

MARIHUANA AND HEALTH

SEVENTH ANNUAL REPORT
TO THE
U.S. CONGRESS

From the
Secretary of
Health, Education,
and Welfare
1977

RM 530

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Seventh Annual Report
to the U.S. Congress
From the Secretary of
Health, Education, and Welfare
1977

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ACKNOWLEDGMENTS

Preparation of the Seventh Marihuana and Health Report was made possible by the contribution of information by members of the research community. Their assistance is gratefully acknowledged.

Special thanks are due to several members of the scientific community who have in the past provided technical reviews of marihuana research on which in part this year's report is based and to those scientists who read the report in draft and offered many helpful suggestions. They include: Dr. Henry Brill, Dr. Sidney Cohen, Dr. Douglas Ferraro, Dr. Leo Hollister, Dr. Reese Jones, Dr. Lissy Jarvik, Dr. Ralph Karler, Dr. Donald Kennedy, Dr. Steven Matsuyama, Dr. William McGlothlin, Dr. Ernest Noble, and Dr. Gene Smith. Scientists on the National Institute on Drug Abuse staff who contributed in a variety of ways include: Drs. Richard Hawks, William Pollin, Louise Richards, and Stephen Szara.

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

Introduction

This edition of Marihuana and Health marks the seventh in a series of annual reports from the Secretary of Health, Education, and Welfare to the Congress as required by Title V of Public Law 91-296. Like previous editions, this report once again attempts to provide an updated answer to the question, "What are the health implications of marihuana use for Americans?" with primary emphasis on developments of the past year. A recurrent problem this year as well as last is the limited number of new findings available to shed light on questions badly needing illumination, but for which definitive answers are elusive. Understandably, the American public would like to have the health issues raised by marihuana use resolved unambiguously. Even if the question of health hazards can not be answered simply, can we not provide clearer indications of the circumstances under which cannabis poses a serious public health threat?

Unfortunately, in many areas we cannot. Some of the critical questions concerning chronic use effects in the United States will require many years to adequately answer. Although animal research may be quite useful in providing indications of possible human effects, interspecies differences in susceptibility to drugs are common and the results found may or may not occur in humans. Research under well controlled conditions that has been done on overseas populations to date involves small numbers which may have missed rarer consequences of use.

A continuing problem throughout the past decade has been the tendency **of many to overinterpret preliminary research findings, to seize** on data from clearly limited research in a desire to resolve important outstanding questions promptly and unambiguously. For example, research on isolated human tissue in the test tube may be of considerable interest and suggestive of hazard. Nevertheless, such work may not accurately reflect the implications of marihuana use in the intact human under more typical conditions of use and its possible implications must be verified clinically.

While the research developments of the past year have added to our understanding of the health implications of marihuana use in the United States, they have by no means resolved the outstanding issues with which we continue to be confronted.

HIGHLIGHTS

Extent of Use

- The number of younger users ages 12 to 17 has jumped 25 percent since 1976.
- The number of current users (in month preceding survey) in the 12 to 17 age group has also increased by 30 percent.
- Three out of five in peak using 18 to 25 age group have used marihuana, over one in four use currently.
- Use continues to be strongly age-related--only 7 percent of those over 35 have ever tried marihuana.
- Among high school seniors nationwide, one in eleven reports using on a daily basis, up from one in twelve in 1976 and one in seventeen in 1975.

Marihuana Use Detection

- Progress continues on simpler methods of detection of marihuana intoxication, but the problem remains of correlating drug levels detected with psychomotor impairment in such tasks as driving.

Developments in Research on Human Effects

- Few new developments have been reported in 1977.
- Increased use by younger age groups (under 18) is a source of concern since this group, because of stage of physical and psychological development, may be at greater risk than other users.
- Others at higher risk may include those with pulmonary or cardiac impairment, those with a history of serious psychological problems.
- Combined use of marihuana and alcohol may be more hazardous than use of either alone.
- Because marihuana is typically smoked and extracts have been shown by skin testing to be carcinogenic in test animals, adverse pulmonary consequences of use both from the material itself as well as from contaminants are a serious concern.
- Evidence remains inconclusive regarding the possible adverse effects of marihuana use on the immune response, an important factor in disease resistance. While there have been both human and animal studies suggesting some impairment, the practical implications of this remain in doubt.

- Effects on endocrine functioning, particularly on testosterone levels in men, have been reported as have been diminished sperm counts and alterations in cellular characteristics of sperm in heavy hashish users. The clinical significance, if any, of these previously reported changes remain in doubt.
- No new evidence concerning chromosomal abnormalities related to marihuana use has appeared. There is no convincing evidence that use causes clinically significant chromosome damage, although the possibility cannot be completely dismissed.
- While research on brain damage reported on last year found no evidence for gross abnormalities suggested by an earlier, less well controlled study, more subtle changes cannot be ruled out. Some microscopic changes in brain cellular structure in monkeys trained to smoke marihuana have recently been reported, but the implications, if any, for humans are presently unknown.
- Overseas studies in Jamaica, Greece and Costa Rica of relatively small numbers of users matched with non-users which found few differences continue to be overinterpreted. Rarer, but nevertheless serious, possible effects of use may have gone undetected and such studies should not be interpreted as indicating marihuana is a "safe" drug.
- Controversy continues over a large Egyptian study suggesting that in a prisoner population cannabis-using prisoners showed greater impairment in psychological functioning than non-using prisoners. A conclusive judgment regarding this study and another conducted in India cannot be reached.
- Serious psychopathology of the type attributed to cannabis overseas continues to be uncommon in the United States. The role of cannabis in "cannabis psychosis" reported in the foreign literature remains in dispute. One small study of the effect of marihuana on schizophrenic patients in partial remission suggests that cannabis use may cause a recurrence of psychotic thinking and that such use should be especially discouraged in these patients.
- Data from the Federal Drug Abuse Warning Network (DAWN) continues to indicate that marihuana ranks third (following alcohol and heroin) as a factor involved in individuals seeking help from "crisis centers". While such figures are not always simply interpretable, they do suggest that marihuana is not an uncommon factor in individuals seeking help.

- As reported last year, there is good evidence from several converging sources that marihuana use at typical social levels impairs driver performance and that driving while marihuana intoxicated should be actively discouraged.
- While there were no major new potential therapeutic applications for marihuana reported last year, its use in the treatment of nausea accompanying cancer chemotherapy and in the treatment of glaucoma remain promising. Other possible therapeutic applications have been reported, but their promise seems more remote.

NATURE AND EXTENT OF MARIHUANA USE IN THE UNITED STATES

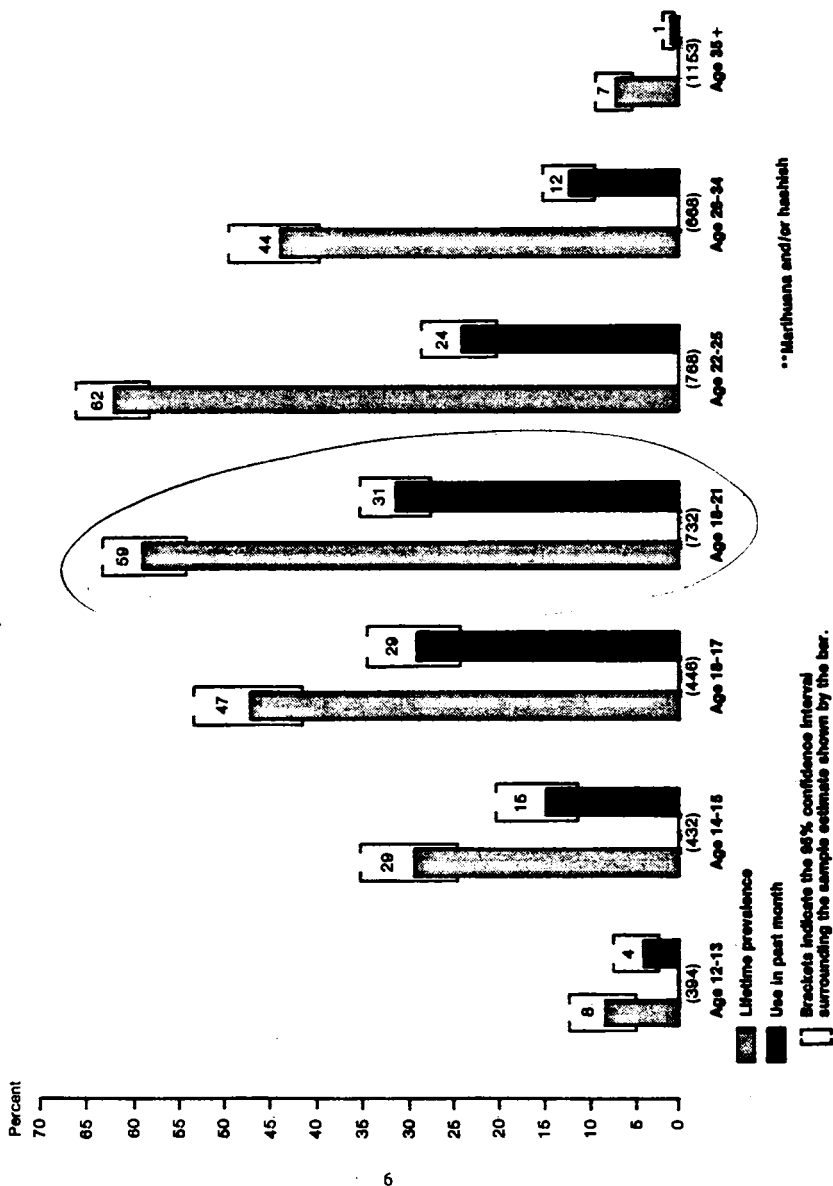
The National Survey on Drug Abuse provides a broad gauge picture of drug abuse in the American population. It is based on a survey of 3,094 persons randomly chosen to be representative of those living in households in the contiguous United States. While not completely representative of the American population (it also does not sample those living in various institutions, the homeless nor those living on military bases and overseas), it does provide a useful indication of the general dimensions of the drug problem in the United States and especially of trends in drug abuse since similar methodology has been employed in the five national surveys that have thus far been conducted under Federal aegis (1971, 1972, 1974, 1976, and 1977).

