irritant as tobacco, and probably more so.

The manner in which marijuana is smoked is a key factor in irritating the lungs. Most modern tobacco smokers are concerned about their lungs and tend to inhale relatively lightly. In contrast, the marijuana smoker inhales deeply and holds his breath to sustain the exposure for maximum absorption of the fumes. Too, the cigarette smoker is likely to buy a filtered cigarette nowadays and will not puff it all the way

.. the ethos of the marijuana smoker is to burn the entire joint. A "roach clip" enables the marijuana user to smoke until there is nothing left except the part that is just touching the lips, maximizing the exposure to tar and other respiratory irritants.

Still another aspect of marijuana smoke is that it contains well-recognized carcinogens. When the smoke is condensed and painted on the skins of laboratory mice, it produces a metaplasia of the sebaceous glands, a cancerous change. The effects of tobacco smoke are not so marked.

So we have evidence that marijuana contains more tar and known carcinogens than tobacco. Moreover, when human and animal lung tissue are exposed to marijuana smoke in a laboratory setting, the resulting cancerous changes are analogous to those produced by tobacco smoke and, in some cases, more frequent. Finding evidence on the development of human lung cancer from marijuana smoke is, I think, just a matter of time.

The evidence piles up

There is yet more evidence that indicates harmful respiratory complications from marijuana use. Some studies have shown severe inflammation of the small airways. Others have demonstrated that the alveolar macrophages, the primary defense against alien bodies in the lungs, are less able to dispose of bacteria and foreign materials when exposed to marijuana smoke.

In addition, there is a rise in the carboxyhemoglobin level in the blood — an increase in the ratio of carbon monoxide to oxygen. One study found that a single marijuana cigarette smoked for 15 minutes produced as high a level of carboxyhemoglobin as ten to twenty tobacco cigarettes smoked in the course of a day. I think the likeliest reason for this difference is the way marijuana is smoked.

So, the evidence suggests that smoking marijuana is harmful to the lungs. Furthermore, everything we now know about the effects of tobacco smoking is applicable to marijuana use in terms of what it does to the lungs — at least, one ought to begin with that assumption until there is evidence to the contrary. We obviously need broad-based epidemiological studies before the final "i" is dotted in this indictment, but I don't know how anyone can believe that marijuana is harmless to lungs in the light of the available data.

Effects of the drug on other parts of the body

Let me cover very briefly the effects of marijuana on other organs of the body. It is important to know that the intoxicating effect of marijuana is profound. The consequences are in some ways like those of alcohol, being of several hours' duration. However, alcohol is soluble in water, and because of this, the water based waste disposal system of blood and urine works quite well to get rid of it. THC, not being water-soluble, tends to be retained in the body, particularly in the brain and the reproductive organs.

A person who smokes one marijuana cigarette has half of the THC in his body five to seven days, later, and measurable quantities are present after a month. This means that if a person smokes as infrequently as once a month, the THC accumulates, and the brain and reproductive organs are continously exposed. There is good evidence that there are profound effects both on brain function and reproductive function from marijuana use.

Hard to reverse the tide

It has proved difficult, even with all the data available in recent years on the health hazards of tobacco smoking, to convince Americans — and especially young people — to quit the cigarette habit or never start it.

Those of us in the marijuana field have found it even harder to turn the tide of the marijuana epidemic because of the perceived lack of sufficient scientific evidence on the dangers of marijuana. This information is just beginning to come to light. As a result, many young people — who make up the majority of marijuana users — have seen no reason not to smoke pot.

Among American high school seniors, about 60% perceive that there is a great health risk in cigarette smoking. Only 35% see the similar peril of cannabis sativa. It is that disparity which is contributing to the explosive growth of marijuana smoking.

The most bizarre thing that strikes me about young people is that so many are concerned about pollution, worried about the environment, believers in eating natural foods, crusaders against the problems of nuclear energy — and yet they continue to smoke marijuana cigarettes. The idea that smoking pot may be hazardous to your health just hasn't cut through all the controversy and the politics surrounding the weed. There is a growing body of information about health risks, and we need to get that across.

I would add that scientific data on the health effects of any drug or product is not, in itself, sufficient to solve the public health problem. However, it is a necessary condition for public health mobilization.

It is actually within only the past year or two that some initial findings on the changes in the body produced by marijuana smoking have been developed. I am convinced that if marijuana smoking were to be taken up as a priority by the American Lung Association, we would take a giant step forward in the education of the public about cannabis.

Smoke is bad for the lungs, whether it's industrial smoke, tobacco smoke or marijuana smoke. We need your help in stemming the marijuana epidemic.

ROBERT L. DUPONT, M.D., is president of the American Council on Marijuana and a former director of the National Institute on Drug Abuse. A practicing psychiatrist, he heads Washington, D.C.'s first phobia treatment program and writes on health topics for local and national television, radio, magazines, and newspapers. He is also president of the non-profit Institute for Behavior and Health, which conducts research and demonstration programs aimed at preventing drug and alcohol abuse.

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PULMONARY HAZARDS OF SMOKING MARIJUANA AS COMPARED WITH TOBACCO

TZU-CHIN WU, M.D., DONALD P. TASHKIN, M.D., BEHNAM DJAHED, M.D., AND JED E. ROSE, PH.D.

Abstract To compare the pulmonary hazards of smoking marijuana and tobacco we quantified the relative burden to the lung of insoluble particulates (tar) and carbon monoxide from the smoke of similar quantities of marijuana and tobacco. The 15 subjects, all men, had smoked both marijuana and tobacco habitually for at least five years. We measured each subject's blood carboxyhemoglobin level before and after smoking and the amount of tar inhaled and deposited in the respiratory tract from the smoke of single filter-tipped tobacco cigarettes (900 to 1200 mg) and marijuana cigarettes (741 to 985 mg) containing 0.004 percent or 1.24 percent Δ^9-tetrahydrocannabinol.

As compared with smoking tobacco, smoking marijuana was associated with a nearly fivefold greater increment in the blood carboxyhemoglobin level, an approximately threefold increase in the amount of tar inhaled, and retention in the respiratory tract of one third more inhaled tar ($P<0.001$). Significant differences were also noted in the dynamics of smoking marijuana and tobacco, among them an approximately two-thirds larger puff volume, a one-third greater depth of inhalation, and a fourfold longer breath-holding time with marijuana than with tobacco ($P<0.01$). Smoking dynamics and the delivery of tar during marijuana smoking were only slightly influenced by the percentage of tetrahydrocannabinol.

We conclude that smoking marijuana, regardless of tetrahydrocannabinol content, results in a substantially greater respiratory burden of carbon monoxide and tar than smoking a similar quantity of tobacco. (N Engl J Med 1988; 318:347-51.)

WE have previously shown that the habitual smoking of 3 or 4 marijuana cigarettes a day is associated with the same frequency of the symptoms of acute and chronic bronchitis[1] and the same type and extent of epithelial damage in the central airways[2] as the regular smoking of more than 20 tobacco cigarettes a day. A possible explanation for these findings is that a greater quantity of smoke particulates and noxious gases is delivered to and deposited or absorbed in the lungs by marijuana than by a similar amount of tobacco, possibly as a result of differences in the way each type of cigarette is smoked. To investigate this possibility, we examined the dynamics of smoking a marijuana or a tobacco cigarette and measured the particulates delivered to the smoker's mouth during the smoking of a single cigarette of each type.

METHODS

We studied fifteen men who were habitual smokers (mean age [±SD], 31.5±7.1 years), each of whom smoked both tobacco and marijuana. The subjects smoked an average of 29.9±16.7 tobacco cigarettes per day and had smoked an average of 16.1±12.2 pack-years of tobacco (one pack-year equals one pack of tobacco cigarettes per day times the number of years of smoking); they smoked an average of 16.5±17.1 marijuana cigarettes per week, and had smoked an average of 54.8±34.8 joint-years of marijuana (one joint-year equals one cigarette [joint] of marijuana per day times the number of years of smoking). All were in good general health and had normal or nearly normal values for forced vital capacity (101±8.7 percent of predicted values[3]) and forced expiratory volume in one second (96±14 percent of predicted values[3]). None reported intravenous drug abuse or smoking other illicit substances besides marijuana.

Each subject was studied on a single day after refraining from smoking tobacco for at least one hour and marijuana for at least six hours. During the study session, each subject smoked his own brand of filter-tipped tobacco cigarette, followed, in single-blind fashion, first by a placebo marijuana cigarette (from which nearly all Δ^9-tetrahydrocannabinol [Δ^9-THC] had been extracted, so that the concentration was 0.004 percent) and next by a marijuana cigarette of similar weight containing 1.24±0.06 percent Δ^9-THC. An interval of approximately 30 minutes separated the smoking of each two cigarettes. The tobacco cigarettes weighed 900 to 1120 mg and had a tar yield of 4.6 to 23.1 mg (mean, 12.0±5.7 mg) and a nicotine yield of 0.4 to 1.4 mg (mean, 0.84±0.32 mg) by Federal Trade Commission analysis. The placebo marijuana cigarettes weighed 741 to 940 mg (mean, 840 mg) and those containing 1.24 percent Δ^9-THC weighed 849 to 985 mg (mean, 907 mg); both were supplied by the National Institute on Drug Abuse, were stored at 4°C to minimize chemical degradation, and were maintained in a humidifier at 60 percent humidity and 21°C for 24 hours before the study, to reduce harshness.

The subjects were asked to smoke both the tobacco cigarette and the two marijuana cigarettes in a manner as similar as possible to their usual pattern of smoking tobacco and marijuana. Peripheral venous blood was withdrawn anaerobically immediately before and two minutes after the first two cigarettes were smoked for measurement of the percentage of carboxyhemoglobin saturation, with use of a carbon monoxide–oximeter (Model 282, Instrumentation Laboratory, Lexington, Mass.). After smoking each of the marijuana cigarettes, the subjects were asked to rate their level of intoxication on a scale of 0 to 100 percent, with 100 percent representing the greatest "high" they had ever experienced.

The volume, duration, and number of puffs and the intervals between puffs were measured with a 00 Fleisch pneumotachygraph (linear from 5 to 100 ml per second) connected through a differential pressure transducer (Model MP54-3, Validyne, Northridge, Calif.) (range, ±2 cm of water) to an oscilloscopic recorder with a differential integrator–computer and a rapid photographic writer (Model VR6, Electronics for Medicine, Pleasantville, N.Y.). To prevent the pneumotachygraph screen from becoming clogged by smoke particles,[4] the pneumotachygraph was connected through wide-bore Tygon tubing (length, 70 cm; internal diameter, 1 cm) to the distal end of a glass cylinder (length, 12 cm; diameter, 5 cm) that contained two ventilation ports (each 1 cm in diameter) and was sealed at its proximal end by a rubber stopper. The tobacco or marijuana cigarette was held in a small plastic holder inserted through the rubber stopper. The ventilation ports were left open between puffs to prevent either the extinction of the lighted cigarette or the excessive accumulation of carbon monoxide. During a puff, the smoker covered the ventilation holes with his index and middle fingers so that the entire volume of air drawn through the cigarette could be measured by the pneumotachygraph. The resistance of the pneumotachygraph (0.0068 cm of water per milliliter per second) was considerably lower than that of the cigarette (0.51 cm of water per milliliter per second for tobacco; 0.17 cm of water per milliliter per second for marijuana); therefore, the pneumotachygraph itself was

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not likely to have a substantial effect on smoking dynamics. The duration of a puff was timed from the pneumotachygraphic flow tracing. The interval between puffs was defined as the period between the end of one puff and the start of the next.

To measure "wash-in" volume (the volume of air inhaled), inductive plethysmographic coils (Respitrace Ambulatory Monitoring Systems, Ardsley, N.Y.) were placed around each subject's rib cage and abdomen.[5,6] A demodulator converted changes in electrical inductance in the coils during respiratory movements into voltage signals proportional to changes in the volume enclosed by the coils. Changes in the volume of the respiratory system were calculated from the weighted sums of the signals from the rib cage and abdomen; the weights were determined by the least-squares calibration method.[7] The accuracy of the calibration was confirmed by comparing the inhaled volumes calculated from respiratory inductive plethysmography with spirometric values; the measurements obtained by spirometry and inductive plethysmography agreed within ±10 percent. The amount of time the inhaled smoke was retained in the lungs (smoke-retention time) was calculated as the interval between the times corresponding to one third of the maximum inhaled volume and two thirds of the maximum volume exhaled following breath holding (Fig. 1). The no-smoking interval was timed from the end of the smoke-retention time to the start of the next puff.

A previously described proportional smoke-trapping device[8] was connected to the apparatus for measuring the volume of puffs in order to measure the amount of smoke particulates delivered to the smoker's mouth. This device consisted of a plastic cigarette holder through which the mainstream smoke was diverted into two parallel pathways, one containing one capillary tube (pathway A) and the other seven parallel capillary tubes (pathway B). A Cambridge filter pad trapped the smoke that passed through pathway A. The tar trapped by the filter was extracted with methanol and analyzed by means of a spectrophotometer (wavelength, 400 nm). A constant fraction of the tar (12.5±0.53 percent) was retained in the filter over a wide range of puff volumes (30 to 60 ml), puff durations (1 to 4 sec), and puff flow rates (20 to 100 ml per second).[8] This apparatus, therefore, permitted the actual quantity of smoke particulates delivered to the mouth to be calculated by multiplying the amount of particulates trapped in the Cambridge filter pad in pathway A by seven. At the end of the period of breath holding after each puff, the subjects turned their heads slightly to one side and exhaled the smoke into the large end (diameter, 26 cm) of an adjacent megaphone device, the distal end (diameter, 4.5 cm) of which was fitted with a high-efficiency filter attached to a vacuum system as described by Hinds et al.[9] After the tar was extracted from the filter with methanol, the exhaled particulates were measured with a spectrophotometer. The amount of smoke retained (deposited) in the respiratory tract was expressed as a percentage of the amount inhaled: percentage deposited = [1 − (amount of exhaled particulates/amount of inhaled particulates)] × 100.

Each subject's measurements were averaged for each cigarette smoked. These mean values, as well as the number of puffs, the quantity of particulates inhaled, the percentage of inhaled particulates deposited, and the increment in carboxyhemoglobin saturation per cigarette, were averaged for all 15 subjects for each type of cigarette smoked. The subjects' ratings of their degree of intoxication after marijuana smoking were also averaged for all subjects for each type of marijuana cigarette (placebo and 1.24 percent Δ^9-THC). Two-way analysis of variance (for subject and type of cigarette) was used to determine the significance of differences in smoking patterns, the delivery and deposition of particulates, and the increase in carboxyhemoglobin saturation among types of cigarette.[10] Pairwise comparisons were then performed using testing for least significant differences[11]; differences were considered significant if P values were <0.05.

Results

Descriptive data about smoking in the group of 15 subjects are shown in Table 1. Placebo marijuana and marijuana containing approximately 1.24 percent Δ^9-THC were smoked in a similar manner. However,

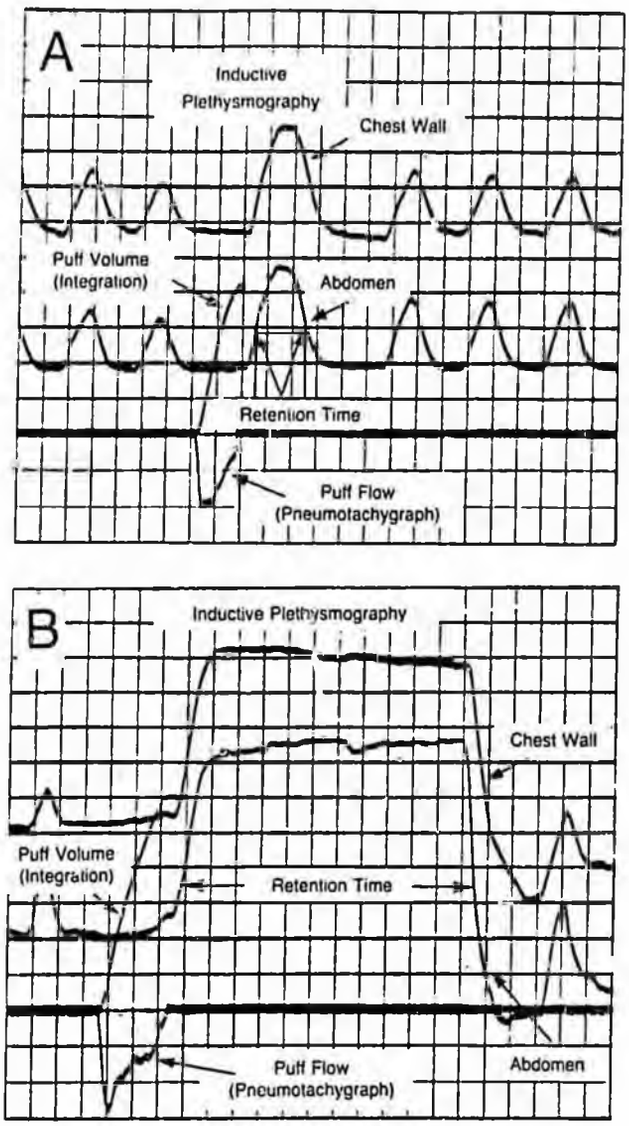

Figure 1. Analogue Tracings of Voltage Signals from Inductive Plethysmographic Coils around the Chest Wall and Abdomen of a Representative Subject and Simultaneous Flow and Integrated Volume Signals from a Pneumotachygraph Incorporated into a Puff-Volume Measuring Device during the Smoking of a Tobacco Cigarette (A) and a Marijuana Cigarette (B).

Note that during marijuana smoking, there is greater amplitude of the voltage signals representing puff volume (measured by the pneumotachygraph) and inhaled volume (measured by the inductive plethysmograph) than during tobacco smoking.

the average volume of puffs was about 70 percent larger (P<0.001) and the duration of puffs about 60 percent longer (P<0.01) during the smoking of marijuana than the smoking of tobacco, regardless of whether the marijuana contained 1.24 or 0.004 percent Δ^9-THC; significantly more puffs were taken from the tobacco cigarette than from either the placebo marijuana cigarette or that containing 1.24 percent Δ^9-THC (P<0.001). Although the interval between puffs was less for tobacco than for marijuana smoking (P<0.05), the no-smoking interval, which did not include the breath-holding time after

Table 1. Characteristics of 15 Subjects' Smoking of Tobacco, Placebo Marijuana (0.004 Percent Δ^9-THC), and Marijuana Containing 1.24 Percent Δ^9-THC.*

Index	Tobacco	Marijuana		P Value†
		0.004% Δ^9-THC	1.24% Δ^9-THC	
	mean ±SD			
Puff volume (ml)	49.4±15.2	88.3±24.8	78.0±22.8	<0.001
Puff duration (sec)	±1.1	3.8±1.9	4.0±2.2	<0.01
No. of puffs	13.5±4.0	7.5±2.3	8.5±3.1	<0.001
Interval between puffs (sec)	27.0±8.2	35.3±12.2	37.6±14.5	<0.05
Inhaled volume (liter)	1.31±0.22	1.82±0.66	1.75±0.52	<0.002
Smoke-retention time (sec)	3.5±1.3	13.8±9.2	14.7±10.2	<0.001
No-smoking interval (sec)	23.5±8.5	21.5±6.4	23.0±8.8	NS

*All subjects were habitual smokers of both tobacco and marijuana. They smoked their own brands of tobacco cigarettes. Δ^9-THC denotes Δ^9-tetrahydrocannabinol; NS denotes not significant.

†P values indicate the significance of comparisons between tobacco and each strength of marijuana; none of the comparisons between the two different strengths of marijuana (0.004 percent vs. 1.24 percent Δ^9-THC) was statistically significant.

smoke was inhaled, was similar for both substances. The mean inhaled volume was 36 percent greater ($P<0.002$) and the smoke-retention time was four times longer ($P<0.001$) during marijuana smoking than tobacco smoking.

The volume of the portion of the proportional smoke-trapping device through which smoke was delivered was approximately 13 ml. After the first puff, this volume was filled with smoke that was delivered in subsequent puffs; thus, after the first puff, no additional volume of air not containing smoke was included in the measurement of puff volume. When the pneumotachygraph was disassembled from the proportional smoke-trapping device and used to measure puff volume, the difference in the mean volume was negligible (4.2±2.0 ml lower without the smoke-trapping device). Similarly, inhaled volumes determined directly from the cigarette by the inductive plethysmograph, without the attachment of either the pneumotachygraph or the proportional smoke-trapping device, were similar to (within 50 ml) the inhaled volume determined when the subjects smoked through these devices.

The amounts of particulates inhaled, the percentage of inhaled particulates deposited in the respiratory tract, and the differences between the carboxyhemoglobin levels before and after smoking each type of cigarette are shown in Table 2. The major significant difference between smoking marijuana cigarettes containing 0.004 percent Δ^9-THC (placebo) and smoking cigarettes containing 1.24 percent Δ^9-THC was that the latter caused a greater degree of intoxication. In addition, the amount of particulates inhaled from marijuana containing 1.24 percent Δ^9-THC was slightly but significantly greater (20 percent) than that delivered from placebo marijuana ($P<0.05$). In contrast, smoking either type of marijuana was associated with the inhalation of 2.8 to 3.3 times more insoluble particulates (tar) and with the deposition of 32 to 35 percent more of these inhaled particulates than smoking the subject's own brand of tobacco ($P<0.001$). Consequently, marijuana smoking resulted in a tar burden to the respiratory tract that was 3.5 to 4.5 times greater than that produced by tobacco smoking in the same subjects. Furthermore, smoking a single marijuana cigarette caused a fourfold greater increment in carboxyhemoglobin saturation ($P<0.001$) than did smoking a single tobacco cigarette.

Discussion

Long-term adverse pulmonary consequences of tobacco smoking have been shown to be related to dose.[12] For example, the incidence of chronic obstructive pulmonary disease or bronchogenic carcinoma in smokers of fewer than 5 to 10 tobacco cigarettes a day is substantially less than in habitual smokers of more than 20 tobacco cigarettes a day.[13] Although regular tobacco smokers consume more than 15 tobacco cigarettes a day, most current smokers of marijuana smoke less than 1 marijuana cigarette a day.[12] Even among the estimated 6 million daily smokers of marijuana in the United States,[14] smoking more than five marijuana cigarettes a day is unusual. In view of the many similarities in the smoke contents of marijuana and tobacco,[15,16] it has been argued that habitually smoking only a few marijuana cigarettes a day may have a proportionately less harmful long-term effect on the lungs than regularly smoking several times more tobacco cigarettes. This argument assumes that the number of cigarettes smoked is directly proportional to the dose of smoke contents inhaled; however, this assumption ignores the ways in which the characteristics of smoking may influence the delivery of the combustion products of cigarettes.[17,18]

Table 2. Inhalation and Deposition of Particulates, Increases in Blood Carboxyhemoglobin Saturation, and Levels of Intoxication Associated with the Smoking of Tobacco and Marijuana in 15 Smokers of Both Substances.*

Index	Tobacco	Marijuana	
		0.004% Δ^9-THC	1.24% Δ^9-THC
	mean ±SD		
Inhaled particulates (optical density)	4.9±2.0	13.5±6.0†	16.3±6.3†‡
Percentage of particulates deposited	64.0±8.9	84.4±6.9†	86.1±6.7†
Increase in carboxyhemoglobin saturation (%)	0.60±0.52	2.99±1.51†	—§
Degree of intoxication (maximum "high" = 100%)	—	15.3±16.9	63.9±18.3‡

*Δ^9-THC denotes Δ^9-tetrahydrocannabinol.