The past year has seen significant changes in marihuana use among the general population. This is in contrast to 1975-76, when few such changes were noted. The most notable 1977 changes were a 25% increase in the total number of those between ages 12 and 17 who had ever used marihuana, as compared to the year before, and a still larger increase in the number of 12-17 year olds currently using marihuana. (3) Nearly three out of ten (28.2 percent) of the 12-17 group reported some experience with marihuana in 1977, up from slightly over two in ten (22.5 percent) the previous year. A still larger increase was noted in the number of 12-17 year olds currently using marihuana (i.e., who had used in the month preceding the survey) in 1977 as compared to 1976. The percentage point increase of 3.7 percent (from 12.4 percent current users in 1976 to 16.1 percent) represents an increase in the number of youthful current users in the 12-17 age group of nearly 30 percent. Among those over 18, current use, again defined as use in the past month, did not increase significantly.

Young adulthood, that is the period between 18 and 25, continues to be the period of peak marihuana use, whether we are looking at the percentages who have ever used or at current use. Three out of five of the 18-25 year old group (60.1 percent) reported having used marihuana at some point in their lives prior to the 1977 National Survey, a significant increase from the slightly over half (52.9 percent) who reported such use in the 1976 survey. Over one in four 18-25 year olds had used marihuana in the month preceding the most recent survey, but the small increase noted (from 24.6 percent to 27.7 percent) was not statistically significant (i.e., it could well have been the result of minor fluctuations in statistical sampling from year to year).

As has been true throughout the past decade of increasing marihuana use, use is closely correlated with increasing age through the period of young adulthood. It drops precipitously in age groups over 35 (see figure A). This is true whether we are talking about those who have ever used the drug or about current use. For example, among children between ages 12 and 13, 8 percent have had some experience

FIGURE A
Marihuana Experience by Age: Lifetime Prevalence and Use in Past Month, 1977**



with marihuana, a figure which climbs to 29 percent for 14 and 15 year olds and to 47 percent for those ages 16 and 17. The 22 to 25 year old group reports the peak level of use--with 62 percent indicating ever having done so. The percentage having used drops to 44 percent in the 26-34 year old group and only 7 percent of those over 35 report any past use. Similar trends are to be found in current use (i.e., use in the month preceding the survey). While 4 percent of the 12 and 13 year olds report current use, the peak years for such use are between 18 and 21. Three out of ten (31 percent) of those between 18 and 21 were current users in the 1977 survey.

Although the percentages of females who had either tried marihuana or were currently using it have generally increased in the course of the five national surveys to date, female use has tended to lag behind that of males. Interestingly enough, among 12 to 17 year olds, the percentage of girls and boys who had ever used remained nearly equal in the three surveys conducted in 1971, 1972, and 1974. However, by 1976 the percentage of males who had used in this age group was significantly greater than that of females (26 percent for males and 19 percent for females). This past year a still greater difference in cannabis use by the two sexes developed in the 12-17 age group (33 percent lifetime male prevalence compared with 23 percent for females). While male use in the 12-17 group increased significantly between 1976 and 1977 female use did not. Among those over 18, by contrast, lifetime prevalence of male use in all five survey years has been consistently higher, about twice that of females up until this past year's survey (1977) in which the gap narrowed. The most recent survey indicates 30 percent of males over 18 have ever used marihuana as compared with 19 percent of females. However, the percentage of females over 18 who had ever used increased significantly between 1976 and 1977 while the male percentage did not. When one examines current use at the time of each of the surveys, generally similar trends are present--male use predominates by a ratio of about two to one among those over 18, while in the 12-17 year old group the difference is smaller. Half again more boys than girls ages 12-17 were currently using in 1977, unchanged from the 1976 findings.

Racial differences are of some interest although the broad statistical breakdown into "white" and "other races" categories precludes more detailed analysis. Among the 12 to 17 age group, white use for most of the five survey years has slightly exceeded use by other races whether we are talking about those who have ever used or about those currently using. In this past year, use by whites 12-17 significantly increased in both the "ever used" and "current use" categories (from 22 percent to 29 percent ever having used and from 12 percent to 17 percent for current use). Among those over 18 the percentages of whites and of other races who have ever tried marihuana are now nearly equal (24 percent of whites have ever used compared to 27 percent of other races) in contrast to previous years in which other races' use by the over 18 group tended to be greater than that of whites. Among current users in the 12 to 17 year age group whites consistently predominate over other races in all survey years (with the significant increase from 1976 to 1977 in white use already noted). Among those over 18, current use by whites and other

rates was approximately equal for all survey years including that of 1977 (8 percent of each group in the current survey).

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

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

If one takes the percentages of cannabis users noted in the 1977 survey and extrapolates to the general population, 43 million Americans had tried marihuana as of spring, 1977. About 16 million of them were currently using the drug (i.e., had used it in the month previous to the 1977 survey).

In addition to the national surveys of the general population, an important source of continuing information on drug attitudes and behavior is a nationwide longitudinal study of high school seniors which has been conducted for the past three consecutive years.(37) This study focuses on a pivotal point in the life of American youth, their final year in high school. It is a useful source of information on attitudes and beliefs about drugs in addition to providing data on personal drug use. Because of the large numbers employed, this survey is a particularly reliable source of information on trends in drug using behavior, which is sensitive to even small changes. Significant increases in marihuana use by high school seniors were found both between 1975 and 1976 as well as between 1976 and 1977. There were increases in current use (the 30 days preceding survey), in the percentage who had used in the past year and in the percentage who had ever used marihuana. Over half of the '76 and '77 seniors (52.8 and 56.4 percent respectively) reported having used marihuana; most of them had used it during the preceding year. About one in three seniors reported use in the month preceding the '76 and '77 surveys (32.2 and 35.4 percent respectively). One in eleven seniors reported daily marihuana use in '77 as compared to about one in twelve in '76 and about one in seventeen in 1975.

Although marihuana was the primary illicit drug used by these high school seniors, about a third (35.8 percent) reported having made non-medical use of such other illicit drugs as stimulants (23 percent), tranquilizers (18 percent), sedatives (17 percent), hallucinogens (14 percent), inhalants (11 percent), cocaine (11 percent),

and opiates other than heroin (10 percent). Less than one in fifty seniors reports ever having tried heroin. (See figure B) Use of these other illicit drugs is, however, far less common than the use of marihuana. One in two hundred or fewer seniors reported daily use of stimulants, the next most popular illicit drug to marihuana. Moreover, use levels of these other drugs have remained relatively constant over the past three years while marihuana use has significantly increased.