†Significantly greater than values for tobacco ($P<0.001$ by analysis of variance and testing for least significant difference).

‡Significantly greater than values for marijuana containing 0.004 percent Δ^9-THC ($P<0.05$ by analysis of variance and testing for least significant difference).

§Not measured.

Few studies have been carried out in which the actual dose of smoke contents delivered to and retained in the respiratory tract during natural smoking has been measured. In our study, both the amount of particulate matter that was inhaled and the amount that was deposited in the respiratory tract were quantified during tobacco and marijuana smoking by means of a simple, new, noninvasive device.[8] These measurements allowed us to compare the actual dose to the smoker of particulate matter from the smoke of marijuana with that from tobacco. At the same time, the characteristics of smoking were determined in order to ascertain the relation between behavioral variables in smoking and the delivery and retention of smoke contents in the respiratory tract for each type of cigarette. The proportional smoke-trapping device had little measurable influence on smoking dynamics.

Findings from the present study indicate that approximately three times as much particulate matter is delivered to the smoker's mouth during the smoking of a single marijuana cigarette than during the smoking of a single tobacco cigarette of the smoker's own brand. These results are similar to those obtained in studies that used smoking machines to simulate conditions thought to be representative of marijuana and tobacco smoking.[19,20] Our results also revealed that approximately one third more of the particulates inhaled from the smoke of marijuana are retained in the respiratory tract than is the case when tobacco is smoked. Consequently, the net respiratory burden of particulates was approximately four times greater during marijuana smoking than tobacco smoking.

Several explanations are possible for the greater burden of particulates to the lungs from marijuana than from a similar quantity of tobacco. First, in all 15 cases, the tobacco cigarettes were more densely packed than the marijuana cigarettes and, unlike the marijuana cigarettes, were filter-tipped; therefore, the filtration efficiency of the tobacco cigarettes was greater. Second, the average residual length of the marijuana cigarettes (23±13 mm) was smaller than that of the tobacco cigarettes (37±12 mm), thereby further reducing the filtration efficiency of the marijuana cigarette. However, because the tobacco cigarettes were initially longer and because the filter tip was included in the tobacco butt, the actual quantities of tobacco and marijuana consumed were similar. Third, the subjects' patterns of inhalation in smoking the two types of cigarettes were markedly different; marijuana was smoked with a puff volume that was more than two thirds larger, an inhaled volume one third greater, and a retention time four times longer than the values for tobacco. Although the larger puff volumes for marijuana were partially offset by a smaller number of puffs, this factor may still have contributed to the greater mass of smoke particulates delivered to the mouth in marijuana smoking. The deeper inhaled volumes and, in particular, the severalfold longer retention times during marijuana smoking than during tobacco smoking may have accounted for the greater percentage of the inhaled particulates from marijuana smoke deposited in the respiratory tract.

The four-to-five-times-greater increments in carboxyhemoglobin saturation during marijuana smoking than tobacco smoking were probably due mainly to differences in how the cigarettes were smoked rather than in the amount of carbon monoxide produced, since syringe-simulated puffs of similar volumes and durations from lit cigarettes yielded approximately 25 percent lower concentrations of carbon monoxide from marijuana than from tobacco. This finding is consistent with the more complete combustion of the more loosely packed marijuana. On the other hand, the subjects' deeper inhalations and, in particular, their considerably longer retention of smoke in the lungs during marijuana smoking than during tobacco smoking made possible a greater uptake of carbon monoxide by the pulmonary microcirculation by means of passive diffusion. We measured the increment in blood carboxyhemoglobin after placebo marijuana (from which the cannabinoids had been extracted), and not after marijuana containing Δ^9-THC. However, we would not expect appreciable differences between the effects of real marijuana and those of placebo marijuana on blood carboxyhemoglobin levels, since the smoking dynamics and the carbon monoxide delivery of the two types of marijuana cigarettes were similar. The expected physiologic consequences of the markedly greater boost in carboxyhemoglobin levels from a single marijuana cigarette are a higher degree of impairment in oxygen transfer in the lung,[21] a reduction in the oxygen-carrying capacity of the blood, and impairment in the release of oxygen from hemoglobin in the tissues.[22] Moreover, the Δ^9-THC in marijuana causes dose-related increases in heart rate[23,24] and thus in cardiac work and myocardial oxygen requirements. Therefore, in persons with underlying coronary artery disease who smoke marijuana, the combined effects of a marked rise in the level of carboxyhemoglobin and the cardioacceleration induced by Δ^9-THC could lead to a critical imbalance between reduced myocardial oxygen supply and increased demand.

Interestingly, no significant differences in smoking dynamics were noted between placebo marijuana and marijuana containing 1.24 percent Δ^9-THC, despite marked differences in the subjects' perceived level of intoxication. These findings differ from previous observations in tobacco smokers that puff volume increases when low-nicotine cigarettes are smoked.[25] Our results in marijuana smokers are consistent with data from other studies,[26,27] however, and suggest that the pattern of smoking marijuana is not immediately adjusted to alter the inhaled dose of Δ^9-THC but, instead, probably represents a learned technique based on previous experiences and interactions.

In conclusion, our findings demonstrate that smoking behavior differs markedly between marijuana and tobacco smoking and that these differences are associ-

ated with a respiratory burden of smoke particulates and absorption of carbon monoxide that are approximately four times greater in the case of marijuana smoking. These results may account for previous findings that smoking only a few marijuana cigarettes a day (without tobacco) has the same effect on the prevalence of acute and chronic respiratory symptoms[1] and the extent of tracheobronchial epithelial histopathology[2] as smoking more than 20 tobacco cigarettes a day (without marijuana). These observations justify concern about the potential long-term pulmonary consequences of the habitual smoking of only a few marijuana cigarettes a day.

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Now, striking evidence of short- and long-term consequences

How the lungs are affected by marijuana smoking

ABSTRACT: Short-term use of marijuana causes bronchodilation, an alteration in ventilatory control, and a substantial increase in end-expired carbon monoxide. Long-term use produces tachyphylaxis and airflow obstruction, and potentiates tobacco in causing airway hyperreactivity. Marijuana smoking appears to have its major impact on the large airways, in contrast to tobacco smoking, which primarily affects the peripheral airways and alveolated regions. Bronchoscopic studies of the mucosa of marijuana smokers have revealed abnormalities such as loss of cilia, basal cell and goblet cell hyperplasia, squamous metaplasia, and inflammation. (*J Respir Dis* 1987;8(11):87-107)

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Marijuana has been used for centuries for its mind-altering effects. Yet careful studies of the biologic properties of marijuana in humans and animals have been conducted only recently because Δ^9-tetrahydrocannabinol (THC)— the psychoactive component of marijuana—and related cannabinoid compounds were not identified and synthesized until the 1960s. Further, despite its ancient history in some cultures, marijuana acquired widespread popularity as a smoked substance in our society only within the last 25 years.

Smoking marijuana in the form of cigarettes ("joints") or in pipes (bongs or water pipes) increased dramatically during the 1970s and peaked in 1979. Since then, self-reported use has gradually declined. Nevertheless, according to the most recent nationwide survey, as many as 18.2 million Americans, mostly persons 25 years and younger, admit to smoking marijuana within the past month. Of these current users, about 6 million reportedly smoke marijuana one or more times daily.

In view of the widespread, habitual use of marijuana, there is concern about the risk of long-term pulmonary consequences, based on the well-known effects of regular tobacco smoking on the lung. However, because of the relative recency of the marijuana "epidemic" in countries where health is carefully monitored, the extent of lung damage due to heavy, habitual marijuana use may not yet be clinically evident.

In this article, we briefly review

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Marijuana smoking

Now, striking evidence of short- and long-term consequences

the results of studies evaluating the effects of marijuana smoke on the lungs of animals. We then discuss human studies dealing with the possible short- and long-term respiratory effects of marijuana smoke, and compare these effects with those of tobacco smoke.

ANIMAL STUDIES

Research with animals has revealed that both histologic and functional pulmonary abnormalities develop after exposure to marijuana smoke.

Histologic changes

Chronic marijuana inhalation in controlled animal studies results in histologic abnormalities in both the airways and lung parenchyma. During a 365-day exposure to marijuana smoke, rats demonstrated a dose-related spectrum of histopathologic lesions in the alveoli and the interstitium—including granulomatous inflammation; accumulations of alveolar macrophages, neutrophils, and mononuclear inflammatory cells; and focal pneumonitis. These abnormalities did not reverse following a 30-day recovery period.

Tracheotomized dogs exposed to the smoke from four standardized marijuana cigarettes daily for 30 months had a significantly higher incidence of bronchiolitis and squamous metaplasia in the trachea than unexposed control animals. Detailed morphometric analysis of the tracheal epithelium in rats exposed to marijuana smoke for only 31 consecutive days showed a 30% decrease (relative to control animals) in secretory cell density but significant increases in the number of secretory cells and glycoprotein volume per cell staining positive with Alcian Blue and with periodic acid-Schiff stains. Further, the epithelial thickness was increased in these animals.

These histopathologic changes are similar to those noted following experimental exposures to tobacco smoke and other inhaled irritants. However, the effects of chronic marijuana smoke inhalation on respiratory epithelial function, such as mucociliary transport, are as yet unknown.

Functional effects

Marijuana smoke has deleterious effects on the cellular defense functions of the lung. Alveolar macrophages obtained from normal rats by bronchoalveolar lavage exhibited dose-dependent depression of bactericidal activity against *Staphylococcus albus* when incubated with different amounts of marijuana smoke. This in vitro finding was confirmed by in vivo evidence from a study in which rats were first exposed to marijuana smoke and then submitted to an aerosolized challenge with *Staphylococcus aureus*. The impairment of macrophage antibacterial defense mechanisms may be related to a water-soluble, gas-phase cytotoxin in marijuana smoke.

Studies of mouse, hamster, and human lung explants exposed to marijuana smoke have shown abnormalities in mitosis, deoxyribonucleic acid content, and number of chromosomes. These abnormalities were more marked than those noted in cultured lung cells exposed to tobacco smoke. Tobacco or marijuana smoke alone caused irregular growth and accelerated malignant cell transformation of cultured hamster lung cells within three to six months of exposure. These findings underscore the carcinogenic potential of habitual marijuana smoking.

HUMAN STUDIES

The pulmonary physiologic, clinical, and histopathologic findings in persons who smoke marijuana are summarized in Tables 1, 2, and 3.

Short-term effects

Initial studies addressed the short-term effects of marijuana smoking on lung function.

Table 1—Pulmonary physiologic effects of smoked marijuana

Short-term

- Bronchodilation (pharmacologic effect of Δ^9-tetrahydrocannabinol (THC) dose-dependent mechanism undefined)
- Decreased maximal oxygen consumption during exercise (possibly due to cardioaccelerator effect of THC with premature achievement of maximal heart rate)
- Increased resting oxygen consumption
- Increased or decreased central ventilatory drive (conflicting experimental data)
- Marked boost in end-expired carbon monoxide and carboxyhemoglobin following a single "joint" (more than three times greater than the increase noted after a single tobacco cigarette)

Long-term (in frequent, habitual smokers)

- Tachyphylaxis to acute bronchodilator effect of THC
- Airflow obstruction (mainly affecting large airways, probably due to chronic irritation leading to structural changes)
- Nonspecific airway hyperreactivity (noted in smokers of both marijuana and tobacco; suggestive evidence of interaction between effects of both substances)

• *Bronchodilation:* Marijuana smoke caused moderate but statistically significant bronchodilation both in healthy volunteers and subjects with mild asthma and even reversed artificially induced bronchospasm in persons with asthma. These results were in marked contrast to the mild transient bronchoconstrictor effect of tobacco smoke.

Marijuana-induced bronchodilation was noted immediately after smoking and lasted for at least two hours; it was not observed after smoking marijuana from which the cannabinoids had been extracted with methanol. That marijuana-related bronchodilation is a pharmacologic response specific to THC was confirmed by experiments demonstrating that synthetic oral THC produced dose-dependent bronchodilation.

Efforts to explore the therapeutic potential of the bronchodilator properties of THC have not succeeded for several reasons: Only slight bronchodilation was achieved with oral THC, and unacceptable side effects resulted when THC was given systemically. When THC was administered as an aerosol, it had an irritating effect on the tracheobronchial tree, and it provoked bronchospasm in some patients with asthma. Further, synthetic analogues of this substance appear to have only negligible bronchodilator properties.

Although bronchodilation is an immediate response to THC, administration of this compound by smoking marijuana is not an appropriate therapeutic strategy for bronchospastic disease because of the many irritating gases and particulates in the smoke that are likely to have an adverse long-term impact on the airways. In addition, tachyphylaxis to the acute bronchodilator effect of THC has been demonstrated after long-term regular use.

Table 2—Clinical findings in marijuana smokers

Increased prevalence of chronic cough, sputum, and wheezing; increased frequency of acute bronchitic episodes in heavy, habitual smokers
Pneumothorax and/or pneumomediastinum (isolated reports)
Cough and hemoptysis temporally related to smoking paraquat-contaminated marijuana
Bronchopulmonary allergic aspergillosis (case report)
Aspergillus pneumonitis in immunocompromised smoker (case report)

The mechanism of THC-induced bronchodilation remains unclear. The bronchodilator effect is not caused by stimulation of β-adrenergic receptors or blockade of muscarinic receptors because it is not inhibited by β-adrenergic blockade and THC does not prevent bronchospasm provoked by a cholinergic agonist. Attempts to elucidate the mechanism of bronchodilation produced by THC have been hampered by failure to elicit a bronchodilator response in experimental animals. Although it has been suggested that marijuana-induced relaxation of airway smooth muscle could be mediated by the effects of THC on the central nervous system (CNS), the observation that aerosolized THC causes bronchodilation without any significant CNS intoxication casts doubt on this possibility.

Table 3—Bronchoscopic findings in heavy, habitual marijuana smokers*

Endoscopic visualization
Acute tracheobronchitis indicated by hyperemia or erythema
Increased secretions
Vocal cord inflammation
Tracheobronchial histopathology
Squamous metaplasia
Hyperplasia of basal and goblet cells
Cellular disorganization of epithelium
Cellular atypia with hyperchromatic nuclei and increased frequency of mitosis
Basement membrane thickening
Chronic cellular inflammation
Bronchoalveolar lavage cells
Increased numbers of alveolar macrophages and polymorphonuclear neutrophils
Impaired killing of *Candida* by alveolar macrophages
Numerous, large complex cytoplasmic inclusions in alveolar macrophages

*With or without concomitant tobacco smoking

• *Maximal oxygen consumption during exercise:* After smoking a single marijuana cigarette containing 10 mg of THC, maximal oxygen consumption was measured during an exercise protocol that employed a multistage, rapidly incremented workload. When this marijuana cigarette was smoked, oxygen consumption was slightly but significantly less than when placebo marijuana (containing a negligible amount of THC) was smoked. Maximum heart rate was similar. The mechanism of this impairment in maximal exercise performance may be secondary to premature achievement of maximal heart rate caused by the cardioaccelerator effect of THC.

• *Ventilatory drive and resting oxygen consumption:* Results of studies of the effects of smoked marijuana on respiratory control in small numbers of experienced users have yielded conflicting results. One group of researchers noted an

acute depressant effect on ventilation from smoking marijuana containing 19.8 mg of THC. Other investigators observed significant ventilatory stimulation and an increase in resting oxygen consumption during the hour after a marijuana cigarette containing 11 mg of THC was smoked.

It is unclear whether this discrepancy resulted from differences in the methodology used by these two groups of investigators when measuring ventilatory responses, individual variations in ventilatory response to marijuana, or a dose-dependent bimodal effect of marijuana on ventilatory control.

Long-term effects

In India and Jamaica, the prevalence of chronic bronchitis has been noted to be greater among habitual marijuana smokers than among nonsmokers, but these conclusions were based largely on uncontrolled observations. In contrast, a few small-scale studies in Costa Rica, Jamaica, and Greece failed to find evidence of a higher frequency of pulmonary disease or clinically significant physiologic abnormalities in habitual smokers of marijuana compared with control tobacco smokers.

These studies, however, were flawed by the small size and nonrepresentative nature of the samples of subjects examined, and were insufficiently controlled with regard to tobacco smoking. In addition, the cross-sectional design of these studies may not have been sensitive to the detection of long-term consequences of habitual marijuana smoking within individual subjects.

Tennant reported a high prevalence of respiratory symptoms and tracheal histopathologic findings in young, heavy smokers of hashish. (Hashish, which is derived

Marijuana smoking

Now, striking evidence of short- and long-term consequences

from the resin scraped off the top leaves of the cannabis plant, has a much higher THC content than marijuana, which is usually prepared from the whole leaf.) Tennant studied 200 patients who reported to a military medical facility in West Germany with complaints of pharyngitis (75%), rhinitis (13%), bronchitis (10%), and/or asthma (2%), which were temporally related to hashish smoking.

Of this group, six patients with bronchitis who smoked 50 g or more of hashish a month (as well as one pack of tobacco cigarettes a day) underwent bronchoscopy and tracheal biopsies. The mucosa appeared congested in all six, and random biopsy specimens of tracheal epithelium showed multiple abnormalities, including loss of cilia, epithelial cell hyperplasia, and atypical cells with hyperchromatic nuclei. Squamous metaplasia was present in one patient, while basement membrane thickening and chronic inflammatory cells were noted in all six patients. The fact that over 90% of the 200 hashish smokers also smoked tobacco may have biased these results.

A subsequent three- to 24-month study found that respiratory symptoms were less frequent in seven smokers of only hashish than in 23 smokers of both hashish and tobacco, although both groups had a similar prevalence (greater than 70%) of rhonchi, rales, or wheezes. Bronchoscopic results revealed that the smokers of hashish alone did not have erythema or congestion, which were present in smokers of both hashish and tobacco. Histopathologic lesions were also fewer in the hashish smokers (two of seven subjects) than in the smokers of both hashish and tobacco (23 of 23 subjects). However, the symptomatic nature of the patients, the method of recruitment, and the small numbers of patients examined may have skewed the results of the study.

An intermediate-term prospective study of 29 regular smokers of marijuana who markedly increased their consumption of marijuana from about one joint a day to an average of five joints a day for six to eight weeks showed a modest but significant worsening of several indices of airway function during the period of increased marijuana use. These changes reverted to baseline within 14 weeks of cessation of the increased use.

Extrapolation of the marijuana-related decreases in lung function in these subjects results in a yearly decline in forced expiratory volume in one second about 20 times greater than the expected rate in nonsmokers (about 30 mL/yr). This markedly accelerated decline in pulmonary function predicts the development of respiratory disability within a few short years. Since such an outcome should be obvious clinically, it is likely that these observations represent an initial steep decline in pulmonary function that would not have progressed at the same accelerated rate even if the subjects had continued to smoke marijuana more heavily than usual. Prospective studies are needed to ascertain the real rate of decline of lung function in smokers of marijuana compared with that of nonsmokers, while considering the effect of concomitant tobacco smoking.

A prospective, longitudinal study of heavy, habitual smokers of marijuana (more than two joints a day for more than five years), either alone or with tobacco, smokers of tobacco alone, and nonsmokers is currently under way at the University of California, Los Angeles. A cross-sectional comparison of 144 smokers of marijua-

na alone, 135 smokers of marijuana plus tobacco, 70 smokers of tobacco only, and 97 nonsmokers conducted from 1982 to 1985 yielded the following results:

- Smokers of marijuana alone, tobacco alone, and marijuana plus tobacco had similar incidences of acute and chronic bronchitis, which were significantly higher than those of nonsmokers.
- Habitual smokers of marijuana, either alone or with tobacco, had a significantly higher frequency of abnormalities in tests of large-airway function (airway resistance, specific airway conductance) than nonsmokers.
- Regular smokers of tobacco, irrespective of concomitant marijuana use, had a significantly higher frequency of abnormalities in tests of small-airway function and diffusing capacity than nonsmokers.
- Habitual smokers of both marijuana and tobacco, but not smokers of either substance alone, had a significantly higher frequency of nonspecific airway hyperreactivity than nonsmokers.

From a functional standpoint, therefore, habitual marijuana smoking appears to have its major impact on the large airways, while tobacco primarily affects the peripheral airways and alveolated regions of the lungs.

Why might marijuana be more harmful than tobacco?

Daily smoking of only a few marijuana joints appears to be comparable with smoking over 20 tobacco cigarettes a day in its effects on the prevalence of acute and chronic respiratory symptoms, tracheobronchial histopathologic findings, and the number of alveolar macrophages recovered in bronchoalveolar lavage fluid.

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

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

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

Bronchoscopic findings

The previously mentioned findings of chronic respiratory symptoms and functional abnormalities in a relatively high proportion of habitual, heavy marijuana smokers were complemented by bronchoscopic biopsy results in a subset of subjects from the same cross-sectional study.

We found airway hyperemia in 88% of 16 smokers of only marijuana, 92% of 13 smokers of both marijuana and tobacco, 100% of six smokers of only tobacco, and 25% of four nonsmokers (Figure 1). Light and scanning electron microscopic evaluation of proximal airway biopsy specimens showed two or more histopathologic abnormalities in all smokers (Figures 2 and 3). Squamous metaplasia was observed in all smokers of both marijuana and tobacco and in approximately 50% of the smokers of marijuana or tobacco alone.

Hyperplasia of basal and goblet cells was more prevalent in the marijuana smokers (80%) than in the combined smokers (50% to 67%) or the nonsmokers (0%). Further, cellular disorganization was more prevalent in the marijuana smokers (53%) than in the other groups.

These results indicate that relatively young, habitual, heavy marijuana smokers have a high inci-

Analysis of the mainstream smoke of a single marijuana cigarette and a single tobacco cigarette*

	Marijuana	Tobacco
Gas phase		
Carbon monoxide		
Volume %	3.99	4.58
mg	17.6	20.2
Carbon dioxide		
Volume %	8.27	9.38
mg	57.3	65
Ammonia (μg)	228	198
Hydrocyanic acid (μg)	532	498
Isoprene (μg)	83	310
Acetaldehyde (μg)	1,200	980
Acetone	443	578
Acrolein (μg)	92	85
Acetonitrile (μg)	132	123
Benzene (μg)	76	67
Toluene (μg)	112	108
Dimethylnitrosamine (ng)	75	84
Methylethylnitrosamine (ng)	27	30

	Marijuana	Tobacco
Particulate phase		
Total particulate matter, dry (mg)**	22.7	39.0
Phenol (μg)	76.8	138.5
o-Cresol (μg)	17.9	24
m- and *p*-Cresol (μg)	54.4	65
2,4- and 2,5-Dimethylphenol (μg)	6.8	14.4
Cannabidiol (μg)	190	—
Δ^9-Tetrahydrocannabinol (μg)	820	—
Cannabinol (μg)	400	—
Nicotine (μg)	—	2,850
Naphthalene (ng)	3,000	1,200
1-Methylnaphthalene (ng)	6,100	3,650
2-Methylnaphthalene (ng)	3,600	1,400
Benz[a]anthracene (ng)	75	43
Benzo[a]pyrene (ng)	31	22.1

*The reference marijuana cigarette is 85 mm and 1.115 mg; the reference tobacco cigarette is 85 mm and 1,100 mg.

**There is 40.7 mg of dry particulate matter in sidestream marijuana smoke and 57.3 mg in sidestream tobacco smoke.

Reproduced from Cohen S, Tashkin DP (eds): *Marijuana Smoking and Its Effects on the Lung*. New York, The American Council on Marijuana and Other Psychoactive Drugs, Inc, 1981.

dence of abnormal airway appearance and tracheobronchial histopathologic findings, irrespective of concomitant tobacco smoking, justifying the concern about potential long-term clinical sequelae, such as the development of chronic airway disease and lung cancer. Moreover, the combined habit of marijuana and tobacco smoking could have additive or possibly synergistic effects on the airways.

Additional studies using bronchoscopy have also provided important information about the effects of habitual marijuana smoking on bronchoalveolar cell populations: The total number of cells and the number of alveolar macrophages recovered in bronchoalveolar lavage (BAL) fluid are significantly increased in smokers of marijuana and/or tobacco. The number of neutrophils from BAL fluid is significantly higher in smokers of both marijuana and tobacco and smokers of tobacco only than in nonsmokers. Preliminary ultrastructural evaluation of alveolar macrophages from marijuana smokers indicates a greater variety of large, complex, frequently multilayered cytoplasmic inclusions than is seen in macrophages of nonsmokers or tobacco smokers. With respect to function, the mac-

Figure 1 – *Increased hyperemia of the tracheobronchial wall is a common bronchoscopic finding in heavy, habitual marijuana smokers.*

rophages from marijuana or tobacco smokers exhibit decreased killing of *Candida albicans;* the clinical significance of this microbicidal defect is as yet unknown.

Other potential complications

• *Barotrauma:* Isolated occurrences of pneumothorax and/or pneumomediastinum have been reported in association with marijuana smoking. In these instances, the barotrauma was believed to be caused by an increase in intrathoracic pressure from Valsalva's maneuver during breath-holding after deep inhalation of the smoke.

• *Effects on plasma theophylline clearance:* Hydrocarbon components of marijuana (and tobacco) smoke can induce hepatic microsomal enzymes to speed up the metabolic breakdown of theophylline. As a result, plasma theophylline clearance is increased and serum theophylline half-life is shortened in habitual marijuana (and tobacco) smokers who are taking theophylline. In patients treated with theophylline, therefore, it is important to inquire about a history of regular marijuana smoking, as well as tobacco smoking, because such practices can influence dosing requirements.

• *Pulmonary effects of marijuana contaminants:* Government efforts to control marijuana use have included spraying of marijuana fields with paraquat, a herbicide that can cause severe oxidative lung injury if swallowed in a concentrated solution. When instilled into the lungs of experimental animals paraquat causes pulmonary edema, eventually leading to lung fibrosis. However, since paraquat is largely destroyed by the heat of combustion, only a minute fraction of this compound is released in the smoke of paraquat-contaminated marijuana. Moreover, since paraquat is highly water-soluble, the small fraction that does survive pyrolysis is likely to be largely removed by absorption in the moisture of the upper airways.

Paraquat, when pyrolyzed, is degraded to a bipyridine, a respiratory irritant. Therefore, the cough and hemoptysis that have been reported after paraquat-contaminated marijuana was smoked are most likely caused by respiratory tract irritation from bipyridine or other combustion products in marijuana smoke, rather than from paraquat itself. However, the possibility of chronic pulmonary fibrosis developing after repeated exposure to even minute quantities of paraquat by heavy, habitual users of contaminated marijuana cannot be completely discounted.

Contamination of marijuana with *Aspergillus fumigatus* can cause lung disease in humans, as illustrated by two case reports—one of a patient with allergic bronchopulmonary aspergillosis and another of *Aspergillus* pneumonitis in a young patient with impaired immunity that developed after smoking several pipesful of marijuana contaminated with the fungus. In addition to fungal contaminants, potentially pathogenic gram-negative bacteria have also been found frequently as contaminants of marijuana.

Marijuana is sometimes smoked by cancer patients to prevent chemotherapy-induced nausea. However, unless the marijuana cigarettes are sterilized before use to eliminate potential pathogens, serious pulmonary infection could ensue because these patients already have impaired lung antimicrobial defenses due to malignancy and immunosuppressive drug therapy. Marijuana smoke may also have a direct effect on the ability of alveolar macrophages to phagocytize and kill potential pathogens which could further predispose patients receiving chemotherapy to lung infections.

FUTURE STUDIES

The nature, extent, and clinical significance of the pulmonary conse-

quences of habitual marijuana smoking have not yet been adequately defined. Further studies are needed to assess the long-range impact of habitual marijuana smoking on respiratory symptoms, lung dysfunction, tracheobronchial histopathologic findings, and alveolar macrophage structure and function. The long-term effects of marijuana smoking on immunologic and nonimmunologic defenses against lung injury also need further evaluation.

Additional research is needed to evaluate the interactive effects of tobacco and marijuana on the lungs and to determine the extent to which marijuana-related abnormalities in lung structure and function can be reversed with cessation of smoking.

In recent years, smoking of cocaine "freebase," including dealer-

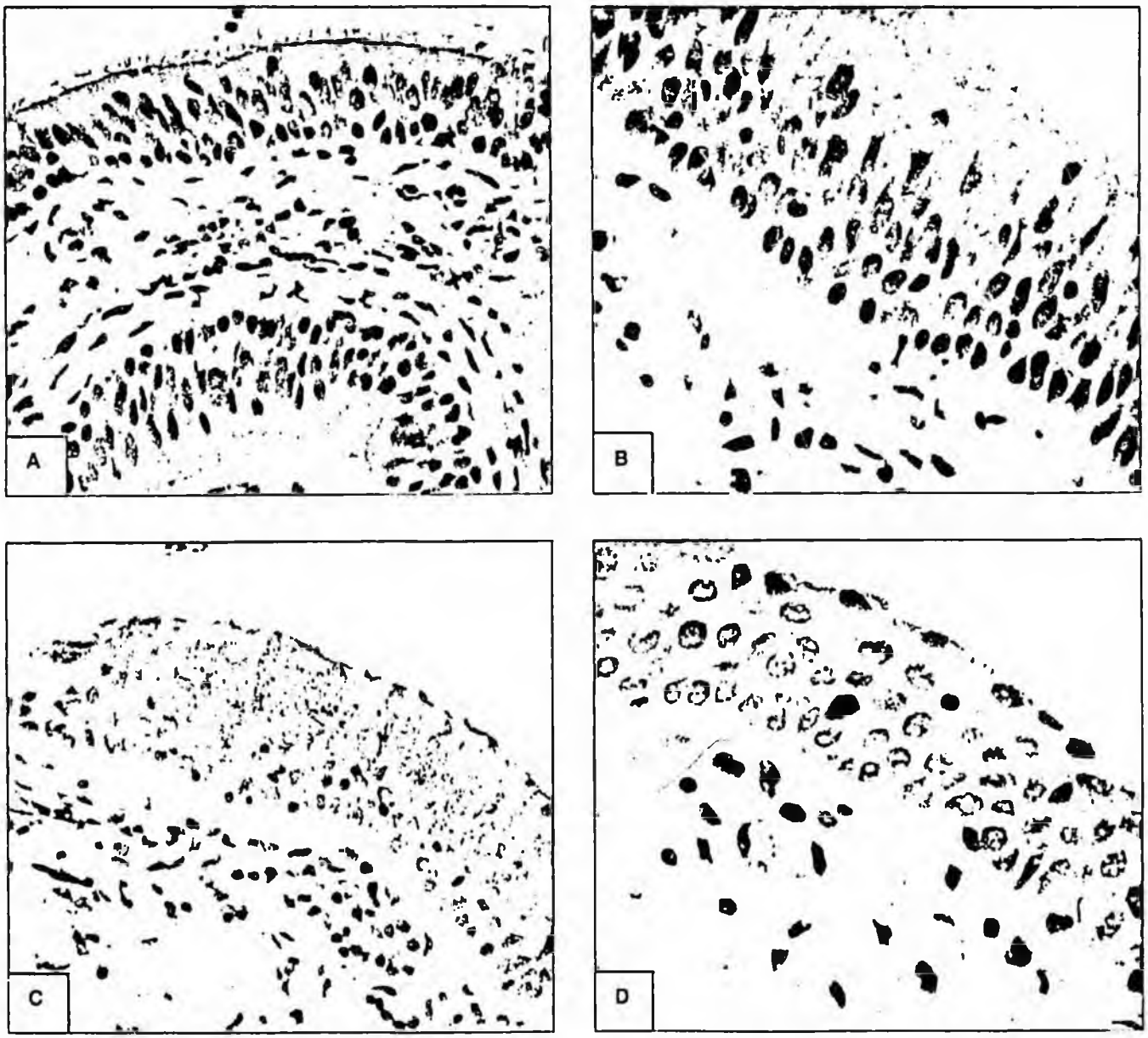

Figure 2 – *Occasional goblet cells and numerous ciliated epithelial cells are the normal findings of light microscopic evaluation of a bronchial biopsy specimen from a healthy nonsmoker (A) (× 130). In contrast, basal and goblet cell hyperplasia, intraepithelial inflammation, and numerous mucus-filled goblet cells are evident in the bronchial biopsy specimen from a marijuana smoker (B and C) (× 250).*

The bronchial mucosa specimen from a marijuana plus tobacco smoker reveals loss of normal ciliated epithelial covering and replacement by squamous epithelium, indicating squamous metaplasia. Note the mitotic figure present in the center of the mucosa (D) (× 250).

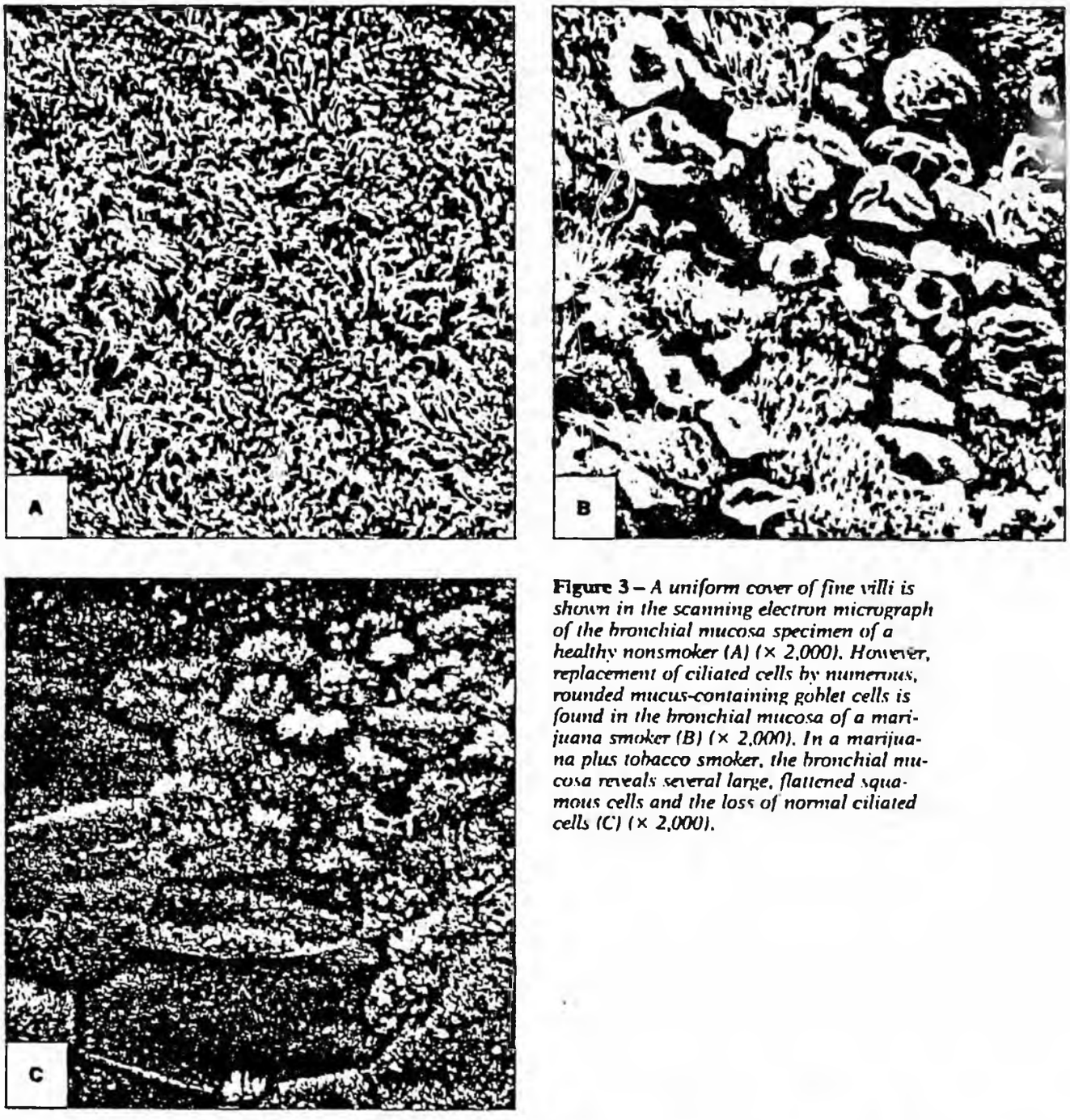

Figure 3 – *A uniform cover of fine villi is shown in the scanning electron micrograph of the bronchial mucosa specimen of a healthy nonsmoker (A) (× 2,000). However, replacement of ciliated cells by numerous, rounded mucus-containing goblet cells is found in the bronchial mucosa of a marijuana smoker (B) (× 2,000). In a marijuana plus tobacco smoker, the bronchial mucosa reveals several large, flattened squamous cells and the loss of normal ciliated cells (C) (× 2,000).*

prepared alkaloidal cocaine ("crack"), has become increasingly prevalent in our society, especially among habitual smokers of marijuana. Therefore, future studies also need to address the independent and interactive effects of smoking cocaine and marijuana on various aspects of pulmonary structure and function.

WHAT YOU CAN DO

Since habitual marijuana smoking has significant effects on health, it is important for us to ascertain, through nonjudgmental history taking, whether and to what extent our patients smoke marijuana. This information can be clinically useful in several ways.

- Symptoms of bronchitis can be due to marijuana smoking and should resolve following cessation of marijuana use. ▶

ZANTAC® 150 Tablets **BRIEF SUMMARY**
(ranitidine hydrochloride)
ZANTAC® 300 Tablets
(ranitidine hydrochloride)

The following is a brief summary only. Before prescribing, see complete prescribing information in ZANTAC® product labeling.

INDICATIONS AND USAGE: ZANTAC® is indicated in:
1. Short-term treatment of **active duodenal ulcer**. Most patients heal within four weeks.
2. **Maintenance therapy** for duodenal ulcer patients at reduced dosage after healing of acute ulcers.
3. The treatment of **pathological hypersecretory conditions** (eg, Zollinger-Ellison syndrome and systemic mastocytosis).
4. Short-term treatment of **active, benign gastric ulcer**. Most patients heal within six weeks and the usefulness of further treatment has not been demonstrated.
5. Treatment of **gastroesophageal reflux disease** (GERD). Symptomatic relief commonly occurs within one or two weeks after starting therapy. Therapy for longer than six weeks has not been studied.

In active duodenal ulcer, active, benign gastric ulcer, hypersecretory states, and GERD, concomitant antacids should be given as needed for relief of pain.

CONTRAINDICATIONS: ZANTAC® is contraindicated for patients known to have hypersensitivity to the drug.

PRECAUTIONS: General: 1. Symptomatic response to ZANTAC® therapy does not preclude the presence of gastric malignancy.

2. Since ZANTAC is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function (see **DOSAGE AND ADMINISTRATION**). Caution should be observed in patients with hepatic dysfunction since ZANTAC is metabolized in the liver.

Laboratory Tests: False-positive tests for urine protein with Multistix® may occur during ZANTAC therapy and therefore testing with sulfosalicylic acid is recommended.

Drug Interactions: Although ZANTAC has been reported to bind weakly to cytochrome P-450 in vitro, recommended doses of the drug do not inhibit the action of the cytochrome P-450 linked oxygenase enzymes in the liver. However, there have been isolated reports of drug interactions which suggest that ZANTAC may affect the bioavailability of certain drugs by some mechanism as yet unidentified (eg, a pH-dependent effect on absorption or a change in volume of distribution).

Carcinogenesis, Mutagenesis, Impairment of Fertility: There was no indication of tumorigenic or carcinogenic effects in lifespan studies in mice and rats at doses up to 2 000 mg/kg/day.

Ranitidine was not mutagenic in standard bacterial tests (*Salmonella / E. coli*) for mutagenicity at concentrations up to the maximum recommended for these assays.

In a dominant lethal assay, a single oral dose of 1,000 mg/kg/day to male rats was without effect on the outcome of two matings per week for the next nine weeks.

Pregnancy: Teratogenic Effects: Pregnancy Category B: Reproduction studies have been performed in rats and rabbits at doses up to 160 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to ZANTAC. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: ZANTAC is secreted in human milk. Caution should be exercised when ZANTAC is administered to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Use in Elderly Patients: Ulcer healing rates in elderly patients (65 to 87 years of age) were no different from those in younger age groups. The incidence rates for adverse events and laboratory abnormalities were also not different from those seen in other age groups.

ADVERSE REACTIONS: The following have been reported as events in clinical trials or in the routine management of patients treated with oral ZANTAC®. The relationship to ZANTAC therapy has been unclear in many cases. Headache, sometimes severe, seems to be related to ZANTAC administration.

Central Nervous System: Rarely, malaise, dizziness, somnolence, insomnia, and vertigo. Rare cases of reversible mental confusion, agitation, depression, and hallucinations have been reported, predominantly in severely ill elderly patients. Rare cases of reversible blurred vision suggestive of a change in accommodation have been reported.

Cardiovascular: Rare reports of tachycardia, bradycardia, and premature ventricular beats.

Gastrointestinal: Constipation, diarrhea, nausea/vomiting, and abdominal discomfort/pain.

Hepatic: In normal volunteers, SGPT values were increased to at least twice the pretreatment levels in 6 of 12 subjects receiving 100 mg qid IV for seven days, and in 4 of 24 subjects receiving 50 mg qid IV for five days. With oral administration there have been occasional reports of reversible hepatitis, hepatocellular or hepatocanalicular or mixed, with or without jaundice.

Musculoskeletal: Rare reports of arthralgias.

Hematologic: Reversible blood count changes (leukopenia, granulocytopenia, thrombocytopenia) have occurred in a few patients. Rare cases of agranulocytosis or of pancytopenia, sometimes with marrow hypoplasia, have been reported.

Endocrine: Controlled studies in animals and man have shown no stimulation of any pituitary hormone by ZANTAC (ranitidine hydrochloride) and no antiandrogenic activity, and cimetidine-induced gynecomastia and impotence in hypersecretory patients have resolved when ZANTAC has been substituted. However, occasional cases of gynecomastia, impotence, and loss of libido have been reported in male patients receiving ZANTAC, but the incidence did not differ from that in the general population.

Integumentary: Rash, including rare cases suggestive of mild erythema multiforme, and rarely alopecia.

Other: Rare cases of hypersensitivity reactions (eg, bronchospasm, fever, rash, eosinophilia) and small increases in serum creatinine.

OVERDOSAGE: Information concerning possible overdosage and its treatment appears in the full prescribing information.

DOSAGE AND ADMINISTRATION: Active Duodenal Ulcer: The current recommended adult oral dosage is 150 mg twice daily. An alternate dosage of 300 mg once daily at bedtime can be used for patients in whom dosing convenience is important. The advantages of one treatment regimen compared to the other in a particular patient population have yet to be demonstrated.

Maintenance Therapy: The current recommended adult oral dosage is 150 mg at bedtime.

Pathological Hypersecretory Conditions (such as Zollinger-Ellison syndrome): The current recommended adult oral dosage is 150 mg twice a day. In some patients it may be necessary to administer ZANTAC® 150-mg doses more frequently. Doses should be adjusted to individual patient needs, and should continue as long as clinically indicated. Doses up to 6 g/day have been employed in patients with severe disease.

Benign Gastric Ulcer: The current recommended adult oral dosage is 150 mg twice a day.

GERD: The current recommended adult oral dosage is 150 mg twice a day.

Dosage Adjustment for Patients with Impaired Renal Function: On the basis of experience with a group of subjects with severely impaired renal function treated with ZANTAC, the recommended dosage in patients with a creatinine clearance less than 50 ml/min is 150 mg every 24 hours. Should the patient's condition require, the frequency of dosing may be increased to every 12 hours or even further with caution. Hemodialysis reduces the level of circulating ranitidine. Ideally, the dosage schedule should be adjusted so that the timing of a scheduled dose coincides with the end of hemodialysis.

HOW SUPPLIED: ZANTAC® 300 Tablets (ranitidine hydrochloride equivalent to 300 mg of ranitidine) are yellow, capsule-shaped tablets embossed with "ZANTAC 300" on one side and "Glaxo" on the other. They are available in bottles of 30 (NDC 0173-0393-40) and unit dose packs of 100 tablets (NDC 0173-0393-47).

ZANTAC® 150 Tablets (ranitidine hydrochloride equivalent to 150 mg of ranitidine) are white tablets embossed with "ZANTAC 150" on one side and "Glaxo" on the other. They are available in bottles of 60 tablets (NDC 0173-0344-42) and unit dose packs of 100 tablets (NDC 0173-0344-47).

Store between 15° and 30°C (59° and 86°F) in a dry place. Protect from light. Replace cap securely after each opening.

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Glaxo

Glaxo Inc
Research Triangle Park, NC 27709

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- A history of marijuana smoking is occasionally associated with otherwise unexplained hemoptysis or pneumothorax.
- Marijuana use could predispose to pulmonary infection, especially in patients with preexisting impairment in immunity.
- In patients receiving therapy with theophylline, inadequate serum levels could result from the enhancement of hepatic clearance of theophylline by components in marijuana smoke.
- Several lines of evidence strongly suggest that habitual marijuana smoking may be a causative factor in the development of bronchogenic carcinoma.

The latter possibility is further supported by the several-fold greater deposition in the lower respiratory tract of tar particulates from the smoke of one marijuana joint compared with that from one tobacco cigarette. However, there is a long lag period between initiation of daily exposure to tobacco tar and the development of frank neoplasia. Moreover, smoking-related pulmonary malignancy will develop in only a small, albeit significant, percentage of smokers.

For these reasons, it will be difficult to document empirically a link between heavy, habitual marijuana smoking and lung cancer. In the case of tobacco smoking, this link was established by autopsy and epidemiologic studies. To permit pathologists and epidemiologists to ascertain an analogous association for marijuana, we need to ask patients about their marijuana smoking habits and to include this information in the medical record.

A strong physician message to patients informing them of what we do know about the harmful effects of marijuana on the lung and other organs may persuade some of them, especially those with man-

juana-related symptoms, to quit smoking.

Patients and parents of children who smoke marijuana who want further advice and assistance can contact the following organizations: PRIDE (Parent Resource Institute for Drug Education), Atlanta; National Federation of Parents for Drug-Free Youth, Silver Springs, Maryland; The American Council for Drug Education, Rockville, Maryland; or their local chapter of the American Lung Association. □

SUGGESTED READINGS

The authors recommend these references for physicians seeking further information:

- Barbers RG, Gong H Jr, Tashkin DP, et al: Differential examination of bronchoalveolar lavage cells in tobacco cigarettes and marijuana smokers. *Am Rev Respir Dis* 1987;135:1271-1275. Bronchoalveolar lavage yielded about two to three times as many alveolar macrophages from the lungs of marijuana-only or tobacco-only smokers than from nonsmokers.

- Gong H Jr, Fligiel SEG, Tashkin DP, et al: Tracheobronchial changes in heavy, habitual smokers of marijuana with and without tobacco. *Am Rev Respir Dis* 1987;136:142-149. Microscopic abnormalities were seen in both marijuana and tobacco smokers, with a possible additive effect in those patients who smoked both.