As in previous years, when comparisons are made between non-medical drug use and the use of such licit drugs as alcohol and tobacco, use of the latter significantly exceeds that of marihuana, the most popular of the illicit substances. Among the youngest (12 to 17) age group in the National Survey for example, nearly a third (31.2 percent) reported having drunk an alcoholic beverage in the month preceding the most recent survey as compared to about half that number (16.1 percent) who had used marihuana during the same period. About two-thirds of those 12-17 who had drunk an alcoholic beverage the previous month consumed beer; less than one in ten drinkers reported using hard liquor in the same period. Slightly more than one in five of the 12-17 group (22.3 percent) were current cigarette smokers. Among high school seniors, however, the percentage who had used cigarettes in the month preceding the survey only slightly exceeded the percentage who had used marihuana in a like period (38.4 percent reported cigarette use vs. 35.4 percent who reported marihuana use). It should, however, be emphasized that cigarettes were used much more frequently than was marihuana. Daily use of cigarettes (28.8 percent of '77 seniors) was more than three times that of marihuana.

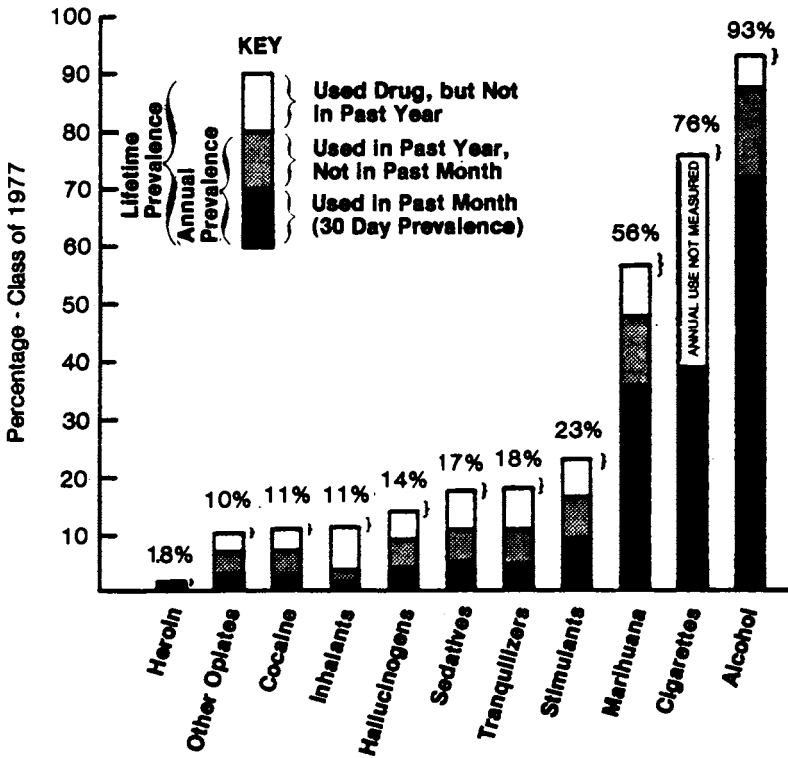
For all three consecutive senior classes, daily marihuana use was about twice as common among males versus females (8.1 percent male vs. 4.0 percent female in 1975; 10.8 vs. 5.0 percent in 1976 and 12.4 vs. 5.6 percent in 1977). However, at less frequent levels of use, the sexes are approximately equal.

There has been a significant trend toward initial use at increasingly younger ages. For example, while 16.9 percent of the Class of 1975 had used by the end of the ninth grade, the corresponding proportions in 1976 and 1977 were 22.3 percent and 25.2 percent. Finally, those seniors who were college bound were found to use less frequently than those who were not or who planned to go to college for less than four years.

Summary -- Nature and Extent of Marihuana Use

There has been a significant increase in both the number of 12 to 17 year olds who have ever used marihuana and who are currently using marihuana (up 25 percent from 1976 for lifetime use and 30 percent for current use)--nearly three in ten have ever used, one in six use currently. Among 18-25 year olds one in four uses currently; three out of five have ever used. Use is closely correlated with age--only seven percent of those over 35 have ever tried the drug. Male use, especially current use, predominates in all age groups. Among high school seniors nationwide, both lifetime use and current use increased

FIGURE B
Lifetime, Annual, and Thirty-Day Prevalence of Use,
(and Recency of Use) for Eleven Types of Drugs, Class of 1977



NOTE: The bracket near the top of a bar indicates the lower and upper limits of the 95% confidence interval.

between 1976 and 1977--over half have ever used, a third currently, one in eleven daily. Daily use is twice as common among males as among females; at less frequent levels the sexes are approximately equal in their use.

CURRENT ATTITUDES AND BELIEFS ABOUT MARIHUANA

As part of both the National Survey and the Survey of Drug Use Among American High School Students, questions were asked about their current drug attitudes and beliefs. While such attitudes and beliefs may, of course, change in response to new information and do not necessarily reflect objective reality, they are nevertheless of interest for the information they supply concerning the psychological context of use. To the extent respondents' drug use reflects their beliefs and attitudes toward drugs, their responses may also be of value in understanding present behavior and, perhaps, predicting future drug use.

Among both youth (12-17) and adults over 36, attitudes toward marihuana have become increasingly positive. However, in neither group is there majority support for making possession for personal use legal (39 percent of youth find that solution acceptable; 28 percent of older adults do). About three out of five youth and adults over 26 (62 percent of both groups) advocate continuing to keep possession, use and the sale of marihuana illegal. Nearly the same number would find stricter marihuana laws acceptable (59 percent of youth; 65 percent of adults 26 and over). However, when we turn to the attitudes of young adults in the peak marihuana using years from age 18 to 25, there is majority support for making possession for personal use legal (53 percent) or for having marihuana become a closely regulated product (57 percent would treat it similarly to alcohol). Among this young adult group there has been a fifty percent increase in the acceptability of marihuana as a regular commercial product (from 18 to 27 percent) in 1977 compared to the same age group in 1971. There has been a less marked, but still statistically significant increase in the percentage who regard as acceptable social policy making the possession of marihuana for personal use legal (up from 38 percent in 1971 to 53 percent in 1977). And, as one might expect, there has been a corresponding decrease in the percentage of 18 to 25 year olds who believe in keeping marihuana use illegal (from 49 percent in '71 to 40 percent in '77). Attitudes of those 26 and older have also shifted significantly toward a greater acceptance of some degree of legal use (such as treating possession for personal use as legal--up from 20 to 28 percent--or making marihuana a closely regulated product--up from 25 percent in '71 to 31 percent this past year). While there has been an increase in the percentage of adults 26 and over who find some degree of legalization of marihuana use acceptable, there has also been an increase in the percentage who feel possession, use and the sale of marihuana should continue to be illegal (up from 57 percent in 1971 to 62 percent in 1977). Although the percentage of this older age group which advocates still stricter marihuana laws has dropped (from 77 percent to 65 percent in 1971 and 1977 respectively) such an approach remains acceptable to two out of three adults in the over 26 group. Earlier

survey data indicates that as young adults assume more traditional adult roles marihuana use diminishes. It will be interesting to see if their attitudes toward others' use changes as those 18 to 25 years old now who have used marihuana in such large numbers enter the older age group.

When we turn to the question of what is regarded as an "ideal solution" to the problem of marihuana in our society, it is noteworthy that youth (12-17), young adults (18-25) and older adult groups (26+) all contain substantial proportions advocating either marihuana continue to be illegal or that our present laws be made still stricter. Seventy-four percent of youth and 79 percent of older adults take this tack. Even among the peak using 18-25 year old group, 40 percent support in about equal proportions the position that marihuana continue to be illegal (20 percent) or that ideally the laws be made still stricter (also 20 percent of the group).

The question of acceptability of "decriminalization," that is continuing to regard marihuana possession as illegal, but eliminating criminal penalties for its personal possession, was not specifically included in the National Survey although it would be subsumed under the category "having, using or selling marihuana is illegal." Other public opinion polling has, however, indicated that a majority of the population would favor the removal of criminal penalties for simple possession.

Respondents in the National Survey were also asked to indicate which of a list of drugs each regarded as "addictive," ("that is, anybody who uses it regularly becomes physically and psychologically dependent on it and can't get along without it."). Alcohol and heroin were classified as "addictive" by about four out of five or more respondents in the 12 to 17, the 18 to 25 and the over 26 age groups. Tobacco was also typically classified as "addictive" with the percentages so classifying it increasing with age (youth: 62.4 percent; young adults: 78.6 percent and older adults: 83.1 percent). Marihuana, by contrast, was classified as "addictive" by less than half of youth and young adults (47.3 percent and 43.7 percent respectively), but so classified by over three out of five (63.6 percent) older (26+) adults.