- Hoffmann D, Brunnemann KD, Gori BH, et al: On the carcinogenicity of marijuana smoke. *Recent Adv Phytochem* 1975;9:63-81. Comparison of the smoke contents of a marijuana joint and a tobacco cigarette revealed 60 cannabinoid compounds in marijuana that are not in tobacco, and about 50% more of the carcinogenic polycyclic aromatic hydrocarbons in marijuana.

- Institute of Medicine: *Marijuana and Health*. Washington DC, National Academy Press, 1982. An excellent review of published reports concerning the health effects of marijuana prepared by a distinguished panel of scientists.

- Tashkin DP, Coulson AH, Clark VA, et al: Respiratory symptoms and lung function in habitual heavy smokers of marijuana alone, smokers of marijuana and tobacco, smokers of tobacco alone, and nonsmokers. *Am Rev Respir Dis* 1987;135:209-216. Results revealed a significantly and comparably higher prevalence of acute and chronic respiratory symptoms in all the smoking groups compared with the nonsmokers. Tobacco smoking was associated with impairment in diffusing capacity and small-airway function, while marijuana smoking adversely influenced large-airway function.

- Tashkin DP, Shapiro BJ, Frank IM: Acute pulmonary physiologic effects of smoked marijuana and oral 9-tetrahydrocannabinol in healthy young men. *N Engl J Med* 1973;289:336-341. Study participants smoked five joints a day instead of their customary one for six to eight weeks and showed a dose-related decrease in large- and small-airway function; these changes reverted to baseline within one to four weeks of cessation of heavy daily marijuana use.

- Tashkin DP, Shapiro BJ, Lee YE, et al: Subacute effects of heavy marijuana smoking on pulmonary function in healthy men. *N Engl J Med* 1976;294:125-129. Smoking of marijuana was followed almost immediately by significant bronchodilation that lasted at least one hour; smoking of tobacco resulted in mild transient bronchoconstriction. Ingestion of Δ^9-tetrahydrocannabinol produced dose-dependent bronchodilation with a peak effect at 1½ to three hours and a duration of four to six hours.

- Tennant FS Jr: Histopathologic and clinical abnormalities in the respiratory system in chronic hashish smokers. *Subst Alcohol Actions Misuse* 1980;1:93-100. Bronchoscopy revealed extensive histopathologic abnormalities in smokers of both hashish and tobacco, but fewer changes in those who smoked only hashish or tobacco, suggesting an additive or synergistic effect on airway pathology.

REPORT OF THE COUNCIL ON SCIENTIFIC AFFAIRS

Proceedings American Medical Association
House of Delegates
December, 1980

Report: B
(I-60)

Subject: Marijuana in the '80s

Presented by: Rogers J. Smith, M. D., Chairman

Referred to: Reference Committee E
(Grant V. Rodkey, M.D., Chairman)

It is perhaps ironic that concomitant with emerging therapeutic possibilities for cannabis and its constituents, new evidence has appeared that marijuana is hazardous to health.

On the one hand, we are at the threshold of providing symptomatic relief to some patients who suffer extreme nausea from cancer chemotherapy and for whom existing anti-emetic agents are ineffective. On the other hand, we face the growing prospect of an appreciable number of marijuana users incurring physiological and psychological impairment.

Marijuana is the drug of the young. More than two-thirds of 18 to 25 year old persons in the United States have tried it on at least one occasion.(1) Some have been chronic users. For the children, adolescents and young adults who do smoke marijuana regularly there is considerable risk ahead. The risk for them, and for society, is of a nature and magnitude that belies the characterization of marijuana as a "soft drug." It can be hard on its user, and inflict a great deal of harm.

The Council on Scientific Affairs has on two previous occasions called attention to the health aspects of marijuana use. In a report adopted by the House of Delegates in December 1977 (Report D: I-77), the Council expressed concern over evidence of a range of adverse effects that had been appearing in the scientific literature.(2) Two years later, in December 1979 (Report I: I-79), the Council reaffirmed its concern to the House, and emphasized in particular the dangers of pulmonary involvement and possible carcinogenesis.(3) The Council also took cognizance of investigations into possible medical applications of marijuana, and urged that research be more rigorously designed and conducted in the future.

In adopting the second Council report, the House asked the Council to prepare a subsequent report on "(1) increased regular use of marijuana by youth, (2) the proliferation of the paraphernalia industry and so-called 'headshops,' and (3) the subverting of FDA laws and regulations by state laws that legalize marijuana use for medical purposes."

This report was developed for the Council on Scientific Affairs by a special panel on drug abuse consisting of Joseph H. Skom, M. D., Chicago, chairman; Henry Brill, M. D., Brentwood, Long Island; Sidney Cohen, M. D., Los Angeles; David E. Smith, M. D., San Francisco; and Jokichi Takamine, M. D., Los Angeles. Rogers J. Smith, M. D., Portland, Oregon, chairman of the Council, participated as an ex-officio member of the panel.

Past House Action: A-80:212; I-79:178-181; I-77:188-193

Then, in July 1980, the House referred to the Council Resolution 3, introduced by the Wisconsin delegation, proposing that, in view of growing evidence of health hazards, the AMA "officially declare marijuana to be a dangerous drug."

This report, which constitutes a response to these requests, comes in the wake of three documents released earlier this year by the National Institute on Drug Abuse (NIDA): Marijuana and Health: 1980,(4) HEW's eighth annual report to Congress; A Drug Retrospect: 1962 to 1980;(5) and The National Survey on Drug Abuse: 1979(1) Taken together, these publications paint a disquieting picture of a growing proportion of young people exposing themselves to dangers that no longer are in the area of tenuous speculation.

Use of Marijuana by Youth

NIDA's latest national survey reflected significant changes in marijuana usage from 1971 to 1979.(1)

In 1971, one of 10 adolescents aged 14 and 15 reported ever using the drug. By 1979, the rate for this age group had tripled, climbing to 32 per cent. In the same period life time prevalence for 16 and 17 year olds had risen from 27 per cent to 51 per cent.

Looking at the 12 to 17 year olds who said in 1979 that they smoked marijuana on a fairly regular basis, the survey showed that 8.4 per cent reported using the drug on five or more days during the previous month. Over 22 per cent of young adults (18 to 25 years old) reported this frequency of usage. These figures, based as they are on a survey of households, undoubtedly are conservative; it can be assumed that a sizable number of chronic users detach themselves from family settings, and that students living away from home -- who were not interviewed -- might include a proportionately larger number of regular users than the surveyed population.

Although the NIDA survey indicated that only 8 per cent of 12 and 13 year old children in 1979 had ever tried marijuana, this figure is a third larger than the percentage of children of that age in 1971 who said they had ever used it. Moreover, other surveys conducted in two states found a greater proportion of children than this who used marijuana. In 1978, one in five 8th graders questioned in Maryland said they were currently smoking marijuana, and one in 11 said they were doing so daily or several times a week.(6) In Maine the same year, 56 per cent of 13 to 15 year olds who were sampled said they had used the drug at least once, and 42 per cent reported being regular users.(7)

As pointed out in the two previous Council reports on marijuana, regular use can constitute a hazard for anyone; especially vulnerable, however, are children and adolescents, who are in crucial phases of psychological and physiological development. Additional findings of adverse effects of marijuana use in animals and humans, coupled with evidence of substantial regular use by young people, therefore have serious implications for the health of a new generation.

Some of the major recent findings as summarized in the 1980 Marijuana and Health report [4] that have particular relevance to youth can be grouped under the headings of brain function, psychomotor effects, reproductive function, pulmonary involvement, and psychopathology.

It should be emphasized that most deleterious effects are related to chronic or consistent, as opposed to episodic, use of marijuana. Metabolites of delta-9-tetrahydrocannabinol (THC) can be found in fatty tissue for up to eight days following intake, so that a cumulative build-up takes place with regular use. (THC is the most prominent psychoactive component of marijuana.) The quality of the marijuana is also significant; in this regard, it is noteworthy that cannabis preparations in use today are as much as five times as potent in THC content as those available five years ago.

Brain Function

Conclusive evidence of macroscopic brain damage is lacking. Microscopic cellular changes, however, have been found in brains of rhesus monkeys who received the equivalent of one marijuana cigarette daily for six months.[8] Similar measurements have not been made in humans.

Yet, the possibility that such changes, which may or may not be reversible, can take place in man as well as in another primate cannot be dismissed out of hand. Moreover, damage does not necessarily have to be visible to result in impaired mental functioning.

In that regard, there are abundant anecdotal reports, if not controlled studies, on the lack of academic drive on the part of students who regularly use high doses of marijuana. Long-term sedative and other effects from chronic intake may combine with acute intoxication effects to initiate or to reinforce inattention to schoolwork or the wish to drop out.

The NIDA report[4] alludes to "dozens of experimental studies" which consistently have shown adverse acute effects of marijuana use on cognition and immediate memory; so that for "substantial numbers of high school students (who) are using marijuana during the course of the school day...a detrimental effect on their classroom functioning and knowledge acquisition" is likely.

Psychomotor Effects

The Council in its 1977 report on marijuana singled out motor vehicle crashes as potentially the most serious consequence of psychomotor impairment resulting from acute intoxication. Subsequent studies have indicated that as many as eight of ten marijuana users sometimes drive when they are "high."[4] NIDA predicts that "as use becomes increasingly common and socially acceptable and as the risk of arrest for simple possession decreases, more users are likely to risk driving while high."[4]

A recent study in California, involving blood samples of 1,800 motorists arrested for driving while intoxicated, detected marijuana in 16 per cent of the cases, nearly all of them in conjunction with the presence of alcohol.[9]

The concomitant use of marijuana and alcohol, which is quite common, has its greatest implications in the area of highway safety. Reduction in reaction time, poor cognition and impaired coordination that have been observed with the use of either substance alone are markedly amplified when the two drugs are taken in combination.(10)

Reproductive Function

Possible disturbances in endocrine function of adolescents and young adults are of greatest interest insofar as they adversely affect sexuality and reproduction. In 1977, the evidence for such effects was sparse. Now, although inconclusive and often preliminary, there is a growing body of data from studies of chronic heavy use in animals and humans that point to diminished fertility and that substantiate danger to the fetus.

For males, there is conflicting evidence regarding the lowering of testosterone levels, especially as to whether such effects are long-term and attendant upon chronic use, or transitory as a result of acute administration. In either case, interesting research questions can be raised concerning aphrodisiac qualities of marijuana that have been alleged by some users. Reduced sperm counts, which were found in one controlled study, probably are not as significant for decreased fertility as are abnormalities in structure and impaired motility, also detected in sperm in this study.(11)

For females, chronic marijuana use may cause abnormal menstruation, including failure to ovulate, and fetal damage. Menstrual problems were evident in a controlled study of street users in St. Louis,(12) although concomitant use of alcohol by some of the subjects could have had some influence on the results. Experiments with rhesus monkeys have implicated THC as a disruptive influence on the reproductive system, with effects apparently mediated through inhibition of pituitary gonadotropin secretion, and also possibly through direct action on reproductive tissues.(13) In another study, female monkeys treated with THC over a period of three to five years at levels comparable to daily human consumption of one or two marijuana cigarettes, suffered four times the incidence of fetal deaths, abortions and resorptions as did drug-free controls.(14) Although demonstrable fetal effects have been largely embryocidal, the possibility of abnormal fetal development as a result of the mother smoking marijuana during pregnancy cannot be ruled out.

Pulmonary Involvement

The two previous Council reports cited evidence of bronchial impairment and lung damage, including carcinogenic risks, associated with chronic and heavy marijuana smoking, and with combined marijuana and tobacco use. Additional supporting data come from a study done with rats who inhaled marijuana smoke daily for a period of one-eighth to one-half their life spans and suffered degenerative changes in their lungs more severe than those caused by cigarette tobacco.(15).

Although the degree of comparability of marijuana and tobacco smoke in pulmonary effects is still debatable, one study of bronchoconstriction found

that smoking less than one marijuana cigarette per day diminished vital capacity of the lungs as much as smoking 16 tobacco cigarettes.(16) Because smoking several marijuana "joints" daily is not unusual among young people, their risk of incurring pulmonary problems may be far greater than that of heavy users of tobacco. The combination of tobacco and marijuana smoking, a common practice, is probably additive in its pulmonary side effects.

The 1979 Council report also dealt with the issue of spraying marijuana crops with paraquat, a herbicide found to have possible toxic pulmonary effects, although no evidence of paraquat toxicity in humans from smoked marijuana has been noted. This spraying reportedly has been discontinued; nevertheless, it would be advisable, in any future consideration of applying herbicides to marijuana plants, to determine and evaluate the health hazards of the chemicals involved before actually putting them into use.

Psychopathology

It has been known for some time that marijuana use can produce panic reactions, flashbacks and other emotional disturbances, and that children and adolescents are at high risk psychiatrically when they abuse psychoactive substances.

It is now also clear that persons with a history of schizophrenia or other major mental disorders place themselves in jeopardy by using marijuana, because even acute use has been shown to precipitate psychiatric symptoms in such individuals.(17)

The fact that the marijuana being smoked today is far more potent than that used just a few years ago may bring an increasing number of psychiatric casualties into emergency rooms, crisis centers, and physician's offices. It might also produce confirming evidence of the "cannabis psychosis" reported in other countries where typical dose levels and drug potency have been higher than those heretofore found in the United States.

Implications of the Research

Marijuana is a dangerous drug. A growing body of evidence from both animal and human studies and from clinical observations attests to its deleterious effects on behavior, performance, and functioning of various organ systems. There undoubtedly must be improvement in research design and techniques before definitive incontrovertible data can be secured in certain areas. But that is no reason to hesitate in calling attention to the potentialities for harm as they become clearer and more widespread.

In view of the evidence of possible adverse effects of marijuana use, the sale of, or other trafficking in, marijuana should be subject to stringent penalties and vigorous prosecution.

The AMA has long opposed excessive and unrealistic penalties for possession of small amounts of this drug for personal use. Nevertheless, legislative action that is designed to moderate penalties for possession should be of

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Behavioral, Psychosocial, and Academic Correlates of Marijuana Usage in Adolescence

A Study of a Cohort Under Treatment

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In 1985 approximately 120,000 American high school seniors smoked marijuana daily. We interviewed 35 middle-class, cannabis-dependent adolescents with a mean age of 16 years who were patients in a drug treatment program. The patients also completed a lengthy self-assessment questionnaire designed to elicit information on drug-related problems. Our results show that family harmony, school attendance, and school achievement deteriorated once these young people began to use marijuana at least 4 days a week. The following behaviors were noted: remaining away from home without permission or parental knowledge for at least 7 consecutive days (29%), a D or F grade average on the last report card before they entered the drug treatment program (43%), involvement in a motor vehicle accident when the driver was under the influence of marijuana (26%), suicide attempts (20%), and convincing a "marijuana-naive" younger sibling to smoke the drug (20%). Despite such seemingly apparent signs of possible drug use by these 35 adolescents, a mean time of 12 months elapsed before parents suspected their children of marijuana abuse. In many cases mental health professionals consulted by a number of the children when they were using drugs were likewise unaware of the marijuana abuse.

THE PROPORTION of high school seniors who admit to smoking marijuana daily has declined from a peak of 10.8 percent in 1978 to five percent in 1985.[1] Thus, 120,000 seniors in American high schools intoxicate themselves daily by smoking marijuana. The average age of first-time users of marijuana is currently between 13 and 14 years. Of all young people who smoke marijuana even once, an estimated 10 percent will progress to daily use of the drug.[1]

Previous claims that marijuana is not injurious to health were based in large measure on the results of studying the effects of relatively low-potency *Cannabis* smoked by large numbers of young adults between 1960 and 1975. Today, ordinary marijuana, at 3.6% Δ9-tetrahydrocannabinol (THC), has four times the potency of the marijuana generally smoked during the 1970s.[2] Indeed, marijuana is now a bit more potent in Δ9-THC than hashish, at least in the United States.[2] Sinsemilla (seedless marijuana), which adolescent "aficionados" prefer and use almost exclusively when available, contains an average of 7% Δ9-(THC).[3] This is approximately six times the concentration of most marijuana smoked in 1975 and twice the concentration of Δ9-THC in hashish.

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Inhibition of Cellular Mediated Immunity in Marihuana Smokers

Abstract. *The cellular mediated immunity of 51 young chronic marihuana smokers, as evaluated by the lymphocyte response in vitro to allogeneic cells and to phytohemagglutinin, was significantly decreased and similar to that of patients in whom impairment of T (thymus derived) cell immunity is known to occur. This inhibition of blastogenesis might be related to an impairment of DNA synthesis.*

It has been previously reported (*1*) that delta-9-tetrahydrocannabinol (Δ^9-THC), a psychoactive substance of *cannabis*, when administered to rodents alters their cellular mediated immune responsiveness, and it was suggested that similar changes might also occur in man. In our study the mixed lymphocyte culture (MLC) and phytohemagglutinin (PHA) responsiveness of 51 marihuana smokers, 16 to 35 years old (median age 22), were studied. Only subjects who had used *Cannabis* products (at the exclusion of other drugs) at least once a week (average four times a week) for at least 1 year (average 4 years) were selected for this investigation.

Eighty-one healthy volunteers, 20 to 72 years of age (median age 44) were used as controls. Purified lymphocyte suspensions were prepared from fresh samples of venous blood by the Ficoll-Isopaque density gradient method (*2*). A microculture system was used for screening of cellular responsiveness (*3*). For the MLC test, 1×10^5 responding cells were incubated, per well, with 2×10^5 stimulating cells pooled from a panel of ten donors, phenotypically different (allogeneic cells in which 25 different HL-A specificities were represented (*4*)).

For the PHA test, 2×10^5 responding cells were incubated per well with 1 μg of purified PHA. The medium used was RPMI 1640 with penicillin, streptomycin, and glutamine, to which 25 percent autologous serum was added.

Results are summarized in Table 2 and compared with data obtained in 60 patients with cancer, 20 patients with uremia, and 24 renal allograft recipients with iatrogenically induced immunosuppression. The mean values registered in the group of marihuana users were significantly lower than those of the normal, but much older, [illegible] relation exists between cellular immunity, as reflected by in vitro lymphocyte blastogenesis and aging (*5*), results obtained in the group of marihuana smokers may be interpreted as being indicative of cellular hyporesponsiveness. Supporting this conclusion is the close similarity between the depressed MLC and PHA responsiveness of marihuana users and that of cancer (*6*), uremia (*7*), and immunosuppressed transplant patients in whom impairment of T (thymus derived) cell immunity is known to occur. Furthermore, we observed that in vitro inhibition of PHA-induced blastogenesis of normal human lymphocytes started with 1.6 μM THC and was complete with 20 μM.

The major psychologically active constituent of *Cannabis sativa* is Δ^9-THC. This substance, as well as its metabolites, is insoluble in H_2O, but is very fat soluble, and has a half-life of several days in tissues where it might exert a cumulative and pharmacological effect (*8*). Such an effect might be related in a still unknown way to the depressed cellular immune response in vitro of chronic marihuana smokers. The effect of THC on adrenergic receptors (*9*) might also play a role in its immunosuppressive activity, as was suggested for other drugs administered continuously over a long period (*10*).

This inhibition of blastogenesis might result from an impairment of DNA synthesis. One of us (A.M.) sampled lymphocytes from four marihuana smokers, cultivated the cells for 72 hours, and then observed a decreased number of cells during the period of DNA synthesis (S period of the cell cycle). There was also an increased incidence of chromosomal breakages.

Table 1. Comparative cellular mediated immunity of normal subjects, marihuana smokers, and patients with impairment of T cell immunity. The in vitro blastogenic response of lymphocytes was studied by the MLC and the PHA tests. The incorporation rate of [^{3}H]thymidine of the T lymphocytes is given in counts per minute ± the standard error.

Subjects	MLC		PHA	
	No. tested	[^{3}H]Thymidine incorporated (count/min)	No. tested	[^{3}H]Thymidine incorporated (count/min)
Normal controls	81	26400 ± 200	81	23250 ± 210
Cancer patients				
Primary tumors	16	14894 ± 792	16	17501 ± 124
Regional spread	23	15816 ± 420	23	13345 ± 530
Distant spread	21	8968 ± 459	21	10516 ± 580
Uremic patients	26	12001 ± 272		
Transplant patients*	24	12307 ± 357		
Marihuana smokers†	34	15679 ± 499	51	13779 ± 169

* After 1 to 4 years of immunosuppressive therapy. † At least 1 year, at least once a week; no other drug taken.

Black American Manual - 1985 Edition

MARIJUANA

What is marijuana?

Marijuana ("grass", "pot", or "weed"),comes from a common plant with the botanical name Cannabis Sativa. It is not a single substance, but a crude drug -- a "complex chemical factory" which contains at least 421 different chemicals. The main psychoactive ingredient in marijuana is delta-9-tetrahydrocannabinol, or THC. This, and 60 other cannabinoids, are chemicals which are found only in the marijuana plant. Because of the complexity of marijuana's chemical composition, its instability, and its wide variation in potency due to different varieties, climates, and growing conditions, no two batches of marijuana will be the same. And, as with any other street drug, people who buy marijuana can never be certain what else it may be mixed with, or if it even is marijuana.

What is THC?

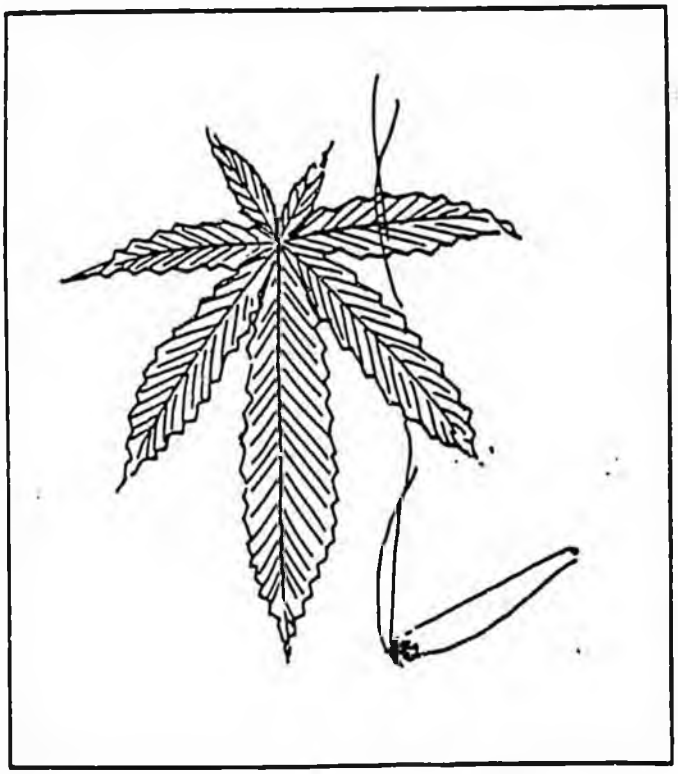
THC Is the chemical in pot that produces the "high". It is the THC content of marijuana that determines its potency.

THC is toxic. (Toxic means "poison".) It is an intoxicant.

THC actually stands for delta-9-tetrahydrocannabinol. THC is the best-known of the 61 cannabinoids in marijuana. All cannabinoids are fat-soluble chemicals. They accumulate in the fatty lining of the cells in the body and brain and are cleared from the body very slowly.

What is hash?