Despite the shift toward a more "permissive" attitude regarding marihuana use, it is noteworthy that in the national high school senior study two-thirds (65.5 percent) of the 1977 seniors disapprove of smoking marihuana regularly. A similar percentage disapprove of smoking a pack or more of cigarettes or of taking one or two alcoholic drinks (beer, wine, liquor) nearly every day. However, while the percentages disapproving of cigarette smoking or of drinking one or two drinks on a daily or nearly daily basis have not changed significantly in the past year, the percentage disapproving of regular marihuana use has dropped slightly but significantly (from 69.5 percent in '76 to 65.6 percent in '77). Moreover, there has been a significant and continued decrease in the percentages of seniors who disapprove of marihuana use on an experimental (once or twice) or occasional basis. Whereas nearly half (47 percent) of the 1975

seniors disapproved of even experimenting with marihuana, only a third of the Class of 1977 (33.4 percent) disapproved. The corresponding percentages of each of the classes disapproving of occasional use were 54.8 percent of the Class of '75, 47.8 percent of the Class of '76 and 44.3 percent of the Class of '77.

When we turn to the question of public policy on marihuana, about a third (34 percent) of the 1977 seniors believe marihuana use should be entirely legal. Another third (31 percent) feel "it should be a minor violation--like a parking ticket--but not a crime" (essentially decriminalized) and little more than one in five seniors (22 percent) feel "it should be a crime." The '77 seniors predict that they would not be markedly affected by marihuana's legalization and sale; about half (51 percent) indicated they would not use it even if it were legally available, approximately another quarter (27 percent) maintained they would use it about as often as they do now. About one in fourteen seniors (7 percent) indicates that his or her personal use would increase. A similar proportion say they do not know how they would respond to legalization. The percentages of seniors favoring treating marihuana use as a crime have steadily dropped over the past two years (30.5 percent in '75, 25.4 percent in '76 and 21.7 percent this past year) as have the percentages opposing legalized sale.

Although marihuana-related attitudes have clearly shifted, attitudes toward other drug use even on an occasional basis continue to be largely disapproving (examples: 96 percent of the Class of '77 disapprove of taking heroin even occasionally; 79.1 percent disapprove of even experimenting with cocaine; 83.9 percent disapprove of experimenting with LSD). With the exception of cocaine (for which there has also been a shift in the direction of smaller percentages disapproving of use), the attitudes toward the other major drugs of abuse have remained relatively stable over all three years studied ('75, '76 and '77).

Summary -- Current Attitudes and Beliefs About Marihuana

Although attitudes in the general population have become increasingly positive toward marihuana, the only age group in which there is majority support for making marihuana possession legal or marihuana a closely regulated product similar to alcohol, is the 18-25 year old peak using group. Less than half of those from 12 to 25 perceive marihuana as "addictive" although substantial majorities of all age groups so classify alcohol, tobacco and heroin. Among high school seniors, two-thirds of the Class of 1977 disapprove of smoking marihuana regularly, about the same number who disapprove of daily use of a pack or more of cigarettes or daily alcohol use. Few high school seniors (one in five) feel marihuana use should be a crime, a third believe it should be a minor violation, another third that use should be legal. Substantial majorities (four or more out of five) disapprove of even experimenting with such drugs as cocaine, LSD and heroin.

CHEMISTRY AND METABOLISM OF CANNABIS

The chemistry and metabolism of cannabis (i.e., the ways in which marihuana is broken down and transformed chemically by the body) despite their technical complexity are of considerable practical importance. Earlier reports in this series have repeatedly stressed the fact that marihuana is not a single chemical substance. While Δ -9-tetrahydrocannabinol (Δ -9-THC) is generally conceded to be the principal psychoactive ingredient in cannabis, other constituents may be important in modifying THC's effects in addition to having their own physiological actions.

Detection of marihuana in the human body is an important chemical problem with major legal and research implications. As marihuana has come to be more widely used, it is used increasingly while driving or under other conditions which may endanger the user and others. Because Δ -9-THC and other cannabis constituents are rapidly transformed into other chemical substances (metabolites) and because of the very small quantities involved, simple detection methods continue to pose a difficult problem.

In 1976, a major monograph on the progress made in developing detection methods was published by the National Institute on Drug Abuse (96). Work continues on the development of simple tests, analogous to blood alcohol determinations that might be useful at the site of accidents and in roadside determinations of possible marihuana intoxication. While there are now a variety of techniques suitable for detection, none is sufficiently simple or inexpensive to be practically useful for routine use. Even if such assays do become available, it is presently questionable how useful they will be for law enforcement purposes. For legal use in relation to charges of driving under the influence of marihuana it would be important that the levels of marihuana-related material detected be consistently related to impaired driving ability.

Chemical research has also emphasized synthesizing the various naturally occurring cannabis constituents, their biological transformation products (i.e., metabolites) and related chemical substances. The production of such chemically pure substances provides essential tools for determining possible effects of each constituent alone as well as in combination with other marihuana ingredients.

Availability of these synthetic materials in research quantities has accelerated research on marihuana detection in body fluids as well as other work on its pharmacological effects. By radioactively labelling some of the active substances involved, it is possible to trace their passage through the body. Availability of these constituents and related materials also has implications for assessing their potential therapeutic value. Since cannabis has some therapeutically undesirable side effects (e.g., accelerated heart action and an intoxication that is disturbing to some), it would be useful to find related drugs with the desired therapeutic effects (such as control of nausea for cancer patients or reduction of intraocular pressure in glaucoma), but free from undesired side effects. The

synthesis of chemically related substances may make this possible.

Some of the metabolites of marihuana are very active in themselves, making an understanding of them important to our knowledge of the parent substance. Additionally some constituents can block important drug metabolizing enzymes in the liver (i.e., block natural chemicals which play an essential role in metabolizing drugs or preventing the accumulation of potentially injurious substances). Such blocking might cause toxic reactions were marihuana to be ingested simultaneously with other drugs normally detoxified in the liver. It is, therefore, important to understand this aspect of marihuana's action.

Tests with dogs and rats have suggested that the major marihuana metabolites produced by the lung may be different from those produced by the liver (12, 94). Thus the effects of cannabis may be partly determined by the route of administration (e.g., smoking vs. eating). Similar differences have been reported in humans.

The identification of cannabis metabolites that remain in the body for days following marihuana use is an important development because they can then be synthesized and evaluated for possible toxicity (52).

The finding that there is an interaction between cannabidiol, a major marihuana constituent, and Δ -9-THC, marihuana's principal psychoactive ingredient, may ultimately shed light on the common belief among users that different varieties of cannabis with varying composition have different effects only partially related to THC level (54).

Summary -- Chemistry and Metabolism of Marihuana

Research is continuing on such problems as marihuana detection in the human body with emphasis on simpler techniques. Levels detected ultimately must be correlated with impaired performance to be most useful. While the principal psychoactive constituent (Δ -9-THC) is important, other cannabis ingredients or biological transformation products (metabolites) may be important in modifying the effects of marihuana or its possible toxic effects.

ANIMAL RESEARCH

A considerable amount of animal research on the effects of marihuana continues. Unlike humans, animals' genetic and learning histories can be accurately specified thus enabling the researcher to separate the drug's role from that of other aspects of life style and development. The shorter life span of animals permits the study of chronic effects over proportionately much longer periods of their lives. Drug dosages can also be employed that are much higher than would be ethically possible in humans. As in previous years, much of the animal work is primarily of interest to the research specialist; however, some of the behavioral findings are of more general importance.

Marihuana and related drugs have consistently been found to suppress aggression in animals when they are not under stress (1, 2). These findings concur with less systematic human observation suggesting

that marihuana is considerably less likely to facilitate the expression of aggression than is alcohol. With animals under stress, however, it has been found that marihuana tends to increase aggression. Whether similar results would be obtained with humans in stress situations is not known. Further research to better specify human implications of use under conditions of stress is obviously desirable.