Hashish or "hash" is a dark brown resin from the tops of the marijuana plant. The resinous secretions of the plant are collected, dried, and then compressed into "bricks." The Middle East is the main source of hash used in the United States. In the past, hash was stronger than marijuana, but with the increasing potency of pot, hash is often a weaker drug, averaging about two percent THC content.



What is hash oil?

Hash oil is a tarlike substance smoked in small amounts on tobacco or marijuana or in small glass pipes. It is distilled from the marijuana plant and is extremely potent, with a THC content from five to 40 percent or more. It is so potent that one drop of high potency oil could produce an hallucinogenic effect. Hash oil is produced in a manner similar to percolation of coffee.

How potent is today's marijuana?

Marijuana is a far more powerful drug today than it was 10 years ago when the average THC content was only about .5 percent. Marijuana being smoked today is often from Colombia and contains four to six percent THC. U.S.-grown Sinsemilla is especially cultivated to have a THC content of up to 11 percent or higher.

Wouldn't it be better to sell marijuana legally so the potency could be controlled?

The idea that people will one day be able to buy "joints" in a grocery store in packages with a label describing the THC content is a fantasy, because marijuana is such an unstable drug. Even after a joint is made, the chemical composition of the THC and other chemicals changes. The strength of marijuana varies according to the length of time it's stored, the place it is is stored in, the temperature it is stored at, and a variety of other factors.

Are other drugs sometimes added to pot?

PCP ("angel dust"), LSD, hash oil, and other chemicals are often added to marijuana -- often without the knowledge of the purchaser.

KIDS: STAY AWAY FROM POT

DEAR ABBY: I was glad to see your warning about angel dust. Everything you said about it was true. It makes you violent and can really mess up your head. I know. I was in high school, ready to graduate, when I smoked that dust. I didn't even know it. I smoked some pot that had been laced with angel dust. I didn't get high. I just went crazy.

I was sent to a mental hospital where I spent three months. I put my poor parents through hell. I'm out now, but I have to see a social worker every week. I'm still on medication, and my head still hurts. But at least I can dress myself and comb my own hair. My biggest fear is that one day I will go completely crazy again and end up back in the hospital. I saw kids there who'd had that experience.

My God, what a terrible price to pay for wanting to get high. Abby, please keep telling kids to stay away from pot. You never know what's in it. I am signing my name and address just to prove this letter is not a phony, but if you print it, sign me...

PAID A BIG PRICE
Nonpareil
July 6, 1982

Besides other dangerous drugs, are there other impurities found in marijuana?

Dried oregano looks like marijuana; dried parsley looks like marijuana; dried cow manure looks like marijuana. All these substances are candidates for filler in marijuana. All have been used. Besides being a waste of money, smoking pot can cause disease from the bacterial organisms found crawling all over the plant.

DOCTORS SAY CONTAMINATED POT CAUSED FOOD POISONING EPIDEMIC

Boston (AP) -- Researchers have discovered that germ-laden marijuana can cause an illness like food poisoning, and they attribute a nationwide outbreak last year to bad pot.

The research provides the first evidence that marijuana can spread disease-causing bacteria.

Doctors from the Centers for Disease Control in Atlanta found that marijuana was the source of an outbreak of food poisoning in Ohio and Michigan in January 1981. The marijuana, probably imported from Colombia or Jamaica, was contaminated with salmonella bacteria from animal manure which had been added to the marijuana.

The doctors tracked down the source of the outbreak, which also affected marijuana users in Georgia, Alabama, California, Arizona and Massachusetts, by asking people whether they used drugs. In Michigan, they found that 76 percent of the victims were exposed to marijuana.

Symptoms of the infection included diarrhea, fever, abdominal pain, nausea and vomiting. The illness lasted an average of eight days, and 62 percent of the victims had to be hospitalized.

World Herald

What are the immediate effects of smoking pot?

In most people, the use of marijuana produces a sense of well-being, a state of relaxation, altered perception, particularly of distance and time, impaired short-term memory and impaired coordination. The "high" usually lasts from two to three hours after smoking one joint. High doses of THC can cause image distortion and hallucinations.

The most commonly observed adverse reaction to marijuana is the acute anxiety reaction. A single dose of THC can cause this reaction even in mentally healthy people. Persons suffering an acute anxiety reaction are anxious and may become paranoid. There can be a sense of general suspicion to a fear of losing control and going crazy. Some reactions require professional treatment, and approximately 10,000 Americans are treated in hospital emergency rooms each year suffering from the reaction.

Unfortunately, all pot smokers get their "high" from the poisonous effects of THC in the brain, where it first stimulates and then damages the cells in the brain's pleasure center, depriving users of a desire to obtain natural, non-chemical "highs."

POT SMOKER LEAPS TO HIS DEATH FROM HOTEL

Gedelle King told authorities that she and her husband Jay were smoking marijuana with friends in their Atlanta, Georgia, hotel room when Jay asked what time it was. Before she could answer he said, "It's time to end the world," ran outside and jumped 30 feet to his death below.

Atlanta Journal
Nov. 9, 1983

What is so dangerous about marijuana?

Marijuana is a special drug because it appears to be harmless. This appearance leads many people to believe that it really is harmless, and therefore not dangerous to use or to experiment with. In other words, the fact that there are no dramatic effects is one of its dangers. Marijuana is such a subtle drug that people don't realize how it is affecting them. Marijuana is dangerous precisely because it is not a killer weed. Its effects on the user at usual doses are often mellow, compared to alcohol intoxication. As long as marijuana users continue to use the drug, they do not permit themselves to consider the possibility that they are damaging themselves with the drug.

> "I believe (marijuana) to be our most dangerous drug because of widespread use, especially by our youth, and because the psychological as well as the physical effects are insidious and ultimately devastating."
>
> - Dr. Robert DuPont

> "Marijuana is our most dangerous drug because of its nation-wide prevalence and because people use it thinking nothing bad is happening to them. By the time it does psychological harm, the pot smoker's ability to judge that harm is impaired to such an extent that he rejects the evidence that is obvious to everyone else."
>
> - Dr. Harvey Powelson
> Director
> Psychiatric Department of the Student Health Service
> University of California, Berkeley

If pot is dangerous, then why do so many people think it's harmless?

Without question, in the past two decades, the cultural messages people picked up about drugs were, for the most part, pro-drug. One of the factors that encouraged use of marijuana was the one-sided publicity given to statements of scientists and others who advocated liberalizing marijuana laws. At the same time, there was a virtual blackout of scientific information describing the dangers of marijuana use. Dozens of pro-drug books were published and sold in the "popular" market, while no anti-drug books were published for that market, although such books were written. Not a single commercial film has been made in the past two decades which presents marijuana use in a cautionary light. At the same time, well-funded lobbying groups to promote drug interests were organized at the local, state and national levels. As a result, many intelligent people concluded that the bulk of the scientific evidence "proved" that marijuana was "harmless." The evidence, of course, "proves" exactly the opposite.

There is still more ignorance about marijuana than about any other widely used drug in society, and this is as true among some drug counselors as it is among users and the lay public.

Don't some scientists say marijuana is harmless?

Marijuana use is a major health problem in the United States, and the harmfulness of the drug is now widely perceived. No scientific authority argues today that marijuana is a harmless drug. That argument is over. Now, all medical authorities agree that marijuana use has hazards.

While knowledge of all the consequences of marijuana use is incomplete, studies finished so far demonstrate a variety of significant risks and dangers. No scientific study has found the drug to be completely safe. Over 8500 research papers have been done on the drug and none of them gives pot a clean bill of health.

Both the American Academy of Pediatrics and the American Medical Association strongly condemn use of marijuana by teenagers. The Surgeon General has concluded that marijuana is dangerous and harmful to health. Also, many people who once believed marijuana to be harmless have now concluded that it may be the most dangerous drug in America.

AMA CONCLUDES: 'POT DANGEROUS'

CHICAGO -- The American Medical Association says marijuana is not a "harmless amusement" and frequent use can lead to problems in the brain, circulatory system, heart, lungs, and nervous system.

"Marijuana can hurt you," the AMA said Thursday in promoting its new physicians' drug abuse handbook. "Marijuana is by no means the harmless amusement that many believe it to be. Structural changes occur in the brain with marijuana use, as well as changes in the patterns of brain waves.

"There is now no doubt at all that marijuana is a dangerous drug with great potential for serious harm to young American users," the AMA said.

Middlesex News
July 24, 1981

What about the books and authors who say pot is okay?

Marijuana research is a young scientific field. More research has been done in the past two decades than in all previous history. Most of the important physiological research on pot was done after 1972. Marijuana research is very difficult because marijuana is a very complex substance. Also, many of the early studies that supposedly "proved" that marijuana wasn't too harmful used amounts of THC that were much smaller than is found in pot on the street today. Thus, it is important to find recent research on marijuana.

It should also be remembered that it was only after many years of use by millions of people that the heart disease associated with smoking cigarettes was recognized. When the controversy about tobacco smoking was raging in the late 1950s, some scientists came to the defense of cigarettes, the way others do to marijuana today. For example, the chairman of the Cancer Commission of the California Medical Association, and one of the state's foremost cancer specialists, testified before a Congressional committee that "a pack of cigarettes a day will keep lung cancer away."

What organizations still say marijuana is harmless?

The Do It Now Foundation says that "marijuana has not been proven harmful, even in remote ways." It advises young people that "the mild psychological changes that occur in many people" are "generally beneficial in nature." In other words, marijuana may even be good for you. Not only that, but Do It Now also says that marijuana may be a cancer cure."

So, how can you be sure that Do It Now isn't right? Well, first, common sense says that becoming a burnout is not a "mild psychological change" and is not "generally beneficial". Secondly, it would be easier to believe Do It Now if it would tell readers who says smoking marijuana will cure cancer. It would be nice if they would cite a single study printed in a reputable scientific journal that says smoking dope helps cure cancer. It would be nice if they could find a single doctor in the whole world who treats his lung cancer patients by having them toke on a joint.

Who is Do It Now, anyway? Who writes their pamphlets?

The Do It Now staff relies for its "realistic" drug information on "over 150 collective years of former drug use and experimentation". Some of its writers regularly contribute articles to High Times magazine and Dean Latimer, the Executive Almighty Editor of High Times often writes articles for Do It Now. Vic Pawlak, once described as the "concept person" for Do It Now's Institute for Chemical Survival, became an expert on drug abuse while writing for underground newspapers. Dean Latimer admits in his articles that he has been a heavy pot and speed user. Do It Now's opinion about the harmfulness of drugs is at odds with the positions of the American Medical Association, the American Academy of Pediatrics, the National Institute on Drug Abuse, the Addiction Research Foundation, the World Health Organization, the Food and Drug Administration, the Institute of Medicine and the hundreds of physicians and scientists across the country who think pot is not only harmful, but dangerous.

Another pro-drug organization is N.O.R.M.L. -- the National Organization for the Reform of Marijuana Laws. They're the people who want to legalize dope. They get alot of their money from the businessmen who manufacture pipes and bongs. Their "official policy" is that they don't encourage people to use any drugs and they "strongly discourage" teenagers from using pot. Even N.O.R.M.L. admits marijuana can be dangerous, but they believe that it's no more dangerous than booze or cigarettes, so it should be made available in the same ways.

But, remember, N.O.R.M.L. is a lobbying organization. It doesn't want your money (although it will sell you a student membership). What it does want is votes. The more pot

smokers there are, the easier it will be to elect politicans who'll vote to ease up on dope. So, N.O.R.M.L. has a vested interest in having lots of adults use marijuana -- and lots of potential future voters turned on to pot.

N.O.R.M.L. says it provides "straight-forward", "assembled medical information", too. This is their idea of "straight-forward."

At one time, N.O.R.M.L. was working on a pamphlet called "NORML On Family Drug Awareness". In that pamphlet, the organization said that evidence of harm from pot was "tentative" and "inconclusive" (just like the American Tobacco Institute says proof of harmful effects from smoking cigarettes is exaggerated). To prove that claims that marijuana is harmful are "scare tactics", they claim to take some "selections" from the testimony of Dr. William Pollin to Congress in the fall of 1981. This is how N.O.R.M.L. quoted the director of the National Institute on Drug Abuse's report on evidence of lung damage:

> "On Lung Damage: 'There does not yet exist an animal model for the development of lung cancer by...marijuana. At this juncture, it is not possible, to predict what precisely the health effects in later life will be on those young people today who are regular marijuana smokers."

What follows is what Dr. Pollin really told the Senators:

> "The concentration of benzo(a)pyrene in marijuana tar is 70 percent higher than in the same weight of tobacco tar. There does not yet exist an animal model for the development of lung cancer by either tobacco or marijuana. However, in animal tests marijuana smoke residuals produce skin tumors. In fact, human lung tissue exposed in the test tube to marijuana smoke shows greater cellular changes than when exposed to similar amounts of standard tobacco smoke. Critical longitudinal studies are needed and are being supported by NIDA to evaluate the risk of long-term use."

Elsewhere in "NORML On Family Drug Awareness", the pro-pot lobby proposed to tell young people that Dr. Pollin said:

> "Thus, any attempt to compare the health impact of marijuana with that of alcohol and tobacco at current levels of use is certain to minimize the hazards of marijuana."

But, this is how that comment reads when taken in context:

> "Thus, any attempt to compare the health impact of marijuana with that of alcohol and tobacco at current levels of use is certain to minimize the hazards of marijuana. But any comparison at levels of anticipated use involves many assumptions that are at best dubious

> and at worst may be dangerously misleading. Such a comparison seems, therefore, useless and undesirable until such time as the parameters of risk are better specified than they can be at present.

Why do you suppose N.O.R.M.L. wanted to be "dangerously misleading" by making a "useless" and "undesirable comparison?"

Finally, there are some books that show up in a few book stores now and then that are classified as "non-Fiction", but when it comes to reporting on marijuana, their facts are fairy tales. Recreational Drugs is one such book. It is recommended reading by High Times magazine. The authors of the book, none of whom are physicians, never bother to cite a single footnote or study by name so that you can look it up on your own. There is no way you can find out how well they researched their material.

Recreational Drugs says "marijuana appears to be remarkably safe". Who says so? The authors don't say. They also tell you that the National Commission on Marijuana and Drug Abuse "verified the safety of marijuana" in a report that was rejected by President Nixon. But wait! You probably can't even remember when Nixon was president. How old is this study, anyway? Well, it's ten years old! It was prepared in 1972. That report never verified the "safety" of marijuana. It did admit that there was much more to learn about marijuana. Since 1972, we have learned much more.

Recreational Drugs also says that "much of today's reliable information about marijuana" comes from a 1972 study done in Jamaica. Since the dope promoters always refer to this study, and because they criticize every research study that says pot is harmful you need to take a good look at what evidence they think is reliable.

For example, the Jamaica study supposedly "proved" that "there was no difference in rate of employment, job stability, or academic achievement" between straights and potheads. What the authors of Recreational Drugs don't bother to tell you is that the small number of people studied were unskilled, uneducated, illiterate laborors who hoed sugar cane fields for a living. How do you test job stability or "academic achievement" among ditch diggers? You are also never told that this "reliable" study was never published by the government agency that sponsored it, that it does not have the support of Jamaican doctors, and that it was never printed in a single, reputable scientific journal. Besides, the Jamaica study is ten years old. What about all the studies that have been done in 1973, 1974, 1975, 1976, 1977, 1978, 1979, 1980, 1981, 1982, 1983 or 1984?

A partial list of popular books which favor or advocate social accaptance of drugs, while minimizing their damaging effects....

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Grinspon, M.D., L., Marihuana Reconsidered, Second Edition, Harvard University Press, Cambridge, 1977.

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Lieberman, M., The Dope Book, Praeger Publishers -- a Division of Holt, Rhinehart & Winston, New York. Ninth Printing 1978.

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Phillips, J.L. and Wynne, R.W., Cocaine The mystique and the Reality, Avon Books - A division of the Heart Corp., New York, 1980.

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Ashley, R., Heroin, The Myths and the Facts, St. Martin's Press, 1972.

King, R., The Drug Hang-Up; America's Fifth Folly, W. W. Norton, 1972.

Lindesmith, A.R., The Addicts and the Law, Vintage Books, 1965.

Musto, D., The American Disease, Origins of Narcotic Control, Yale University Press, 1973.

Zinberg, N.E., Robertson, J.A., Drugs and the Public, Simon & Schuster, 1972.

Is it true that nobody has ever died from using marijuana?

Do people who smoke cigarettes and get lung cancer die from lung cancer or cigarette smoking? Do people who overdose on alcohol die of heart failure or alcohol overdose? Does a drug with 50 percent more cancer-causing tar than tobacco cigarettes cause death if the smoker eventually dies of lung cancer or emphysema?

It is true that nobody has ever proven that human beings have overdosed on pot and died, although such cases have been reported. At this point, few physicians would know how to diagnose a death caused, or contributed to, by marijuana. The fact that death from smoking marijuana does not happen immediately after using the drug, or cannot be proved, does not mean that it cannot happen.

> "And people who try to tell you there have been no deaths from marijuana should visit the cemeteries. Do you know that drug-related suicide is the number one cause of death among college students today? The number two cause of death is alcohol and drug-related traffic accidents. And in almost every case illegal drug use starts with marijuana."
>
> - Dr. Robert Heath

Who uses marijuana?

The United States has the highest level of marijuana and other drug use among young people of any developed country in the world. In America, the mainstream child is just as likely to use marijuana as the obviously deviant or rebellious kid. As a matter of fact, more high school seniors smoke marijuana than smoke tobacco cigarettes. Marijuana use begins as early as 12 years, although the most frequent ages of first use are around 14 and 15. Widespread use of marijuana by adolescents and females is unprecedented in human history.

Are there many parents who have smoked pot?

Unfortunately, many kids who grew up in the '60s smoking pot have grown up enough to have kids of their own, but haven't grown up enough to stop smoking weed. Their kids face an uphill battle if they want to be straight themselves. Many persons in the 35 to 49 age group are presently raising teenage children, and surveys show that one-fourth of those parents have at least tried marijuana. One in five parents of children aged 12 to 17 have tried marijuana at some point during their lives.

Why do kids smoke pot?

Teenagers know better why kids smoke pot than adults do. Many adults, especially those who work in drug treatment centers, are convinced that all kids who use drugs have "problems" which cause them to use drugs. They insist that solving the "underlying problems" is the way to battle drug abuse. However, increasing numbers of professionals and parents are beginning to understand that for many, if not most kids, drugs are the cause of their drug problems, and getting kids off drugs permits them to solve their drug problem and other problems with a healthy mind that is functioning normally.

The majority of adolescents who use marijuana and other drugs do so because of ignorance of the long-range harmful effects and because of the need to belong to a group. Many teenagers who use drugs have everything going for them. Their families are intact, their parents love them, they get good grades in school, they are involved in extracurricular activities, they have interesting hobbies, they have lots of friends and they are very popular. They aren't escaping reality, because their world isn't that unpleasant. To them, marijuana and other drugs are "mild, harmless intoxicants", which they can handle -- they think. What these kids lack is information about how drugs that make them feel good can hurt them, especially in ways that they cannot see or "feel".

Don't lots of people just "try" pot?

Just "trying" pot isn't a good idea because for many people, the first "try" produces no "high". Therefore, the experiment is repeated several times in order to achieve an effect. Surveys show that few persons who "try" marijuana stop after merely "trying it to see what it's like" on one or two occasions. Among kids 12 to 17, less than one in three of those who admit they have "ever used" marijuana say that they used pot just once or twice. About one-half of adults who tried marijuana before the age of 16 report that they eventually used marijuana on a daily basis.

Isn't it okay to use pot in "moderation"?

Even moderate use of marijuana is associated with school drop-out, psychoses, panic states and adolescent behavior disorders. Besides, how many current "burnouts" ever planned to become burnouts? Doesn't everybody think their pot use is "moderate" when they start? Doesn't every pothead still think his pot use is "moderate", even though to everyone else it is clear that he has become a burnout?

How long do the chemicals in marijuana stay in the body?

Marijuana is a unique drug because its chemicals accumulate in the user's body in much the same way as DDT. A week after a person smokes one joint, 30 to 50 percent of the THC remains in the body; it is estimated that four to six weeks are required for all the THC to leave the body. In other words, a kid who gets "high" on Saturday night and again on Wednesday night will build up the amount of THC in his body. His brain will never be free of the drug. At least a full month of not smoking would be necessary to rid the body of all the THC.

Since marijuana stays in the brain long after the user feels "high," it is very deceptive. Many professionals are worried that the slow, subtle accumulation of THC in the body and brain is responsible for the personality and behavior changes seen in users. And, the longer the drug remains in the system, the greater time it has to affect the other tissues of the body.

> "There is no other drug used or abused by man which stays in the body as long as cannabis does. And there is no other drug, legal or illegal, which affects every major organ of the body. And every system in the body. And every single cell in the body."
>
> - Dr. Carlton Turner, Deputy Assistant to the President for Drug Abuse

Where in the body does THC accumulate?

THC, and the other cannabinoids in marijuana, are stored in the fatty tissues of the brain and lungs. They are also accumulated in the ovaries and testicles for long periods of time.

How does marijuana affect the lungs?

Marijuana smoking constitutes the greatest single new threat to the health of lungs in the United States. Not only is the possible damage to the lungs very severe, but the changes associated with heavy pot smoking can appear within 18 to 24 months, which is a relatively short period of time.

Marijuana is much more harsh and irritating than tobacco. That is why users often cough and gag as they inhale the smoke. Marijuana smoke contains THC and other chemicals which irritate the lungs, as well as poisons like carbon monoxide and ammonia. The effect is so severe that some scientists have concluded that five joints irritate the lungs as much as 112 tobacco cigarettes.

Following exposure to marijuana, the lungs' defense systems against bacteria are impaired. Alveolar macrophages, which

are special cells designed to attack and destroy foreign material and bacteria in the lungs, have reduced effectiveness.

Chronic bronchitis and chest pain are common in teenagers who smoke pot. There have been studies of human users which have reported laryngitis, cough, hoarseness, asthma, sinusitis, pharyngitis, bronchitis and precancerous lesions in the lungs much like that found in heavy cigarette smokers. Emphysema, a deadly lung disease, also has been found. Studies done on U.S. Army soldiers in West Germany who had been smoking cannabis for a year or less found lung damage that was more severe than that found in older soldiers who had smoked at least 1½ packs of cigarettes a day for 10 years or more. The doctors were startled to find emphysema and bronchitis in the lungs of 18-year-old hash smokers. These lung diseases are rarely found in people under 45 years of age.

Unlike tobacco cigarettes, "joints" are unfiltered and smoked to a very small "roach". As a result, the lungs of the marijuana smoker are more blackened than those of tobacco smokers and there is extreme breakdown of the lung structure. Experiments have demonstrated that significant worsening of lung function occurs only six to eight weeks after smoking a few joints a day. These tests show that heavy pot smoking causes a narrowing of breathing passages. Vital capacity, the amount of oxygen the lungs can inhale and exhale in one breath, is decreased more by one or two joints than by a whole pack of regular cigarettes.

There is still a great deal to learn about the effects of pot on human lungs. It took many years of cigarette smoking before the ill effects of cigarettes were documented. It may take another 20 years before all the effects of pot smoke on lungs are learned.

Can marijuana cause cancer?

Since marijuana smoke is deeply inhaled and contains many chemicals known to be cancer-producing, it is virtually certain that heavy use can cause lung cancer. However, it takes 30 to 40 years for lung cancer to grow. Thus far, in the United States, people have been smoking pot heavily for only a decade or two, so there aren't many dead bodies yet. However, preliminary laboratory evidence is convincing -- and scary.