Another important area of animal research concerns the possible long term chronic effects of marihuana. Two previously reported studies failed to find any residual effects of Δ -9-THC on learned behavior in chimpanzees following discontinuance of the drug after 150 days of use or after seven months of intermittent administration (18, 19). More recently, an impairment in maze learning was found following six months of heavy use (17). Because of the high doses, the relevance of these findings to human experience is questionable. The possibility that heavy doses of cannabis administered during pregnancy might impair learning in the offspring of rats has been raised by one animal study (93). Here, too, the relevance to human use is uncertain. In general, however, it should be emphasized, as it has been in previous editions of this report, that the use of cannabis by pregnant women is especially unwise since the implications of such use in humans have not been adequately explored.

A report of animal research in which a combination of a bacterial endotoxin and THC markedly increased the toxicity that might be expected from either substance alone or additively has led to some speculation that a similar effect injurious to human health might occur (6). However, the absence of any clinical or epidemiological evidence that there has been any increase in disease or debilitation of the type which might be expected were such an effect occurring in human users makes the clinical implications of this finding doubtful.

Summary -- Animal Research

Animal research, because it permits the use of higher drug doses over much longer periods of an animal's life span in an organism of known genetic and learning history, continues to be an important area of research emphasis. Work reported in last year's report indicating that marihuana in animals under stress tends to increase aggression, but reduces it under non-stressful conditions suggests that the relationship of marihuana to aggression may be more complex than originally thought. Research with high doses of marihuana suggesting possible learning impairments in the offspring of pregnant animals treated with the drug is of uncertain relevance to humans because of the high doses employed. Research reporting that THC given in combination with a bacterial endotoxin increased the toxicity much beyond what might ordinarily be expected has created speculation that similar effects might occur in humans. At present there is no clinical or epidemiological evidence that this in fact occurs.

HUMAN EFFECTS

Because many of the human effects of marihuana have been extensively described in prior editions of the Marihuana and Health Report as well as in other reviews of the literature, this brief report will be largely restricted to the developments of the past year. While the past year's research has extended our understanding in a number of areas, no new developments markedly altering our perspective have occurred. Use has increased sharply, particularly among youth, after a period of plateau. (Cf. Nature and Extent of Marihuana Use in the U. S., this volume.)

A report on the health aspects of marihuana by the American Medical Association's Council on Scientific Affairs was adopted by the parent organization in December, 1977 (72). It recommends the discouragement of marihuana use, especially by persons vulnerable to the drug's effect and in high risk situations; a modification of state laws to reduce the severity of penalties for possession of marihuana for personal use; and additional concentrated research to determine the consequences of long term marihuana use. Its conclusions regarding the scientific evidence are generally similar to those of the Sixth Marihuana and Health Report, and worth summarizing here.

(A) The nature and extent of marihuana use during the past five years has changed significantly; the typical material used tends to be more potent, is more often used regularly, rather than intermittently; and use is increasing, particularly among youth.

(B) For healthy users, intermittent ingestion rarely constitutes a health or social hazard; however, regular ingestion, or multiple drug use may well do so.

(C) For certain high risk persons, the hazards are potentially greater. These include children and adolescents, persons with physical illness, and persons with emotional problems or instabilities.

(D) There are nine current areas of health concern with regard to marihuana use. These are:

(1) pulmonary effects; chronic administration has been shown to impair lung function in otherwise healthy subjects,

(2) cardiac complications; thus far, apparently relevant only to the elderly, or persons with pre-existent cardiac disorders,

(3) psychopathology; ranging from flashbacks and panic reactions to cannabis psychosis. The latter has not been confirmed in the United States; milder sequelae seem variably to reflect the triggering of pre-existing or latent illness, concomitant phenomena that may have

led to use of the substance rather than be caused by the substance, or toxic effects of the substance,

(4) effects on the immune response system, which may lower resistance to disease. The data thus far is contradictory, with negative findings in some hospital studies using marihuana of known quality, and positive findings in others; several pre-clinical studies are positive, including one showing suppression of circulating antibodies in rats on doses equivalent to heavy human use,

(5) endocrine functioning; the major problem is evidence of decreased levels of testosterone and decreased sperm counts. The significance of these is yet to be evaluated; their major relevance may be in prepubescent or early adolescent boys,

(6) psychomotor impairment; there is clear-cut evidence for impairment of reaction time, motor coordination and visual perception which makes driving, flying and operating machinery dangerous under conditions of marihuana intoxication,

(7) genetic hazards; and

(8) brain damage have not been confirmed by studies attempting to replicate initial reports; though they have not yet been definitely excluded as possibilities,

(9) the amotivational syndrome; there is still uncertainty over whether chronic marihuana use causes or results from apathy, listlessness and associated personality difficulties.

Studies relevant to these areas of health concern, and a number of others, are summarized below.

Cardiovascular Effects

Although cardiovascular effects of marihuana have been investigated extensively, such research in humans has been largely restricted to healthy young male volunteers in whom the effects to date appear to be limited in duration and generally benign. One such study published this past year (68) examined the short range effects of smoking one to three marihuana cigarettes on 21 male experienced smokers participating in a 94 day in-hospital study of heavy marihuana smoking. They found, as have others (9, 76) a significant increase in heart rate after smoking although not as clearly dose related as previous findings. They attribute the lack of a clear dose relation to tolerance that developed for the cardiovascular effects of the drug as a result of chronic use. The changes they found in heart functioning were secondary to temporarily increased heart rate and appeared to be free of adverse consequences. As previous editions of

this report and the most recent American Medical Association report (72) emphasize, however, there is evidence (70) that in patients with already impaired heart function use of marihuana may precipitate chest pain (angina pectoris) more rapidly and following less effort than tobacco cigarettes. This possible difference in the response to marihuana in heart disease patients may prove to be of considerable practical significance if use expands to include older populations or if presently young adult users continue to use cannabis as they progress through middle life. Despite the limited evidence to date, a warning to heart patients and others who may have impaired cardiac function not to use marihuana seems justified.

The authors of a research paper dealing with the side effects of alcohol and marihuana (88) also caution that the use of the two drugs simultaneously may be dangerous for some individual with cardiac disorders. In a study of seven healthy male volunteers aged 20 to 29, they found that four of the seven developed intense nausea and vomiting when they smoked a marihuana cigarette after having consumed a moderate amount of alcohol. The doses of alcohol involved (1 gm. ethanol/kg. of body weight or about 57 cc. of pure alcohol for a man of average weight of 154 lbs.) represented about the equivalent of three drinks containing one and a half ounces each of 90 proof liquor. All four were markedly incapacitated during the height of the adverse effects with recovery occurring after three to four hours. The fact that not all seven subjects were equally affected illustrates that with marihuana alone or in combination (as with other drugs) there are marked individual differences in response. One subject, for example, experienced a marked drop in heart rate under the influence of the drug -- from 150 to 36 beats per minute. When the experiment was repeated with half the amount of alcohol originally used no adverse effects occurred. The authors comment that it was not easy to obtain information spontaneously about similar effects occurring under social conditions of use. Their volunteers only acknowledged such past effects of social use when later asked specifically about them. Given the frequency with which cannabis is used in association with alcohol, it would be desirable to further explore possible interactive effects.

Intravenous Use of Marihuana

In previous years there have been several reports of serious consequences ensuing from the intravenous injection of various crude extracts of marihuana or hashish (23, 31, 42, 43). Two more recent reports on a total of six young adult male patients in two different geographical areas report generally similar findings (16, 61). These include: rapid onset of nausea and vomiting, generalized pain, shaking, chills, fever, rapid heart rate and diarrhea. By contrast with laboratory studies using intravenous injection of pure THC (the principal psychoactive ingredient in cannabis), marked drops in blood pressure occurred. Cardiac symptoms indicative of temporary muscle injury were detectable by electrocardiographic techniques. While these symptoms all disappeared without apparent residual effects following week long hospitalizations, other reports in which fatalities have occurred (31, 66) illustrate the serious dangers of attempting

to inject extracts of cannabis. Fortunately, this mode of cannabis use is rare.

Pulmonary Effects

Because marihuana is typically smoked, possible adverse effects on the lung and pulmonary function have been a continuing concern. Earlier reports in this series have cited clinical and histological evidence that heavy marihuana and/or hashish use produces some effects similar to those of cigarette smoking (32). Residuals of smoked marihuana have been shown to be carcinogenic by skin tests (although not yet by smoking) in animals, and other previously discussed research on isolated lung tissue exposed to marihuana smoke (53) has suggested that tissue changes as serious or possibly more so than those found in heavy cigarette smokers may occur when cannabis is used chronically. While it has been argued that the less frequent use of smaller quantities of marihuana as compared to tobacco cigarettes might be expected to reduce this hazard, the custom of deep inhalation and the practice of consuming virtually all of each joint may more than offset this. Moreover, heavier, more frequent use of marihuana has become increasingly common. Very heavy marihuana smoking by healthy young male subjects under controlled experimental conditions has been demonstrated to cause mild but statistically significant airway obstruction (89a). Under conditions of ready availability there is evidence that the number of marihuana cigarettes consumed (up to ten "joints" daily) may approach that of tobacco cigarettes (13). Thus the suggestion in last year's report that heavier chronic use of marihuana could well lead to clinically important pulmonary changes similar to those found in heavy cigarette smokers continues to be justified.