There is evidence that the products of marijuana smoke cause the growth of cancer cells in the test tube in a way similar that caused by the tar in tobacco cigarettes. There is evidence that heavy pot smokers have precancerous lesions in their lungs. These lesions have been found in samples of tissue removed from the lungs of smokers of cannabis in their early 20s. Similar lesions are found in heavy tobacco smokers only after they reach the age of 40.

None of these results is surprising considering the fact that cannabis produces 50 percent more tar than the same weight of regular cigarettes. Also, because a joint is smoked down to a tiny roach, more tar is inhaled than in a tobacco cigarette -- particularly if it is a filtered cigarette. Cannabis tar contains more than 150 hydrocarbons, including cancer-causing chemicals. These chemicals from marijuana tar produce skin tumors in laboratory tests.

Because marijuana has more cancer-causing chemicals than tobacco, it may take fewer joints than cigarettes to produce cancerous changes. Compounding the damage to the lungs is the fact that most pot smokers also smoke regular tobacco cigarettes.

Does marijuana affect the heart?

It is clear that marijuana changes heart function; it increases heart rates, and it changes the distribution of blood; it causes significant increase in chest pain in individuals who have heart diseases.

POTLUCK

A former Dade County Circuit Court Clerk will be spending time in jail for serving marijuana-laced brownies that sent 22 co-workers to the hospital.

One court clerk supervisor suffered a mild heart attack and was hospitalized for several days.

American Bar Association Journal
Jan., 1984

Marijuana stimulates the nervous system and causes quickened heart beat and irregular heart rhythm. Marijuana increases heart rate as much as 50 percent and can bring on chest pain in people experiencing a poor blood supply to the heart. During the early phases of cannabis intoxication, heart rate can increase up to 160 beats per minute or more, along with causing a decrease in standing blood pressure.

THC seems to have far more profound effects on the cardiovascular system than does nicotine. There is evidence that in patients with impaired heart function the use of marijuana may precipitate chest pain more rapidly and following less effort than tobacco. One study found that a single marijuana cigarette smoked for 15 minutes produced as much carbon monoxide in the blood as 10 to 20 tobacco cigarettes smoked in the course of a day.

How does marijuana affect personality?

Psychiatrists and physicians have begun to recognize severely harmful effects of marijuana on personality, especially in maturing adolescents. Marijuana affects judgment, motivation, perception and learning. It can lead to an overall deterioration of personality and an estrangement from the mainstream of life. Users tend, quite often, to

socialize only with other potheads who exhibit the same problems. At the same time, they withdraw from their families, causing disruption and sometimes devastation in the home.

AIR AGENCY PROBES MECHANIC'S POT CASE

Miami (AP) -- The Federal Aviation Administration said it is investigating a year-old marijuana case against one of two Eastern Airlines mechanics, whose mistakes almost forced a jumbo jet to ditch in the Atlantic.

World Herald
May 22, 1983

The most consistent and notable changes that are reported in marijuana smokers include apathy, lack of motivation, which is called the "amotivational syndrome", and reduced interest in socializing. There is less concern for the future. Some users lose contact with reality and suffer from hallucinations. It's clear that a larger percentage of children who are involved with marijuana drop out of school and do not achieve as well in school as children who don't smoke pot regularly. It is also important to note that kids who stop smoking pot often show dramatic changes in behavior. They become more interested in school and being on time, getting better grades and forming meaningful relationships with their friends, and they are less hostile. Sometimes they take more interest in their personal appearance and habits.

While not all, or even most, pot smokers become "burnouts", almost all marijuana smokers deny any damage to themselves from using the weed. The marijuana user does not realize that he has changed, and if his altered behavior is brought to his attention, he tries to justify it. What the pot smoker doesn't understand is that the very area of the brain that is affected by marijuana is the same area which is responsible for helping him regulate and evaluate his own behavior. As a result, even burned out "space cadets", who may be suffering from very severe drug-related mental impairment, do not consider themselves to be burned out. The marijuana smoker can become a liar and a con artist -- and he seems to be his own biggest victim.

Of particular importance to teenagers is the very real danger that marijuana use can interfere with growing up. To become an adult, an adolescent must learn to cope with emotional, social, mental and physical growing pains. Drugs like marijuana that protect kids from the stress of growing pains also prevent kids from growing up to be responsible, mature adults.

How does marijuana affect learning?

Marijuana can interfere with learning by impairing thinking, reading comprehension, verbal and arithmetic skills. Marijuana impairs the ability to concentrate, consider complexity, manage tension, postpone rewards, think abstractly, and consider hypothetical solutions to problems. Heavy marijuana users, not surprisingly, often find that their grades become worse because of pot smoking.

Marijuana particularly seems to impair short-term memory. It also seems to interfere with the transfer of information from immediate memory to long-term memory storage. There is now evidence of memory loss so great that some kids actually forget their own birth dates.

Unfortunately, marijuana seems to fool students into believing that pot improves their performance. They think they can drive better, study better, play music better, and play football better when they are "high" -- in spite of the fact that to everyone observing their performance, they have declining abilities.

Are teenagers more susceptible to the bad effects of marijuana?

Youngsters who are undergoing rapid and complex changes of body chemistry and emotional development may be more susceptible to the accumulation of THC and other chemicals in the body than are mature adults.

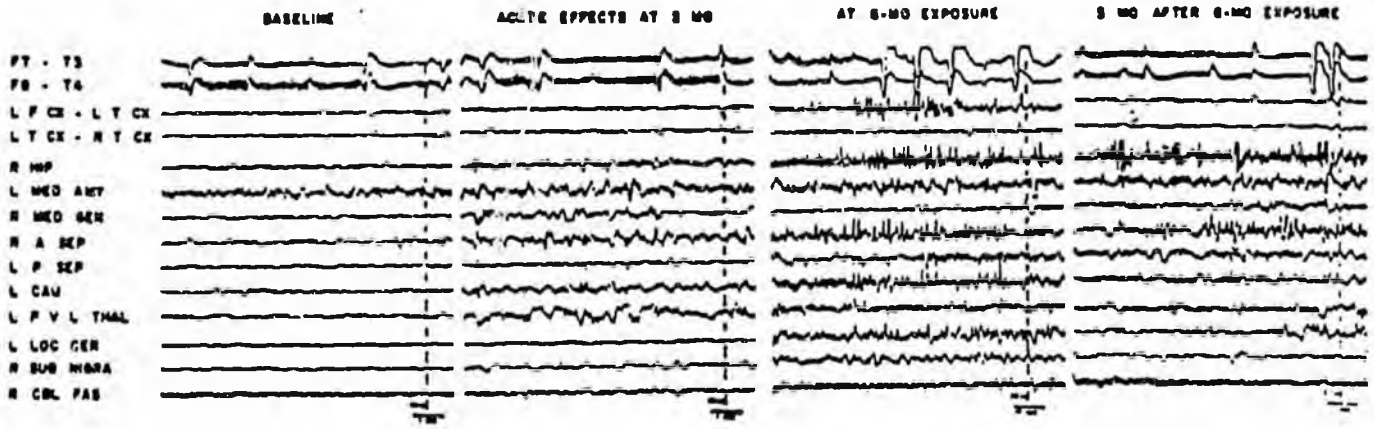
How does marijuana affect the brain?

THC accumulates in the brain. Because of the slow clearance of THC from the body, anyone who smokes more than once a month is never drug-free, and is constantly adding to the level of THC already stored in the body. Since the brain is the thinking organ of the human body, behavior changes could be expected.

There are personality changes in marijuana users. There is evidence that a person needs only to smoke two joints a week for three months before persistent changes in behavior begin to occur. The user may become more "laid back" and not care about things anymore. The user doesn't become upset -- even about things that should be upsetting. The pot smoker changes himself, not his problems. When his diminished mental capacity becomes a problem, he doesn't care enough to change to help himself.

The cause of the pot smoker's lack of concern for anything -- except getting "high" -- may be the result of pot's slowing of brain activity. Studies of brain waves of young people who smoke pot several times a week consistently show an inability of their forebrains to produce fast "beta" wave activity. Inhibiting fast wave activity means inhibiting powers of problem solving, discrimination and analysis. Studies in humans also reveal that continuous usage of marijuana may alter the roles of the right and left hemispheres of the brain with resulting impairment of verbal-analytic tasks.

Results in tests on rhesus monkeys have also yielded disturbing changes in brain wave patterns, as shown below.

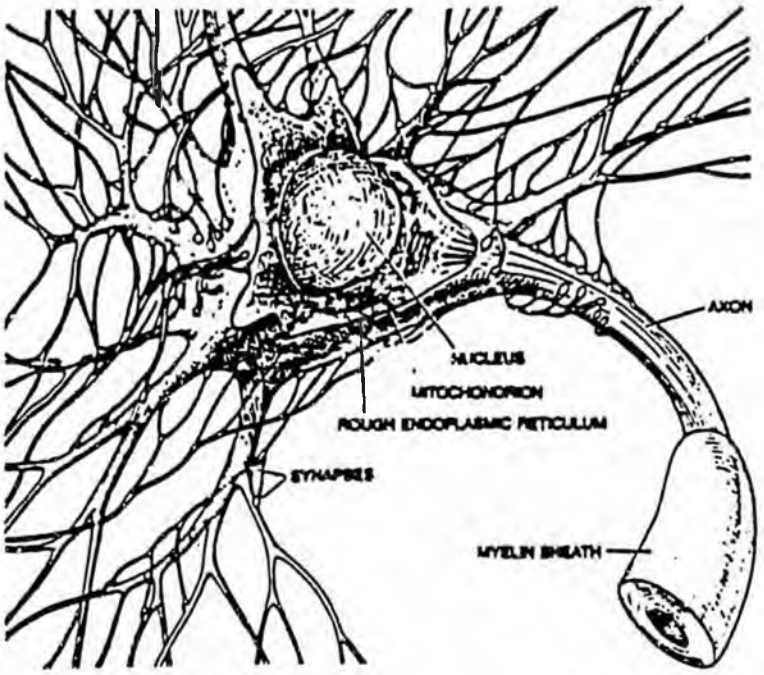


Electrical activity recorded in brain sites of rhesus monkeys. Moving left to right, the first series represents the electrical activity at 14 different brain sites before any exposure to marijuana smoke. The next series shows the acute effects after two months of exposure. The third shows brain waves after six months and the last series shows brain patterns five months after marijuana use was discontinued.

Changes have also been noted in the limbic region of the brain. The limbic, or "old" brain, is where the centers controlling instincts, memory storage, and emotions such as pleasure and reward have been identified. This part of the brain is also associated with the hypothalamus which regulates the sex hormones LH and FSH, both of which are decreased by pot smoking.

Persistent changes in brain wave patterns, which outlast exposure to the drug, have been reported in the limbic regions of the brains of monkeys and rats exposed to humanly-relevant amounts of marijuana smoke. Infant rats treated with THC show fewer structures that make protein, necessary for memory function, in the brain cells. Dr. Robert G. Heath of Tulane University Medical School, has studied the brains of rheaus monkeys treated with THC. His research demonstrates that smoking less than two joints a week for three months (possibly only 20 joints total) causes serious and possibly permanent alteration of brain

function. In addition to changes in brain waves, Dr. Heath found alterations in the structure of the brain cells. There was a widening of the synaptic cleft, the space between the cells, and other microscopic brain changes. Dr. Heath has concluded that users need to use pot only for a short time in moderate to heavy levels before there is evidence of brain damage. Such damage could be the cause of the memory loss, loss of general mental functioning, and paranoid thinking evident in some potheads.



Why isn't there more proof that marijuana causes brain damage?

Drug users demand proof that marijuana causes brain damage. What they fail to understand, however, is that studies to provide such proof are difficult to perform and that, even under to best laboratory conditions, brain cell damage is difficult to identify.

Even where laboratory animals are studied, there are limitations on the evidence of brain dysfunction that can be gathered, because the brains of animals are not as highly developed as humans'. And, even when animal brains can be studied, it is impossible, using present methods of microscopic examination, to inspect damage to cells affecting thought formation. Nevertheless, it is possible to have severe impairment of the brain function that is not visible by visual examination, microscopic examination, or physical testing. It is foolish, therefore, to assume that because damage cannot be seen or fully explained, that it does not exist.

Is marijuana a sexual stimulant?

There has been no research that indicates that marijuana acts as a sexual stimulant. There are reports, however, that among males who have smoked cannabis for five or more years, 20 percent may have impotence problems.

How does marijuana affect the male reproductive system?

Marijuana affects male reproductive function in all species studied.

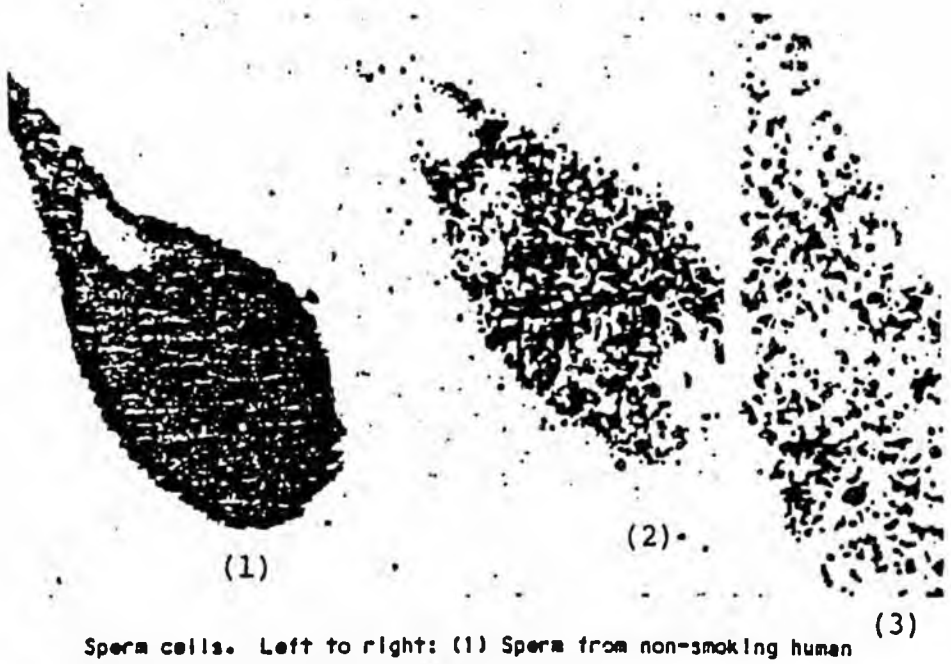
Studies show that THC reduces the amount of LH hormone in males. The LH hormone stimulates the testicles at puberty, causing them to produce the male hormone testosterone. THC produces a longer-lasting and greater depression of LH hormone than morphine, indicating that marijuana is more disruptive to reproductive function than narcotics.

Testosterone levels are reduced in males exposed to THC. The findings of one researcher revealed a five percent decline in testosterone level for each joint (of one percent THC) smoked per week. Scientists are particularly concerned that these results, obtained in mature males, will be even more pronounced and disturbing in adolescent males who are developing sexually.

Because their testicles are producing less testosterone, males exposed to marijuana may observe a decrease in the weight and function of their reproductive organs. And, because the male also produces female hormones, alterations in the balance of hormones has lead to reports of breast development in adolescent males who smoke pot.

The THC in marijuana is absorbed into the testicles and accumulates there. There is evidence that pot causes a significant decrease in sperm count and sperm motility. Thus, the fertility of pot smokers could be decreased. There is also an increase in the number of abnormal sperm. There is a possibility that abnormal sperm could lead to formation of a deformed fetus. Evidence is beginning to emerge that when the male parent alone is exposed to marijuana, there is a significant increase in the number of offspring born with deformities.

There have also been observations that in male animals exposed to marijuana, there is reduced sexual behavior. This is consistent with reports from other parts of the world that human males who use marijuana heavily develop impotence problems.



Sperm cells. Left to right: (1) Sperm from non-smoking human male. (2) & (3) Sperm from chronic hash smokers.

Does marijuana pose special problems for the teenage male reproductive system?

Marijuana's depressing effect on the production of male hormone is one of the greatest risks for adolescents, because a healthy balance of hormones is crucial for normal physical development of young men. The sexual maturation of adolescent boys depends largely on increased testosterone production. However, marijuana may restrict the normal growth of sperm-producing cells, causing under-developed testes. Such results have been produced in laboratory animals treated with THC during puberty. Physicians are concerned that depressed testosterone levels in teenage boys is responsible for the thin body, narrow shoulders, lack of chest, arm and buttocks muscle development, facial pallor and stunted beard growth that is frequently observed in pot-smoking teenage boys.

The study that follows was reported in the Journal of Pediatrics, June, 1980. It demonstrates that, for some boys, the bumper sticker is correct -- "If You Smoke Pot, Your Banana Will Rot".

MARIJUANA SMOKING AND PUBERTAL ARREST

CASE HISTORY

This boy was evaluated at 16 2/12 years of age for short stature and delayed puberty. He had always been in excellent health, growing at the fifth percentile until the age of 11 years when his height fell to below the third percentile. Family history revealed that his mother, who is 167 cm tall, had menarche at 12 years, and his father, who is 188 cm tall, had no delay of puberty. A 14-year-old sister who is pubertal but premenarchal, and an 8-year-old half-brother are in good health.

Pertinent laboratory and physical findings at the first and subsequent examination are summarized in the Table. On the first examination, the

patient was prepubertal in spite of unequivocal testicular enlargment. Six months later, he was found to have had progression of testicular growth without signs of androgen effect. His serum testosterone concentration remained low. At this visit, it was discovered that since the age of 11 years, the patient had smoked at least five marihuana "joints" per day, condoned as well as supplied by his mother. Despite a short period of abstinence followed by a reduction in marihuana exposure for five months, he continued to have testicular enlargment discordant with signs of androgen effect. Studies in addition to those listed in the Table included normal visual field and funduscopic examinations, a bone age of 13 years (at chronologic age of 16 8/12 years), and normal skull radiographs, electrolytes, BUN, creatinine and urinalysis. Prolactin and immunoreactive somatomedin-C values were normal (3.7 ng/ml and 0.86 U/ml, respectively).

			Testicular measurements			Public				
Age (yr)	Height (cm)	Penis (L x W) (cm)	Right (LxW) (cm)	Left (LxW) (cm)	Volume (ml)	Hair Stage (Tanner)	Testosterone (ng/dl)	Serum LH (mIU/ml)	Serum FSH (mIU/ml)	Marihuna Smoking (Joint/day)
16 2/12	152.7	6x2	3.2x1.8	3.0x1.8	6	I	16	-	-	5
16 8/12	154.6	7x2	3.3x2.0	3.2x2.1	8	I	32	2.9	1.9	5
16 9/12	-	-	3.6x2.2	3.4x2.2	9	I	47	4.3	2.2	0 (for 19 days)
17 1/12	156.7	7x2	4.1x2.1	3.8x2.0	12	I	82	4.1	3.0	1
17 3/12	159.3	9x2	4.6x2.4	4.1x2.2	-	-	392	5.7	2.5	0

* All measurements were made by the same observer.

How does marijuana affect the female reproductive system?

Marijuana affects the female reproductive system in a variety of ways:

* Studies show that marijuana users have three times as many defective monthly cycles as nonusers.

* Evidence from animal and human studies suggests that use of marijuana several times a week or more may reduce fertility.

* Animals treated with THC show marked decreases in uterine and ovarian weights as a result cf shrinkage of the organs.

* Marijuana accumulates in the ovaries. The ovary contains a girl's lifetime supply of only about 400,000 eggs at birth, so damage of an egg by marijuana is permanent, and raises the possibility of genetic damage.

* THC decreases the level of important reproductive hormones LH, FSH, and prolactin. Prolactin is a hormone important in producing mother's milk. Nursing could be impaired in marijuana-

using women following childbirth. Many other studies on female animals show that marijuana reduces the level of estrogen, the principal female sex hormone.

* Cannabinoids concentrate in the cells of the breast, and are transferred to the offspring in animals. Some infants have been bombarded with cannabinoids during pregnancy and after through their mother's milk.

Has the number of children born with birth defects increased in the past few years?

Physicians and statisticians who analyze the patterns of birth in the United States have concluded that the number of babies born with physical or mental defects has doubled over the last 25 years. Could marijuana have anything to do with this increase?

"Today's pot smoker may not only be damaging his own mind and body, but may be playing genetic roulette and casting a shadow across children and grandchildren yet unborn."

- Dr. Gabriel Nahas

"It certainly seems that cannabinoids are mutagenic -- they can transmit abnormalities across the generations."

- Dr. Susan Dalterio

Can marijuana harm a developing fetus?

Marijuana's chemicals pass from the mother to the developing fetus in her uterus. As a result, there is a distinct possibility that marijuana use could result in abnormal development.

;TUDY LINKS POT TO
;IRTH DISORDER

Washington -- A federally funded udy at Boston City Hospital has nked marijuana use by pregnant women a serious disorder in their babies own as "fetal alcohol syndrome". Fatal alcohol syndrome infants typally have a cluster of facial abnorlities and often are mentally rerded.

World Herald

In a study in Boston completed in 1982, it was found that babies whose mothers used marijuana during pregnancy were five times more likely than normal to be born with birth defects. The children had features that were similar to those found among women who drink during pregnancy (Fetal Alcohol Syndrome), although the defects occurred more often among pot smokers' babies than among drinkers' babies. While the defects such as specific facial deformities were apparent to

doctors upon the babies' births, there was no way to assess possible damage to the brain. However, researchers are concerned that mental retardation could also occur with greater frequency among the babies of pot smokers.

Even seemingly normal offspring could carry genetic defects which could affect their children as a result of their parents' drug use. When laboratory animals of one generation were exposed to cannabis during pregnancy, birth defects were found in the third generation, suggesting that a gene change had been transmitted through the second generation animals, which had not been exposed to pot except before their birth.

THC, even when given to pregnant animals at doses too small to produce visible defects, may produce changes in the behavior and development of the children. There is evidence that the offspring of mothers given marijuana during pregnancy show learning disabilities. Other studies have shown that when THC or other cannabinoids are given briefly to pregnant or nursing females, abnormal hormone changes occur in the male offspring when they go through puberty. Sons exposed to pot by their mothers are deficient in testosterone and have smaller testicles. At adulthood, the males are not interested in mating, are infertile or impotent. Much like a castrated animal, they are grossly overweight. In addition, there is evidence that there are chromosomal abnormalities which could be passed on to future offspring. There are similar reports of delayed sexual maturation in human males under similar circumstances. These adolescents show sparse beard growth and smaller testes.

Pot smokers' babies are more likely to experience difficulties at birth. They are more likely to suffer from stress and are more likely to need oxygen immediately after birth. Some are born stoned, with THC appearing in the umbilical cord blood. In animal experiments, up to 44 percent of all offspring conceived by THC-treated females are lost before or shortly after birth due to spontaneous abortion or stillbirth.

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CONGENITAL ABNORMALITIES OBSERVED IN BOSTON CITY HOSPITAL STUDY

ajor abnormalities

- Cleft palate
- Hypospadies
- Imperforate anus
- Vertebral anomalies
- Cardiac abnormalities
- Chromosomal abnormality
- Tuberous sclerosis
- Stenotic/atretic ear canals

inor

Head
- Large fontanel plus metopic sutures or third fontanel
- Small fontanel plus metopic sutures or third fontanel
- Large fontanel plus widely space sutures
- Micognathia

Ears
- Abnormal shape
- Low-set ears
- Posterior slant 10°
- Ear tags
- Ear pits

Mouth
- Prominent lateral bridge
- Highly arched palate
- Tounge enlargement
- Carp-shaped mouth

Eyes
- Epicanthic folds
- Slanted eyes
- Wide-spaced eyes

Nose
- Prominent bridge
- Anteverted nostrils
- Abnormal philtrum

Neck
- Short
- Excessive skin folds

Chest
- Accessory nipple
- Wide-spaced nipples

Abdomen
- Inguinal hernia

Genitourinary/anal
- Sacral dimple
- Sacral hair
- Lumbosacral sinus
- Hydrocele
- Large clitoris
- Small penis

Extremities
- Hypoplastic finger or toenails
- Clindactyly
- Syndactyly
- Increased space, toes 1 + 2
- Extra digits
- Metatarsus adductus
- Toe overlap
- Malpositioned toes
- Club feet
- Rocker bottom feet

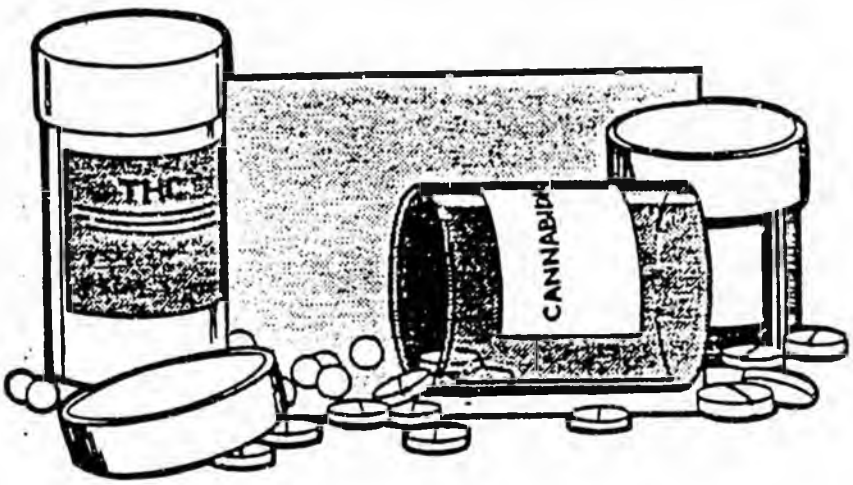
Skin
- Cafe-au-lait spots
- Hypopigmented spots
- Hemangioma
- Lipoma
- Hyperpigmented spots

How does marijuana affect cells in the body?

Changes have been found to occur in the membranes of brain cells, red and white blood cells, and sperm cells due to accumulation of THC in the body.

Many birth defects are related to abnormal number or structure of chromosomes in dividing cells. There are reports of breaks in chromosomes occurring in cells obtained from pot smokers. Other experiments show, however, that pot is more likely to cause abnormally low numbers of chromosomes than chromosome breaks. One study revealed that 30 percent of the white blood cells in marijuana users had reduced numbers of chromosomes compared to normal cells with 46 chromosomes.

THC also depresses cell division. Even small amounts impair manufacture of DNA. The observation that marijuana interferes with DNA in cells and chromosomes indicates that it disturbs the genetic balance of the cells. By altering hereditary DNA, THC could cause genetic mutations.



Does marijuana use effect the immune system?

Animal data consistently show a definite suppression of test animal's immune responses after they use marijuana.

Isn't marijuana being used as medicine?

There isn't such a thing as "marijuana" as medicine. Almost always, studies on the medical use of "marijuana" are studies using THC, or other single chemicals derived from the plant.

Marijuana is a mishmash of chemicals. Most of its chemicals do not have any benefit, and others produce undesirable effects such as bronchial irritation. Even if marijuana does prove to have some medical value, it is unlikely that it will ever be sold as a medicine.

On the other hand, THC appears to show some promise in the prevention of nausea and vomiting that accompany treatment of cancer using chemotherapy. THC weakens the brain's reflex to vomit when a person is poisoned. Some cancer patients say THC reduces the sick feeling their cancer treatment produces. However, marijuana does absolutely nothing to prevent or cure cancer. If anything, it weakens the body's natural defenses against cancer or other diseases. Knocking out the brain's vomiting reflex in a healthy person could cause the person to lose a natural defense against poisoning or drug or alcohol overdose.

Because THC may lower pressure inside the eyeball, it may be useful in treating an eye disease called glaucoma. However, its effects on the heart make the drug a poor choice for elderly patients, the group most likely to need glaucoma treatment. Most eye specialists believe other drugs treat glaucoma better than THC and with fewer side effects. And, many eye specialists also believe that smoking pot might do the glaucoma patient more harm than good by causing serious eye damage.

> "We must not allow a pro-pot publicity campaign to fool the American people into thinking that marijuana is being used as medicine and is, therefore, a safe drug."
>
> - Dr. Carlton Turner

How is marijuana different from alcohol?

Marijuana is different from alcohol in the following ways:

1. THC stays in the body for a long period of time. Alcohol is a water-soluble drug which is washed out of the body relatively quickly. Somebody who drinks too much will get sick and suffer from a hangover the next day as his stomach and liver work to quickly process the alcohol. Most of the alcohol will have left the body within 12 hours. THC, however, is not water-soluble, and its chemicals remain absorbed in the brain, lungs, and reproductive organs for weeks.

2. Marijuana has respiratory irritant effects and the probable effect of causing lung cancer.

3. Marijuana is very unpredictable, because of the huge variation in effects of 421 different chemicals in the body.

4. Marijuana is illegal.

Why shouldn't marijuana be legalized?

Marijuana today is an illegal substance in all 50 states and there are severe criminal penalties for dealing or intending to deal the drug. Cannabis and cannabis products are currently controlled in Schedule I of the 1960 Single Convention on Narcotic Drugs, an international treaty signed by 75 countries, in which it is agreed that marijuana, as well as other drugs, will not be legalized. Schedule I is the most restrictive schedule in the Single Convention. Other drugs included in Schedule I are heroin, morphine and cocaine.

Some people believe that marijuana should be legalized. If marijuana were legalized, a new intoxicant would be made available for use by the population, and there would be greater access to the drug. Once a new drug is accepted by the public, it is difficult to later prohibit its use. That is the lesson learned from Prohibition, when alcohol was considered an illegal drug. How many drugs can be available for general use and still maintain a vigorous and productive society? How will children in the future be able to grow up in a chemical culture?

If marijuana smoking is dangerous, then public policy should not support any policy which encourages increased use of the drug. Many people would incorrectly believe that if marijuana is legal, then it must not be too dangerous, just as people ignorantly assume that alcohol is not "too bad" or else it would be illegal.

It also needs to be made very clear that there is no n
for legislation to make marijuana available for medical
purposes. The legislation now on the books is more tha
adequate to make available any chemical ingredients in
marijuana that might be needed. The use of "marijuana
medicine is not relevant to legalization of the drug f
social use. For example, there are medical uses for m
and cocaine, but their non-medical use is prohibited.

Why not decriminalize marijuana?

Decriminalization is sort of a weird concept. Decriminalization means that the penalty for possession of marijuana is reduced from a jail sentence to a fine. Several state legislatures decriminalized marijuana in the '70s when many people thought pot was a mild drug. Since 1978, no additional states have decriminalized marijuana, although judges have not typically sent people to jail for possessing marijuana in the remaining states where possession of marijuana can still result in a jail sentence.

The problem with decriminalization is that it makes people believe that marijuana must not be "too bad", otherwise the legislature wouldn't have reduced penalties. By decriminalizing the possession of marijuana, the possessor is given more latitude in dealing with criminal suppliers. (Selling marijuana is a criminal offense in all states.) From the dealer's point of view, decriminalization is a boom for business, because his customers are not as reluctant to buy his product. Decriminalization doesn't do anybody any good except for the pothead adults who don't like to obey the law.

What about countries where marijuana has been used for years?

Decades of experience with marijuana in other countries is not necessarily relevant in the United States where a stronger form of pot is used, primarily by young people in their formative years, and where patterns of inhalation are likely to differ. (Eastern smokers don't inhale pot smoke as deeply as Americans). It may be 20 years or more before the necessary studies can be conducted on American heavy users to demonstrate the health effects of marijuana as it is used in the United States.

What about paraquat?

People read about paraquat everytime the government tries to spray illegal marijuana fields with the herbicide. They never hear about it when each year 10.7 million acres of American farmland is sprayed with the chemical. About four million pounds of paraquat is used each year on all kinds of legal fruits and vegetable plants, because it is the most widely used herbicide in the world. The United Nations Fund for Drug Abuse and Control recommends paraquat to all

nations as the safest, most effective agent for the control of marijuana and the government has not documented a single case of human paraquat poisoning from smoking marijuana. The big fuss about paraquat comes from marijuana growers and smokers who really aren't worried about health. (If they were, they wouldn't smoke the stuff anyway.) What they are worried about is the economics of supplying an illegal drug.

Is marijuana an addicting drug?

More and more cases are being reported of people who have trouble stopping a pot-smoking habit. This is not surprising, since marijuana contains powerful "self-reinforcing" chemicals that stimulate the pleasure center of the brain. Once brain cells are stimulated by a pleasure-producing drug, they are imprinted with a chemical "memory" that is associated with a pleasant feeling. This creates a desire to smoke more pot. Teenagers who are "hooked" on pot increase the amount of the drug they smoke because they build a tolerance to it in their bodies. They begin to smoke alone and in hiding. Their personality changes when they are "high". They are unable to control the amount they use, they are preoccupied with pot use, and they continue to use pot in spite of the adverse consequences occurring to them as a result of their drug use. This is evidence of psychological dependency.

Now there is also evidence of withdrawal symptoms when heavy users stop smoking, which indicates that marijuana is a physically addicting drug. Very high, frequent doses of THC produce withdrawal symptoms which include irritability, sleep problems, digestive upsets, and loss of appetite.

Today, marijuana accounts for the second largest number of admissions to drug treatment centers in the United States. The Drug Committee of the World Health Organization has concluded that marijuana fits its definition of an addictive drug.

Do users develop tolerance to marijuana?

It is well-known that pot smokers develop tolerance to the drug's effects. Tolerance to marijuana provides a physical basis for the necessity of the heavy smoker to smoke more pot or to use more potent drugs such as LSD, cocaine or heroin.

Are pot smokers more likely to use other drugs?

Often the first step in becoming involved with drugs is use of marijuana. Marijuana users tend to use other drugs to a significantly greater degree than nonusers. The earlier marijuana use begins, and the heavier it becomes, the stronger this tendency is.

High school seniors who smoke marijuana on a daily basis use other illegal drugs five to seven times more often than the rest of the senior class. People who hang out with people who are using marijuana find they have a whole variety of other drugs being offered to them all the time. And, people who are "high" on pot have impaired judgment, which makes them more likely to consider trying other illegal drugs.

MARIJUANA IS DESTROYING MY LIFE

...For the past three years, I've been smoking pot and thinking I was enjoying it. I'd always heard it was non-addictive. This is not so -- I find I'm psychologically dependent on the drug.

I used to smoke when I felt sad or angry to make myself forget what was bothering me. I soon found I was spending two-thirds of my weekly wages from the checkout counter on pot. I now have a hard time remembering things and I'm starting to stutter.

But that's not half my problem. My best friend has given up on me, and the girl I love is soon to follow. It's surprising that I have any friends at all since I've developed a mean, paranoid streak. At 18, I feel like a worthless bum. I've tried to stop smoking pot plenty of times but only made it for a month at the most. The drug counselors at school are no help.

Star
Oct. 5, 1982

How can you help someone who is using pot?

Like an alcoholic, a chronic pot user does not usually understand the role that marijuana plays in his problems. The user must recognize his problem and decide to stop. He must reorganize his life so that it no longer revolves around marijuana, and he must form new friendships and find new sources of satisfaction that are not drug-related. To help a chronic user who may be addicted to marijuana, you need to become part of a professionally guided intervention team which might include parents, teachers, doctors, counselors, friends, etc.

When experimenting, some people tend to stop smoking pot when they get the medical facts about what the drug is doing to them. Even if, when they stop, they get better. Quite often, that is enough to convince them to stay straight. Once the person is off pot, he can see very clearly that his pot-smoking friends, in spite of what they say, are going nowhere, except downhill.

Nevertheless, even if the marijuana user is convinced that the lifestyle of a pothead and the effects of pot are not what he wants out of life, he is likely to encounter difficulties with friends who are users and who try to pressure him into joining in the "fun" when the joint is being passed around.

See section B of this manual for a more detailed explanation of how you can help a user choose a more productive lifestyle.

All these things suggest important ways that friends can help the marijuana user out-grow marijuana.

27% of those high school seniors who report daily marijuana use, also report daily alcohol consumption, versus only 7% for this age group as a whole.

59% of high school seniors who report daily marijuana use report daily tobacco smoking, versus only 25% for the age group as a whole.

47% of high school seniors who report daily marijuana use report they are current users of amphetamines, generally 4-7 times the average for this age group as a whole.

31% of high school seniors who report daily marijuana use report that they currently use cocaine, generally 5-7 times the average for this age group as a whole.

How do people get high?

People who are "high" are "high" because the part of the brain that gives them memory and intelligence is weakened. The part that registers pleasure is on the loose. That may sound like fun. The problem is that since there is a chemical in the brain that isn't supposed to be there, the brain can't operate the way it is supposed to. When the part of the brain that supplies will power and thought and reason loses control, you've lost control. That's why people who smoke dope can't tell it's affecting them. The only part of the body that can help them see what it is doing to them is itself affected by the drug. At the same time, THC stimulates the limbic (or pleasure) area of the brain, reinforcing the desire to use more dope.

How do people become burnouts?

Burnouts don't become burnouts because they want to be that way. For them, the natural ability to regulate mental functions was lost to THC. They can only return to a normal state when they abstain from using marijuana. Unfortunately, they don't want to abstain because their brains have become so accustomed to THC that they are incapable of experiencing normal pleasure without that alien chemical stimulation.

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State of California

Department of Justice

George Deukmejian

(Pronounced Duke-May-Gin)

Attorney General

CANNABIS:

ADVERSE EFFECTS ON HEALTH

The government of Canada has indicated its intention of introducing new legislation concerning marijuana. All three major parties appear to be agreed that changes are needed. The Addiction Research Foundation understands that a public debate on the issue is likely to take place during the coming year, prior to the introduction of new legislation. One important consideration in the debate will be the consequences to health of cannabis use. The Foundation is anxious to ensure that reliable information on this subject is widely available and to this end has asked scientists on its staff to prepare the following summary.

John B. Macdonald
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Introduction

Since the mid-1960s, the increasing popularity of marijuana use has underscored the need for a valid and objective evaluation of the effects of this drug on health. Much contradictory opinion has been expressed on this matter. The reasons for this are rather simple. First, knowledge of these effects of marijuana is relatively scanty compared to the knowledge on other drugs such as alcohol and tobacco. Second, and probably more importantly, marijuana use, its effects, and the legal controls on its use have created ideological issues that have been quite unnecessarily confused with facts.

The Addiction Research Foundation (ARF), and individual members of its staff, have made periodic statements on marijuana since 1968. Furthermore, the Foundation has studied the problem continuously since 1965, and maintains one of the most complete archives on the marijuana literature anywhere in the world. At present, this amounts to about 5,000 articles, approximately 1,200 of which deal with the effects of the drug on health. This statement is based on a thorough study of this material, and on direct expertise of members of staff on specific experimental areas. We have assessed the evidence on marijuana according to the same medical and scientific standards that we apply to the evaluation of the effects on health of all other drugs, including alcohol. This is important, because much of the confusion about cannabis results from the use of different standards of assessment.

The statement is made at this time to assist in the public discussions that are likely to occur when the Government of Canada deals with a bill to alter the present marijuana laws.

The Drug

Marijuana and hashish are derivatives of the cannabis plant which has been cultivated for centuries for its fibre, oil, and psychoactive resin. There are more than 400 known chemical constituents in this plant. More than 60, known as cannabinoids, are found only in cannabis. One of these is delta-9-tetrahydrocannabinol, also referred to as delta-9-THC. It accounts for the major psychoactive effects of the plant. There are two varieties of the cannabis plant. One is resin-

producing and the other is fibre-producing. THC is found most abundantly in the upper leaves, bracts, and flowers of the resin-producing variety. Marijuana, the dried leaves, may contain up to 5% of this compound; hashish, the dried and pressed flowers and resin, up to 12%; and hashish oil, a crude extract of hashish, up to 60%. The fibre-producing variety has much lower concentrations of THC.

In the liver, THC is rapidly changed to a compound called 11-hydroxy-THC, which is also psychoactive, and to more than 20 other products that are inactive. Until recently, there were no reliable methods for estimating the concentration of THC and its breakdown products in body fluids, other than the measurement of radioactivity in blood and tissues after the administration of a dose of radioactive THC. Measurement of THC and "total cannabinoids" is now possible by either radioimmunoassay or gas-liquid-chromatography/mass-spectroscopy, but these methods are available only in a few research laboratories. This fact has seriously limited the study of the fate of THC and its breakdown products in humans, including the question of how long the THC remains in the body.

Accumulation of THC in the body fat has not been demonstrated unequivocally in humans, and has been observed only under very specific conditions in animals. Furthermore, long retention in the body does not necessarily imply toxicity. However, if a substance is inherently toxic, a long retention-time will increase the risk of cumulative toxicity in the regular user.

Some of the actions of cannabis are unquestionably toxic in that they either directly or indirectly can produce adverse effects on health, but others may be beneficial in certain situation. The use of marijuana, THC, and similar synthetic chemicals, either alone or in combination with other drugs, is currently being investigated as a possible treatment for epilepsy, wide-angle glaucoma, anorexia nervosa, asthma, and the relief of nausea and vomiting produced by anti-cancer drugs. The latter effect is the most promising of the possible therapeutic applications.

The therapeutic use of cannabis is not directly relevant to decriminalization of cannabis. This is clearly shown by the fact that

the medical use of morphine and cocaine is legal, while their non-medical use is prohibited. In contrast, the adverse effects of the non medical use of cannabis clearly constitutes one of the factors that the government will take into account in its debate on possible changes in the present laws. This document focuses on the known and potential health hazards of cannabis following both acute (single dose) and chronic (multiple dose) use. Heavy use is defined here as at least daily use of high potency cannabis. Where relevant, these effects will be compared to those of others psychoactive drugs.

Damage to health induced by any drug is often first suspected by observant physicians on the basis of individual cases. A casual relationship is usually indicated by a higher rate of occurence of the damage among users than among non users of the drug. Experimental prpof that the drug causes a particular health problem is relatively uncommon; for example, there is no experimental proof that alcohol causes liver cirrhosis or tobacco smoke causes lung cancer in humans, even though the connection is clinically and statistically clear. However, conclusions about the frequency of occurrence of a particular health problem among users of the drug can be reached only through large-scale epidemiological studies. Important but relatively infrequent problems, such as lung cancer in cigarette smokers, or liver cirrhosis in alcoholics, can not be detected in studies of a few dozen users, but may require observation of a whole population over many years. So far, our knowledge concerning cannabis is at the level of case reports, some experiments, and small group studies, but the crucial epidemiological observations are still lacking.

Behavioral and Mental Effects

In most individuals, the social use of low to moderate doses of cannabis produces euphoria, a pleasant state of relaxation, altered perception particularly of distance and time, impaired memory of recent events, and impaired physical coordination. The state of intoxication is usually mild and short-lived (two to three hours after one joint). An occasional "high" is probably not physically hazardous unless the user attempts to drive, fly, or operate heavy machinery during the state

of intoxication. It is now well recognized that even reaction time, in judgment probably account for these observations. Until a reliable, inexpensive, and simple method for the estimation of blood levels of THC and its breakdown products, comparable to the breathalyzer test for alcohol, is widely available, the detection of cannabis-intoxicated drivers will remain a major problem.

In some users, an acute dose of cannabis can produce adverse reactions ranging from mild anxiety, through panic and paranoia, to an acute toxic psychosis characterized by detachment from reality, delusions, hallucinations or illusions, and bizarre behavior. These reactions occur most frequently in individuals who are under stress, anxious, depressed, or borderline schizophrenic, and in normal users who inadvertently take much more than their usual dose. Limited evidence from survey studies suggests that the mild reactions have been experienced on one or more occasions by more than a half of regular users, although their exact frequency is unknown. They are mainly self-treated and usually go unreported. The severe reactions, which appear to occur in only a small percentage of users, usually respond well to non specific psychiatric treatment and last no longer than one or two days.

There has been a great deal of controversy about the effects of chronic heavy use of cannabis on brain function. There is evidence that chronic use can lead to lasting behavioral changes in some users. Apathy, lack of concern for the future, and loss of motivation have been described in some heavy users, and psychotic and paranoid symptoms in others. These symptoms usually disappear gradually when regular drug use is discontinued, and recur when use is resumed. These reactions are relatively rare, although case studies suggest that certain cannabis users may be particularly susceptible. Many psychiatrists are concerned about such reactions in youthful drug users (11 to 15 years of age), because of the possibility that regular use may produce adverse effects on psychological, as well as physical, maturation. This concern, of course, applies to the use of all psychoactive drugs by juveniles. For reasons that are still unclear, a few users experience spontaneous recurrences of the symptoms of acute intoxication ("flashbacks") days or weeks after consuming cannabis.

Are there any other changes in brain function that outlast the period of intoxication? Limited clinical evidence suggests that some users do not recover fully when drug use is discontinued. The psychological functioning (perception, coordination, intelligence, etc.) of presumably non intoxicated heavy users has been tested in countries such as Jamaica, Costa Rica, Greece, Egypt, and India. The conclusions from these studies have been conflicting, and confounded in some cases by methodological problems and biased investigators. Studies with the largest groups of subjects (in Egypt and India) have shown significant differences between users and matched non users, while the studies using much smaller samples (in Jamaica and Costa Rica) have not.

Experimental evidence from the ARF laboratory in rats, and elsewhere in monkeys, suggests that long-term exposure to doses of cannabis equivalent to those consumed by very heavy users can produce learning impairment and changes in brain waves that persist months after the end of chronic intoxication. These disturbances are accompanied by subtle changes in brain cell connections that can be seen under the electron microscope. This experimental evidence of brain damage is consistent with clinical observations in humans. On the other hand, the reports of gross brain atrophy, based on air encephalography, have not been confirmed by the more sophisticated tomographic technique ("CAT scan").

Respiratory System

Cannabis is usually smoked, either alone or in combination with tobacco. Smoke is an aerosol, consisting of tiny particles suspended in a vapor phase. The latter consists of gases such as carbon monoxide, while the particles form the solid residue called "tar". Cannabis produces 50% more tar than the same weight of a popular strong tobacco brand. A "joint" is usually smoked to leave as small a butt as possible, thus doubling the tar yield per "joint."

In addition, the tar contains more than 150 poly-nuclear aromatic hydrocarbons, including cancer-producing agents such as benzo(a)pyrene. The concentration of this component in marijuana tar is 70% higher than in the same weight of tobacco tar. Therefore, one cannabis cigarette, totally combusted, yields about five times as much benzo(a)pyrene as

one tobacco cigarette of equal weight, but smoked to a butt of 30 mm. The amount of benzo(a)pyrene retained in the lungs from one "joint" is probably even greater than from five normally smoked tobacco cigarettes, since cannabis smoke is inhaled deeply and held for as long as 30 seconds. Thus, two to three cannabis cigarettes a day may well carry the same risk of lung damage as a pack of tobacco cigarettes.

Cannabis tar, when painted on the skin of mice, causes pre-cancerous changes similar to those produced by tobacco. Cultures of isolated human and animal lung cells also undergo pre-cancerous changes when exposed to cannabis and/or tobacco smoke. In addition, some of these cells, the alveolar macrophages, appear to lose their ability to inactivate bacteria when exposed to certain components of cannabis smoke.