Marihuana and the Immune Response

Because of the importance of the body's immune response in the preservation of health, reports of impairment of this vital function by marihuana must be carefully considered. This question still remains unresolved. Two research reports published subsequent to last year's report are, however, germane to the issue. In one of these (69), thirteen chronic (once a week or more for one year or more) male marihuana smokers from 22 to 26 years of age were compared to a sample of eight matched non-smokers. A comparison of T-lymphocyte functions, that is, of a white blood cell formation central to the immune response, was done. While it was found that marihuana smoking did affect T-cell function, the authors observe that "these effects are transitory, vary significantly from subject to subject, and are closely related to the time at which the samples (i.e., the blood samples tested) are obtained." They conclude that "If, in fact, the effects of marihuana smoking are deleterious to man, it would appear to us that the only way to determine this would be to identify a group of marihuana smokers who have demonstrated alterations in several T-cell functions and to follow them prospectively."

A second study of ten chronic (2x/wk. or more) marihuana smokers who smoked from 5 to 12 marihuana cigarettes under closed ward experimental conditions (15) found alteration in early T-cell rosette formation

although the total number of T-cells in peripheral blood remained unchanged. The authors report that a reduction in early rosette formation has been noted in patients with known reductions in immunity (patients with cancer, some infectious disorders and those receiving immunosuppressive treatment), however, they conclude that the clinical significance of their findings remains in doubt in the absence of clinical evidence of greater disease susceptibility in marijuana smokers.

Three reports based on work in two laboratories have reported reductions in the immune response in mice and rats treated with high, but humanly relevant doses of inhaled marijuana smoke or oral THC in one laboratory and injected with THC in another. In both there was a definite suppression of the animals' immune response (73, 98).

Taking the body of animal and human evidence as a whole, the results to date are far from clear cut in establishing whether or not the human immune response is impaired by marijuana use and if impaired, whether that impairment has practical significance.

Endocrine Functioning

The issue of a possible effect of marijuana on endocrine functioning was first raised as early as 1972 (89) when it was theoretically suggested that the chemical structure of delta-9-THC might lead it to act as a "false hormone" interfering with aspects of normal hormonal function. Experimental evidence that it caused some reduction (though still within normal limits) in serum testosterone, the principal male sex hormone, was first published in 1974 (47). Since then there have been several studies that have produced somewhat contradictory findings (48, 49, 11, 14, 59). There have also been two studies which were cited last year of a diminution in sperm count in otherwise normal young males correlated with their marijuana use and of alterations in the cellular characteristics of the sperm of chronic hashish users in Greece (30, 85). There have been several animal studies which have found reduced testicular weights and lowered levels of plasma testosterone resulting from the administration of relatively high doses of THC. A possible mechanism of action has been described based on recent animal research (24). Nevertheless, since a range of factors influence testosterone levels in men (e.g., variations depending on time of day assay is done and use of other drugs including alcohol) and since, even when reductions have been found, levels have remained within what are normal limits, their clinical significance may be limited to those with already impaired functioning or marginal fertility.

In 1972 an account was published of an increase in male breast development (gynecomastia) associated with chronic cannabis use (26). A subsequent animal study lent some support to these limited clinical observations when it was found that THC stimulated breast development in rats (27). A report published last year carefully matched eleven U.S. Army patients with gynecomastia of unknown origin with soldiers of similar age, race, military rank, length of time stationed in Europe and unit of military assignment (8). Both groups were interviewed under conditions of medical confidentiality. There was no evidence of any difference in history of cannabis use in the two groups. While

these findings do not rule out the possibility that those developing gynecomastia might have an unusual sensitivity to marihuana or to one or more of its constituents, they do suggest that the quantity of marihuana used in itself is not the critical difference and that marihuana may not be directly causal.

Chromosome Abnormalities

There is no new evidence to report in this area. While there were earlier reports of increases in chromosomal breaks and abnormalities in human cell cultures, more recent results have been inconclusive. The three positive studies in humans that have been reported (34, 51, 86) have decided limitations. All were retrospective -- i.e., studies of those who had already used marihuana as compared to non-users. Such variables as differences in life style, exposure to viral infections and possible use of other drugs, all known to affect chromosome integrity, could not be reliably assessed. In two of the studies, the aberrations observed were found only in a minority of the users.

Three other studies done prospectively (i.e., before and after use) have been reported (56, 57, 67). All were negative although they, too, can be faulted for a variety of reasons: most importantly, the subjects of all three had at least some prior experience with marihuana. It is possible that the baseline levels of chromosome deficits may have been elevated by earlier casual marihuana use, thus masking a drug-related effect.

A team investigating the effect of marihuana smoke on human lung cells in laboratory culture has found an increase in the number of cells containing an abnormal number of chromosomes (53). Another investigator who previously reported a high proportion of cells in marihuana smokers with reduced numbers of chromosomes has more recently reported that the addition of delta-9-THC (the principal psychoactive ingredient of marihuana) to human white blood cell cultures also resulted in an increased frequency of cells with abnormally low chromosome numbers (62). The implications of these findings continue to be uncertain.

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

Alterations in Cell Metabolism

The implications of laboratory findings on the inhibition of DNA, RNA, and protein synthesis (all of which are basically related to cellular reproduction and metabolism) are still unknown. Research discussed in last year's Report found that adding delta-9-THC to various types of human and animal cell cultures inhibited DNA, RNA and protein synthesis (5). This study detected no effect on DNA repair synthesis although the uptake of the chemical precursors within the cells was reduced by half.

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

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

Brain Damage Research

A British research report, which originally appeared in 1971, attributed brain atrophy to cannabis use in a group of young male users (7). It continues to be widely cited particularly in the mass media. In the original study, 10 patients, with histories of from 3-11 years of marihuana use, were examined by a neurological technique (air encephalography) used to detect gross brain changes. The authors concluded that their findings suggested that regular use of cannabis may produce brain atrophy. This research was faulted on several grounds: all of the patients had used other drugs, making the causal connection with marihuana use questionable; and the appropriateness of the comparison group and diagnostic technique was questionable. Although little new evidence has appeared, the potential seriousness of the original observations justifies a brief review of several subsequent studies bearing on the original British observations.

In a study of chronic Greek users (20), a different technique (echo-encephalography) was employed to determine whether brain atrophy might be present in heavy users. (Air encephalography was not used because the hazards of that technique were not ethically justifiable for purely research purposes.) The findings from the Greek study were negative; that is, users were not found to differ from non-users in evidence of gross brain pathology.

Two studies (discussed in detail in last year's Report) were subsequently conducted in Missouri and Massachusetts (10, 50). They examined two samples of young men with histories of heavy cannabis smoking using computerized transaxial tomography (CTT), a brain scanning technique for visualizing the anatomy of the brain. In both studies, the resulting brain scans were read by experienced neuroradiologists independent of the drug histories. In neither was there any evidence of cerebral atrophy. As was emphasized last year, several additional points should, however, be stressed. Neither study rules out the possibility that more subtle and lasting changes of brain function may occur as a result of heavy and continued marihuana smoking. It is entirely possible to have impairment of brain function from toxic or other causes that is not apparent on gross examination of the brain in the living organism. Nevertheless, virtually all studies completed

to date (late 1977) show no evidence of chronically impaired neuropsychologic test performance in humans at dose levels studies so far.

Last year the work was reported of a researcher who uses electrodes implanted deep within the brains of monkeys instead of more conventional scalp recording techniques to record brain electrical activity changes related to marihuana use. He has found persistent changes related to chronic use (29). More recently this same investigator has reported that rhesus monkeys trained to smoke a joint of marihuana five days per week for six months show persistent microscopic changes in brain cellular structure following this treatment (28). While both these experiments demonstrate the possibility that more subtle changes in brain functioning or structure may occur as a result of marihuana smoking at least in animals, the implications of these changes for subsequent human or animal behavior are at present unknown. As was reported last year, other studies, using more conventional EEG techniques to measure brain electrical activity, have found changes temporarily associated with acute use, but no evidence of persistently abnormal EEG findings related to chronic cannabis use (20, 46).

Chronic Users -- The Overseas Studies

Although there have been many studies of cannabis users overseas ranging as far back as those of the Indian Hemp Commission in 1893, virtually all of the earlier and much of the contemporary work suffers from multiple deficiencies making the interpretation of their findings difficult. Three studies conducted under Federal aegis in Jamaica, Greece and Costa Rica (11, 74, 84) have been widely discussed, often ignoring important limitations inherent in their design. Despite the extensive reporting and discussion of their findings, a brief review of the three once again placing them in perspective continues to be needed.

In each of the three studies considerable effort was made to match chronic users with non-users of similar background, lifestyle and social characteristics apart from drug use. Such user/non-user matching was rather carefully done in the Jamaican and Cost Rican studies; in the Greek study precise matching was less possible. All subjects were men because male use predominates in all three cultures. The elaborate testing procedures limited the total number studied. This is an important limitation since the limited sample size may have precluded detection of rarer consequences of cannabis use. For example, samples of similar sizes of matched cigarette smokers and non-smokers would probably not have detected some of the known serious consequences of cigarette smoking such as heightened susceptibility to heart disease, lung cancer and emphysema.

A wide range of tests and measurements was employed to detect physical or psychosocial consequences of use. Few differences were found that could be directly attributed to cannabis use. In the Greek study, the heavy hashish users examined showed significantly greater psychopathology. They were classified as having antisocial personality disorders more often than the matched non-users. It was not possible, however, to determine whether their personalities predisposed them to

heavy hashish use or whether use itself played some role in producing their psychopathology (83a).

Data on chromosomal assays collected in Jamaica are sometimes cited as indicating that cannabis use is without chromosomal effects. More accurately, the data must be regarded as inconclusive because of technical deficiencies in the methodology for that phase of the research.

While the overall results of these three studies are somewhat reassuring with regard to grossly adverse consequences of marihuana use, once again it should be emphasized that they by no means demonstrate that cannabis use is free of potentially adverse consequences. The small numbers studied, the possibility that cultural differences may have masked drug related performance differences and the differences in the demands of these less industrialized societies from those of our own, all make direct translation of the results to American conditions hazardous. Since adults with long experience in marihuana use were studied, none of the three projects is directly relevant to the implications of marihuana use by American adolescents at an earlier stage of development and under different social conditions. Use by children and younger adolescents in our culture is a source of concern because of their possible special vulnerability during a period of rapid growth and because use may interfere with necessary skill acquisition.

A retrospective study of an Egyptian prison population of cannabis users compared to non-users was discussed in last year's Report (80, 81). This work compared 850 chronic users with 839 non-cannabis using controls using a number of tests of psychological functioning. Users were reported to be slower in their psychomotor performance and to show impaired visual coordination and memory for designs. These performance deficiencies were found to be more common in younger, better educated users from urban backgrounds than in older, illiterate users from rural areas. This study was sharply criticized in an article published this past year for alleged sampling and psychometric deficiencies and equally sharply defended by its author (21, 82). Despite the apparent disagreement on many points, there was some agreement on the desirability of replicating the work and possibly doing further analysis of the original data. The large samples employed, despite some of the methodological deficiencies, might well make the original Egyptian study more sensitive to modest differences between smoker and non-smoker groups which smaller studies may well have missed. At present the information available does not permit a conclusive judgment of the adequacy of the study's findings particularly if the data were subjected to more elaborate analysis designed to take some of the criticisms levied against the study into account.

A study of chronic cannabis users in Northern India was recently published based on a comparison of 11 male users with eleven male non-users who were matched in terms of age, occupation and marital status (95). Users had all used cannabis equivalent to about 50 mg. THC per day (about the equivalent of 5 to 10 "joints" of typical 1 to 2 percent THC content marihuana) for five years or more. They were given physical examinations including various

laboratory tests of blood and urine as well as chest X-rays, electrocardiogram (EKG), and electroencephalogram (EEG). Subjects were also given a range of psychological tests of intelligence, memory and other intellectual functions sometimes impaired in the brain damaged.

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

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

American studies comparing college student users with non-users have found little in the way of evidence of intellectual performance decrement associated with cannabis use at least as such performance is measured by college grades. As was pointed out in previous reports, the higher levels of motivation of students in the schools studied, the rather modest levels of use compared with that overseas and the possibility that those whose performance was impaired by marihuana use had dropped out earlier, all limit broader interpretation of these more limited findings.

Psychopathology

Although this has been discussed in earlier editions and there is little new evidence in this area, a brief review may be useful. The most common adverse psychological reaction to marihuana use among American users is the acute panic anxiety reaction (25, 60). It represents an exaggeration of the more usual marihuana response in which the individual loses perspective (i.e., the realization that what she or he is experiencing is a transient drug induced distortion of reality) and becomes acutely anxious. This reaction appears to be

more common in relatively inexperienced users although unexpectedly higher doses of the drug can cause such a response in the more experienced as well. The symptoms generally respond to authoritative assurance and diminish in a few hours as the immediate effects of acute intoxication recede.

Transient mild paranoid feelings are common in users and it has been suggested that those who are characterized by more paranoid defense mechanisms are less likely to experience other acute adverse reactions (63). It has been repeatedly emphasized that reactions of users are very much influenced by the set and setting of use. Set refers to the pre-existing expectations the individual has regarding use; by setting is meant the physical environment during use. It is generally conceded that anxiety and mild paranoid reactions are more likely if the user is initially anxious about the experience and/or the circumstances of use are anxiety producing. Some additional research support for this clinical impression is found in a field survey which used a questionnaire to measure acute adverse drug reaction (65). Preliminary work has found that, in a college population, those who are more hypochondriacal, and who feel less in control of their own lives and more at the mercy of external events are more likely to have adverse reactions to marihuana and other psychoactive drugs (64).

An acute brain syndrome associated with cannabis intoxication including such features as clouding of mental processes, disorientation, confusion and marked memory impairment has been reported. It is thought to be dose-related (much more likely at unusually high doses) and to be determined more by the size of the dose than by pre-existing personality (60). This set of acute symptoms appears to be rare in the United States, possibly because very strong cannabis materials are less readily available here than in some overseas locations. Acute brain syndrome also diminishes as the toxic effects of the drug wear off.

Descriptions of a specific cannabis psychosis are to be found principally in the Eastern literature (25, 60) from cultures where use is typically more frequent and at much higher doses than those generally consumed in the United States. It continues to be difficult to interpret such reports because the diagnosis of mental illness is partly dependent upon socio-cultural factors. In addition, the diagnostic picture is frequently complicated by use of other drugs and earlier evidence of psychopathology not necessarily associated with drug use. While the overseas studies conducted under U. S. auspices in Jamaica, Greece and Costa Rica did not find such adverse consequences, the small size of the user samples studied, together with the probable rarity of the disorder, would have made its detection unlikely.

One clinical study in India has contrasted the features of a paranoid psychosis arising in the course of long term cannabis use with that of paranoid schizophrenia. Twenty-five consecutive patients admitted with each diagnosis were compared. The cannabis users, reportedly, had used the drug for five or more years in amounts up to several grams per day in gradually increasing quantities. Those diagnosed as having a cannabis psychosis were characterized by the

authors as showing more bizarre behavior, more violence and panic, an absence of schizophrenic thinking and greater insight into their illness. Patients with the cannabis-related disorder recovered rapidly upon being hospitalized and being treated with a major tranquilizer (90).

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

Some further indication of this is to be found in a paper reporting on four cases of well documented schizophrenia in which the use of marihuana is believed to have led to an exacerbation of psychotic symptoms in patients whose psychoses were in at least partial remission prior to use. The author concludes that "While marihuana can perhaps be safely used by many persons, this is not so with the schizophrenic." He urges that schizophrenics be alerted to the special hazards he feels marihuana poses for them in the same way other patients would routinely be alerted to possible hazardous interactions between their illness and substances they might use (92).

In a detailed review of the relationship between cannabis and violence (2) the author concludes that while marihuana probably does not precipitate violent behavior in the majority of users, nevertheless there may be some individuals with a prior history of poor impulse control or special circumstances of stress which combined with preexisting personality may make use inadvisable. It is not clear, however, he points out, whether it is specifically marihuana which might have the undesirable effect of releasing violence or any of a variety of other drugs including alcohol.