Long-term heavy smoking of cannabis is associated with chronic respiratory symptoms such as sore throat, rhinitis, and bronchitis. Although acute use increases the diameter of the airways, chronic heavy use conversely produces changes suggestive of early obstructive airway disease. In addition, pre-cancerous changes have been found in bronchial biopsies from 20-year-old heavy smokers of hashish and tobacco, that are not normally seen in heavy tobacco smokers under the age of 40. Many cannabis users also smoke tobacco, and the pulmonary toxicity observed is probably a reflection of the total tar inhaled from both sources.

Cardiovascular System

In humans, acute administration of cannabis produces reddening of the eyes, and a dose-related increase in heart rate. In normal individuals, these effects, as well as slight changes in heart rhythms, are transitory and appear to be of little significance. In patients with angina pectoris, however, the increased oxygen requirement associated with the increased heart rate results in an earlier onset of angina pain in response to exercise. The effect of cannabis on patients with irregularities of heart rhythm is not known.

Cannabis-induced changes in blood pressure tend to be inconsistent, although abnormally low pressure in the standing position has frequently been observed.

Chronic administration of large doses of THC to healthy volunteers results in tolerance to the increase in heart rate, decreased blood pressure, and an increased blood volume. The chronic effects of cannabis in patients with cardiovascular disease are not known.

Sex Hormones and Reproduction

Drugs can interfere with reproduction by altering sexual behavior, affecting fertility, damaging the chromosomes of the germ cells of the male or female, or acting directly on fetal growth and development.

Moderate doses of cannabis do not affect sexual behavior consistently, but a decrease in libido has been reported among heavy users in some but not all studies.

Drugs can affect fertility by changing the output of hormones that govern ovulation or spermatogenesis. In male animals, chronic cannabis treatment consistently produces decreased levels of serum testosterone, testicular degeneration, and arrested or abnormal sperm production. The drug appears to act both directly on the testes, and indirectly by suppressing hormone release from the hypothalamus.

In men, the situation is less clear. Decreased testosterone levels (that remain within the lower part of the normal range), decreased sperm counts, and abnormal sperm morphology and biochemistry have been reported in heavy users, although not all investigators have been able to replicate these findings. Differences in experimental methodology probably account for most of the inconsistencies and most investigators now believe that there is some interference with male hormonal function, but this is less marked than with heroin or alcohol. The clinical significance of small decreases in serum testosterone levels in healthy males is probably minimal. These changes may be more significant during intrauterine development of the male fetus, during adolescence, or in adult males with borderline testicular function.

In female animals, THC is known to suppress ovulation by interfering with the hypothalamic release of luteinizing hormone, but tolerance to this effect develops on chronic administration. Virtually no research

has been done in women, but there is preliminary evidence that cannabis smoking is associated with intermittent failure of ovulation. For ethical reasons, it has not been possible to study this effect in controlled experiments.

In some but not all studies, the chromosomes in white blood cells isolated from cannabis users have shown increased rates of breakage and other damage. This is a common finding among users of many street drugs, and more likely reflects the general lifestyle of the users, than the effect of any particular drug. Furthermore, it has never been established that chromosome damage in white blood cells indicates genetic damage in the egg or sperm cells or predicts an increase in the number of abnormal births.

THC does not produce genetic mutations in the test systems studied to date, although other components of the smoke are mutagenic. In animals, reported birth defects appearing in the third generation, after exposure of the first generation to cannabis smoke during pregnancy, suggest that the possibility of genetic damage cannot be discounted.

The ability of cannabis to produce birth defects has been studied in many animal species. Although THC crosses the placenta, very high doses must be given to produce visible abnormalities. However, cannabis smoke containing lower doses of THC has been shown to produce fetal toxicity including an increased number of fetal resorptions, decreased fetal weight, and an increased death rate around the time of birth. This suggests that components other than THC, such as carbon monoxide, are responsible for these effects.

In addition, THC, when given to pregnant animals at doses that are too low to produce visible abnormalities, can produce subtle changes in the behavior and development of the offspring.

Information in humans is scanty. In Eastern countries cannabis has been consumed almost exclusively by males, so that observations on pregnant women are lacking. There have been a few case reports in Western countries of deformed babies born to mothers who had smoked cannabis during pregnancy, but no cause-and-effect relationship can be determined on the basis of this evidence. Further research is

needed, particularly follow-up studies of behavior and development in the infants of marijuana smokers.

Immune System

THC and cannabis extracts and smoke, when given to animals at behaviorally relevant doses, suppress immune reactions. In humans, many but not all studies indicate that heavy use of cannabis may interfere with the function of one component of the immune system--the T-lymphocyte. This component is known to play a role in the resistance to viruses and to cancer. The combination of inhaled carcinogens and depressed T-lymphocyte function could entail a greater risk of cancer. An increased frequency of cancer has not been apparent in countries where cannabis use has been traditional; however, until recently the average life-span in these countries was relatively short, and the users may have died of other causes before cancer had time to develop. The question of decreased immunity in chronic users must be examined in North America and Europe by careful epidemiological studies.

Macromolecular Synthesis

THC and related compounds inhibit the intracellular synthesis of complex biological molecules, including proteins, DNA, and RNA, and inhibit cell division in test-tube experiments. Alcohol and opiates have similar effects. Some investigators have suggested that this inhibition may be responsible for the impaired immune response noted above, and for other effects observed in chronic users. The biological relevance of these test-tube effects is still unclear, because the dose required to produce them in the body is unknown and the consequences of such effects are often difficult to recognize.

Tolerance and Dependence

It has been known for many years that tolerance to some effects of cannabis occurs rapidly in animals, i.e., the drug effects become less intense on repeated administration. In experiments, frequent administration of high doses of cannabis or THC in humans produces tolerance similar to that observed in animals. For example, increasingly

high doses must be given to obtain the same intensity of subjective effects and increased heart rate that are observed initially with small doses.

Frequent high doses of THC can also produce mild physical dependence. Healthy subjects, given by mouth the equivalent of several "joints" a day, or volunteers who smoke comparable amounts, experience irritability, sleep disturbances, weight loss, inhibition of appetite, sweating, and gastrointestinal upsets when the drug is discontinued abruptly. Although this is a true abstinence syndrome, the intensity of the symptoms is not as marked as that produced by moderate chronic doses of other drugs such as alcohol, the barbiturates, or the opiates.

Heavy use of cannabis is also associated with psychological dependence which is responsible for sustained drug-seeking behavior. The existence of compulsive users has been well documented, although the percentage of cannabis users that reach this stage is unknown and probably rather small, as is the case with most other psychoactive drugs.

Miscellaneous

A number of minor effects of cannabis have been reported in humans and in experimental animals. These include gastrointestinal disturbances, reduction of gastric acid secretion, and weight loss in heavy users; true allergic reactions to cannabis and some of its individual constituents; and an increase in the difficulty of medical control of diabetes. Despite the fact that single doses of some constituents of cannabis can suppress seizures, some epileptics actually have more seizures when smoking marijuana. The mechanisms of these effects are not known, nor is their frequency of occurrence, though it is probably low.

Conclusions

Clinical observations from many parts of the world have long suggested that regular heavy use of cannabis may produce lung damage, impair reproductive and endocrine functions, cause long-lasting disturbances of behavior and brain function, and lower resistance to

infection. Well-controlled animal experiments have demonstrated that cannabis, in high dosage, can indeed produce such effects. It is probable that most of the remaining discrepancies among experimental findings will be resolved by standardization of experimental methods, and by the development of accurate sensitive methods for measuring the levels of THC and other cannabis constituents in blood and tissues, so that the exact degree of drug exposure is known.

What is not yet known, however, is the frequency with which these health problems occur among cannabis users, the degree of use needed to produce them in humans, and the percentage of users at risk. Sophisticated epidemiological studies of large populations of users, such as those already done in relation to alcohol and tobacco use, are needed to fill in these gaps in our knowledge. It may also be necessary to carry out studies on large groups of individuals, monitored before, during, and after many years of cannabis use. It is probable that any specific health problem due to cannabis will have a low incidence and prevalence among the total population of cannabis users, and that it will therefore take a generation or more of wide-ranging public health observations to provide a clear picture. This was true of alcohol and tobacco problems, and there is no reason why it should be different for cannabis.

It should also be emphasized that almost all of the available experimental data arise from studies of young healthy adult males. While some of the changes noted above may be relatively unimportant in a healthy young person, they may be very significant in an individual at risk because of age or pre-existing disease. For ethical reasons, however, these individuals cannot be studied experimentally. We feel that people especially at risk with even moderate doses include anxious, depressed, or unrecognized psychotic individuals; heavy users of other drugs; pregnant women; some epileptics; diabetics; individuals with marginal fertility; and patients with chronic diseases of the heart, lungs, or liver. In addition, as with any other psychoactive drug, adolescents who are undergoing rapid physiological and psychological development may be particularly susceptible to the development of a life-long pattern of use, and to the effects of long periods of cannabis

intoxication. They may also be more prone to cannabis-related traffic accidents because of their lack of driving experience, and may be affected more by possible disruptions of hormone balance.

(THE ABOVE ARTICLE WAS COPIED FROM THE JANUARY 1980 ISSUE OF "THE JOURNAL" AND WAS PREPARED BY SCIENTISTS OF THE ADDICTION RESEARCH FOUNDATION OF ONTARIO.)

NATIONAL ORGANIZATION FOR THE REFORM OF MARIJUANA LAWS

NORML

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March 17, 1988

Karla Hart
House Research Agency
Post Office Box Y
Juneau, AK 99811-3100

Dear Ms. Hart:

As per your request, I have researched the scientific basis for the various findings listed in Senate Bill No. 32 (Hess). NORML's comments, with appropriate citations, are listed below after each finding.

Many citations refer to the first chapter of the National Academy of Sciences report, Marijuana and Health, edited by Arnold Relman, M.D. I have enclosed a copy of the entire first chapter so you can evaluate our claims in context. I have also included an pre-publication article about marijuana's potency, a copy of the recent study by Dr. Tashkin on marijuana and smoking, and several copies of a recent "Harvard Medical School Mental Health Letter" on the subject of marijuana and health. I have quoted from these articles in my remarks below, but have omitted listing citations contained within those sources. Additional citations can be garnered from the full copies enclosed.

1) *Marijuana... may contain over 420 different compounds.*

There is no correlation, let alone a causal relationship, between the number of compounds a substance contains and its capacity to pose a serious health hazard. However, it must be pointed out that refined pharmaceuticals tend to be more toxic and hazardous to the body than natural substances - which tend to be more easily metabolized. Coca leaves and opium, for example, are less toxic than their refined by-products, cocaine and heroin. It could be argued that the lower the number of compounds present in a substance the more dangerous it is, but this would be equally as fallacious.

Finding number one suggests that the sheer number of compounds present in marijuana make it dangerous. First of all, it is only "a single cannabinoid, Delta 9 THC, (that) produces almost all the characteristic specific

pharmacological effects of the complex, crude cannabis mixtures."[1]

Secondly, marijuana is not a dangerous drug. A recent textbook for emergency room technicians states that "cannabinoids (marijuana) are very common but of little concern to ER clinicians because of their mild effects."[2]

2) *THC... takes as long as 30 days to be eliminated from the body.*

It is true that extremely small levels of unmetabolized THC remain in the body, however they have no effect on the body. Dr. Arthur McBay, North Carolina's chief medical examiner, holds that the psychoactive components in marijuana are metabolized fairly quickly, whereas the metabolites can be present for 30 days.[3] He also points out that arsenic and lead are present in the human body, but pose no health hazard because of the low amounts involved.[4]

Dr. John Morgan is the Director of Pharmacology at the City University of New York, and has testified before the Senate Judiciary Committee (and elsewhere) as an expert on this subject. He writes that:

> THC is detectable within the urine within 30 minutes of smoking marijuana. It may persist in the urine and in the blood for an appreciable period of time...
>
> (Though) unchanged THC scarcely appears in the urine and falls to extremely low concentrations in the blood within 4 hours of smoking. Although a large portion of smoked or eaten THC will appear in the urine as THC-COOH (the primary metabolite - 11-Nor-delta-9-tetrahydrocannabinol carboxylic acid), the absolute amount is very small. Testing usually detects between 50 and 100 nanograms per milliliter of THC-COOH. A nanogram is one billionth of a gram...

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[1]A.S. Relman (Chairman); Marijuana and Health (Washington D.C.: National Academy Press, 1982), 13.

[2]M. Bishop; J. Duben-Bon Laufen; E. Fody; Clinical Chemistry Principles, Procedures, Correlations (Philadelphia: J.B. Lippincott Company, 1985).

[3]Arthur McBay; "Technical Problems with Urine Testing" (Remarks made at a conference entitled Marijuana Related Problems sponsored by the Council on Marijuana and Health, February, 1987).

[4]Arthur McBay; Personal communication.

> Depending upon the amount of THC in the marijuana and the smoker's efficiency, the serum THC will peak in 15 to 30 minutes somewhere between 100 and 500 ng/ml. A fairly precipitous decline in concentration follows as the THC is distributed from the central compartment (the blood) to the deeper compartment, the rest of the body. The brain is included in the rest of the body. After the THC falls to nearly undetectable concentrations within 3-4 hours (usually less than 2 ng/ml) another process intervenes. Some equilibrium between the THC in the blood and other tissues reenters the blood stream. The concentration of THC in the body now declines very slowly in a second phase... During this lengthy stay in the body, THC is continually metabolized to the THC-COOH which is filtered at the glomerulus and excreted into the urine...
>
> Despite its persistence and its tendency to accumulate in body tissues with repeated dosage, there is no reliable evidence that this burden of THC, much discussed, has any effect on repeated users. The small concentration of THC carried in the blood and storage tissue is below the threshold to provoke an effect.[5]

The National Academy of Science's review of studies reports a variance in the half-lives of Delta-9-THC from 19 hours in experienced users to 57 hours in naive users.[6] Whether the difference is due to the experience of the user was not established, but the range suggests that any buildup of THC or metabolites would also be offset by an increase in the time taken to metabolize the chemicals.

It is incorrect to conclude from finding number two that the active component of marijuana, THC, has the potential to exert its psychoactive effects for a thirty day period. THC has a psychoactive effect only for several hours.

3) *"The buildup... means that... even small doses may lead to an accumulation of the drug higher than levels reached at any time after a single dose."*

In a general sense this is true of any drug, however as explained above the "high" associated with marijuana lasts for approximately four hours. Repeated doses in that time

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[5]J.P. Morgan; "Marijuana Metabolism in the Context of Urine Testing for Cannabinoid Metabolites" (Paper to be published by the Council on Marijuana and Health in the Fall of 1988)

[6]A.S. Relman; (1982), 23.

frame will extend the "high", but not for thirty days. The only way a person can be under the influence of marijuana for thirty days is to smoke marijuana about every four hours for thirty days.

This finding is a virtual quote from the National Academy report.[7] It concludes a paragraph which begins with a report of data from an experiment involving an injection of Delta-9-THC. To infer from the finding that THC builds up in the system and affects an individual far after their use of marijuana is incorrect.

Furthermore, the NAS report warns of difficulty in making any conclusions about marijuana's safety based on individual clinical indications. "The intensity and duration of a drug effect depends on at least three major factors... With cannabis, many or even most of these factors are not always measurable or under control of an investigator."[8]

4) *"The buildup... causes the user to smoke more marijuana to achieve the desired high and may result in loss of sleep, appetite, and initiative, as well as moodiness and depression."*

This finding confuses and merges the symptoms of tolerance and withdrawal, and misattributes them to a buildup of THC which is inadequate to explain these effects. The NAS report on the matter of tolerance:

> Tolerance to most cannabinoid effects has been demonstrated both in animals and human beings. Tolerance can develop rapidly after a few small doses. It disappears at an equally rapid rate for many effects, although after large doses in experimental animals some tolerance may persist for long periods...
>
> The development of such tolerance to cannabis does not necessarily have health implications. However, if tolerance should lead to higher or more frequent doses, adverse consequences, e.g., respiratory effects, associated with higher usage could result.
>
> Physical dependence, manifested by withdrawal signs and symptoms, can develop rapidly in animals and in human beings. The withdrawal syndrome is not life threatening... Withdrawal symptoms can include restlessness, irritability, mild agitation, insomnia, and sleep EEG disturbance.

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[7]A.S. Relman; (1982), 20.

[8]A.S. Relman; (1982), 19.

> Cannabis dependence does not mean the same thing as cannabis addiction. Dependence means only that a withdrawal syndrome can occur when drug taking is stopped. Addiction implies compulsive behavior to acquire the drug. The relationship between dependence and increased drug seeking or drug using is more theoretical than well-documented, particularly in experiments with human beings.[9]

5) *"It is possible for a human being to overdose from the use of marijuana, especially if it is used in conjunction with alcohol, because it increases the effects of alcohol."*

It may be possible, but it is highly unlikely that a human being will die from a marijuana overdose. According to the Harvard Mental Health Letter, "No human being is known to have died of an overdose. By extrapolation from animal experiments, the ratio of lethal to effective (intoxicating) dose is estimated to be on the order of thousands to one." Generally, an oversufficient dose of marijuana will put a subject to sleep. According to the NAS, "delta-9-THC and related cannabinoids have a very low lethal toxicity... The lack of well-authenticated cases of human deaths from acute delta-9-THC or cannabis overdose is consistent with the experimental animal data."[10]

Alcohol abuse can cause accidental death or injury regardless of whether or not marijuana is involved. There has been speculation that because marijuana is effective as an anti-emetic for chemotherapy patients that it could inhibit vomiting on the part of individuals who have consumed unsafe quantities of alcohol. However, marijuana appears to be an insufficient deterrent to vomiting when excessive quantities of alcohol are involved.

6) *"...the THC content... has increased from less than one percent... to as high as 10 percent today."*

According to the Harvard Medical School Mental Health Letter:

> New breeding and cultivation techniques have raised the THC content of marijuana smoked in the United States as much as ten times over the last 20

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[9]A.S. Relman; (1982), 26-27.

[10]A.S. Relman; (1982), 24.

years, from an average of 0.4 percent to 4 percent. Some varieties now contain as much as 10 percent.[11]

There is nothing new, or dangerous, about high potency marijuana, despite the emergence of domestically grown high potency marijuana in the United States.

The high THC potency cannabis preparation 'hashish', has existed and been used, like marijuana, for thousands of years. In an upcoming article in the Journal of Psychoactive Drugs, Drs. Tod Mikuriya and Michael Aldrich cite references to the use of high-potency cannabis preparations in papers written in 1839, 1857, 1860, 1869, 1884, and 1890.[12] Then, as now, the response to stronger preparations is to titrate the dose. More importantly, "From the time of its introduction to Western medicine in 1839, right up to the present day, quite potent cannabis products have been available and have been used in research."[13]

Furthermore, the NAS reports that "about half of the delta-9-THC originally in a cannabis cigarette is lost by combustion, by butt entrapment, in smoke not inhaled, and in smoke exhaled."[14] This factor indicates that potency itself is not an indicator of the amount of THC actually consumed in social use.

8) *"marijuana may cause schizophrenia, illusions,..."*

According to the Harvard Mental Health Letter:

> The idea has persisted that in the long run smoking marijuana causes some sort of mental or emotional deterioration. In three major studies conducted in Jamaica, Costa Rica, and Greece, researchers have compared heavy long-term cannabis users with non-users and found no evidence of intellectual or neurological damage, no changes in personality, and no loss of the will to work or participate in society. The Costa Rican study showed no difference between heavy users (seven or more marijuana cigarettes a day) and lighter users (six or fewer cigarettes a day). Experiments in the United States show no effects of fairly heavy

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[11]Lester Grinspoon, ed.; The Harvard Medical School Mental Health Letter, Vol. 4, No. 5 (Boston: Department of Continuing Education of Harvard Medical School, 1987), 1.

[12]T. Mikuriya and M. Aldrich; "Cannabis 1988: Old Drug, "New Dangers" -- The Potency Question" (San Francisco: Journal of Psychoactive Drugs, April, 1988).

[13]ibid

[14]A.S. Relman; (1982), 21-22

marijuana use on learning, perception, or motivation over periods as long as a year.[15]

9) *"...one marijuana cigarette a day may cause lung cancer in three years."*

If this finding is true, America would have between 15 and 30 million cases of lung cancer directly attributable to marijuana use recorded in this decade alone. The burden of proof for this claim lays with its author.

NORML concedes that marijuana smoke can cause lung damage, and can contribute to respiratory and heart problems. The NAS claims that:

> It is not easy to compare the toxicity of a given number of marijuana cigarettes to a given number of tobacco cigarettes. There are general similarities in the composition of the smoke, but the variations in composition of both tobacco and marijuana cigarettes and differences in smoking techniques make simple extrapolations of risks of tobacco versus marijuana smoking not valid.[16]

A new study published early this year by Dr. Tashkin and his associates concludes that one marijuana cigarette produces the tar and carbon monoxide of approximately four tobacco cigarettes.[17]

However, Dr. Tashkin concedes:

> Long-term adverse pulmonary consequences of tobacco smoking have been shown to be related to dose. For example, the incidence of chronic obstructive pulmonary disease or bronchogenic carcinoma in smokers of fewer than 5 to 10 tobacco cigarettes a day is substantially less than in habitual smokers of more than 20 tobacco cigarettes a day. Although regular tobacco smokers consume more than 15 tobacco cigarettes a day, most current smokers of marijuana smoke less than 1 marijuana cigarette a day. Even among the estimated six million daily smokers of marijuana in the United

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[15]L. Grinspoon, ed. (1988), 3.

[16]A.S. Relman (1982), 15.

[17]D. Tashkin; T. Wu; B. Djahed; J. Rose; "Pulmonary Hazards of Smoking Marijuana as Compared With Tobacco" (Boston: New England Journal of Medicine, Vol. 318, No. 6., 1988), 347 - 351.

States, smoking more than five marijuana cigarettes a day is unusual[18]

Accordingly, despite the presence of four times the tar and carbon monoxide of a tobacco cigarette, a single marijuana cigarette consumed daily presents less of a health risk than a quarter pack of tobacco cigarettes.

Furthermore, the tar and carbon monoxide levels were unaffected by THC potency. The lung damage associated with marijuana use is produced by the physical burning of the plant material, not THC, the active ingredient. Oral ingestion of marijuana does not produce lung damage. Incidently, as far as respiratory effects, high potency marijuana is safer to use because less material is actually burned, thereby exposing the lungs to less tar.

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

The Harvard Letter:

The effects of marijuana on the reproductive system are a more complicated issue. In men, a single dose of THC lowers sperm count and the level of testosterone and other hormones. Tolerance to this effect apparantly develops; in the Costa Rican study, marijuana smokers and controls had the same testosterone levels. Although the smokers in the study began using mariuana at an average age of 15, it had not affected their masculine development. There is no evidence that the changes in sperm count and testosterone produced by marijuana affect sexual performance or fertility.

In animal experiments THC has also been reported to lower levels of female hormones and disturb the menstrual cycle. When monkeys, rats, and mice are exposed during pregnancy to amounts of THC equivalent to a heavy human smoker's dose, stillbirths and decreased birth weight are sometimes reported in their offspring. There are also reports of low birth weight, prematurity, and even a condition resembling the fetal alcohol syndrome in some children of women who smoke marijuana heavily during pregnancy. The significance of these reports is unclear because controls are lacking and other circumstances make it hard to attribute causes. To be safe, pregnant and nursing women should follow the standard

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[18]ibid, 349.