Based on his experience with some five thousand drug-related psychoses encountered while medical director of many youth festivals, the author of a recent paper has summarized his clinical experience including that with marihuana users (4). While agreeing with others about marihuana's relative safety, he offers several sources of concern about its widespread and indiscriminate use. Specifically, he feels that the possibly unexpectedly high potency of some of the cannabis preparations may pose a hazard for those used to weaker materials. Although he believes it to be very rare, he believes that it is possible to have a psychotic reaction to marihuana. He also believes that persistent psychiatric symptoms after psychotic drug experiences are commoner than is generally believed, as many as 5 to 10 percent of those cases which he was able to follow up. While some patients reporting "flashbacks" had their initial "bad trip" on drugs other than marihuana, the flashback re-creation of the disturbing aspects of the original experience frequently occurred following alcohol or marihuana use. He concludes by advising that "Those with a history of emotional disturbances and especially 'bad trips' (i.e., previous drug precipitated emotional disturbances) should avoid intoxicants including alcohol and marihuana." Finally, this author advises that present emergency room and psychiatric hospital procedures should be altered to

make the situation less judgmental, less frightening and coercive, more compassionate and more acceptable to youth, the surroundings more homelike and reassuring.

Marihuana flashbacks--spontaneous recurrences of feelings and perceptions similar to those produced by the drug itself--have been reported. A survey of U.S. Army users discussed last year found that flashbacks occurred in both frequent and infrequent users and were not necessarily related to a history of LSD use. Such experiences may range from the quite vivid re-creation of a drug related experience to a mild evocation of a previous experience. The origin of such experiences is uncertain but those who have experienced them appear to typically require little or no treatment (83).

One source of information about possible adverse reactions to drugs, including marihuana, is the Federally sponsored Drug Abuse Warning Network (DAWN). This is a nationwide reporting system which provides information about the frequency with which various drugs in common use are implicated in patient or client contacts with such facilities as hospital emergency rooms and crisis centers. (A crisis center is a facility established to provide "walk in" or "phone in" assistance to those experiencing personal crises, including adverse drug reactions.) Of 121,000 emergency room episodes involving some form of drug abuse between May 1976 and April 1977, marihuana ranked 13th among the drugs mentioned. But in crisis center contacts, marihuana ranked third following alcohol and heroin as the drug involved. While the interpretation of such figures is made more difficult by ignorance of how the number seeking assistance compares to the total number using a drug during the reference period, it does indicate that marihuana is not an uncommon factor in individuals seeking help.

Complex Psychomotor Performance in Driving and Flying

While there have been no major recent studies, there is now good evidence that marihuana use at typical social levels definitely impairs driving ability and related skills. Studies indicating impairment of driving skills include: laboratory assessment of driving related skills, driver simulator studies, test course performance, actual street driver performance and, as reported last year, a study conducted for the National Highway Traffic Safety Administration of drivers involved in fatal accidents (87).

Despite their commonly expressed belief that their driving skills are impaired by cannabis intoxication, there is reason for believing that more marihuana users drive today while "high" than was true in the past (91).

As use becomes increasingly common and socially acceptable and as the risk of arrest for simple possession decreases, still more users are likely to risk driving while high. In limited surveys, from 60 percent to 80 percent of marihuana users questioned indicated that they sometimes drive while high (44, 45, 78).

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

A study reported last year of drivers involved in fatal accidents in the greater Boston area was conducted by the Boston University Accident Investigation Team. They found that marihuana smokers were overrepresented in fatal highway accidents as compared to a control group of non-smokers of similar age and sex (87).

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

The parameters of impairment for the average driver under various dosages of marihuana can not yet be adequately specified. It is important to develop reliable standards for what constitutes driving under the influence of cannabis so as to encourage more responsible use. At present it is clearly desirable to discourage driving while marihuana intoxicated.

In the interim since publication of the 6th Marihuana and Health report a research monograph summarizing what is presently known about the effects of drugs, including marihuana, on driving and related psychomotor performance has been published by the National Institute on Drug Abuse (96a).

While there have been no recent studies, research thus far indicates that even experienced pilots undergo marked deterioration in performance under flight simulator test conditions while high (35, 36, 58, 97). Thus, flying an aircraft while marihuana intoxicated is clearly dangerous.

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

Combined Use of Marihuana and Other Drugs

The amount of data on the simultaneous use of marihuana and other drugs and their possible combined effects is modest. Based on data from the National Survey and from a study of the drug using habits of 20 to 30 year old males, one investigator has reported that nearly half (46 percent) of regular marihuana users combine its use with that of alcohol (68). This same researcher found that among those who had combined alcohol use with the use of another drug in the 20 to 30 year old male group, four out of five had used marihuana and alcohol in combination.

The combined use of marihuana and alcohol may result in greater skilled performance decrement than the use of either in similar amounts by itself. Given the likelihood that such combined use of marihuana and of other drugs, particularly alcohol, will continue and quite probably increase, it would be desirable to better specify the consequences of such use at least for some high probability combinations and doses particularly in relation to driving and other significant psychomotor performance.

Tolerance and Dependence

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

Several more detailed reviews of tolerance development to the behavioral and physiological effects of marihuana in both animals and humans have been published in recent months (22, 39, 40). A report detailing tolerance development of 30 young adult subjects in a 94 day closed experimental ward environment has also been published which stresses tolerance to both the effects on heart rate and the subjective "high" (68). The practical implications of this work are that experienced, frequent users of marihuana experience less pronounced physiological and psychological changes at a constant level of use than would less experienced users. This is in some contrast with the original impression that users had a "reverse tolerance" -- i.e., a greater sensitivity to marihuana upon repeated use. The latter impression probably derived from the relatively low dose, infrequent use that characterized some of the earlier observations. Under those conditions neophyte users may have become more aware of marihuana's subjective effects with repeated use partly as a result of social learning of what was to be expected from the experience and thus subjectively believed that its effects were enhanced. Since marihuana's metabolites (the transformation products which result as marihuana is metabolized) are also persistent in body fat, it is also possible that repeated low dosage use released some of the previously stored material enhancing the effects. Whatever the ultimate explanation of these earlier impressions, under conditions of heavier, more regular use, tolerance now appears to be well established.

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

ness, decreased appetite, sleep disturbance, sweating, tremor, nausea, vomiting and diarrhea (38, 39). Some of these symptoms were experienced in a similar research study by users who selected their own smoked marihuana doses (59). Such a "withdrawal syndrome" is, however, uncommon and has rarely been reported clinically. Only one research report, from Germany, has noted it (41).

Summary -- Human Effects

Overall there have been few new developments in the past year. The increase noted in use in the 12 to 17 year old age group is a source of special concern because they may be especially sensitive in that stage of development to disruptive psychological and physiological effects of use. A late 1977 Report from the American Medical Association on the health implications of use underscores similar concerns to those noted in this and previous Marihuana and Health reports. These include: possible pulmonary and cardiovascular effects, uncertainty regarding possible effects on the body's principal defense against disease, the immune response, possible decreases in testosterone levels and sperm counts in males which may have clinical implications for young males and the marginally fertile, and psychomotor impairments produced by marihuana intoxication which make driving and other complex motor and perceptual performance hazardous, and possible psychological implications of heavy use. While evidence of adverse cardiovascular effects has not been detected in healthy young males, there is some evidence that use has adverse effects in precipitating chest pain (angina pectoris) in patients with impaired heart function. Additional evidence has appeared stressing the fact that intravenous use of marihuana, fortunately uncommon, can have serious effects including the possibility of death (probably not because of marihuana constituents per se, but as a result of injecting non-sterile particulate matter. Evidence from previous years as well as more recent data suggest that marihuana use, particularly heavy use, is likely to interfere with pulmonary function. Unfortunately, the extent of the added risk is not presently known. While additional animal and human evidence has appeared concerning possible impairment of the immune response, findings are not clear-cut and the clinical implications of such research remain in doubt. The implications of possible alterations in testosterone levels are uncertain. When found, these changes have still been within normal limits of variation. Although the possibility of chromosomal abnormalities related to marihuana use has been previously raised, research findings have been inconsistent and there continues to be no convincing evidence that marihuana causes clinically significant chromosome damage. The limitations of the overseas studies of chronic users are discussed, viz., small numbers of subjects which might have missed rarer adverse consequences of use, cultural differences, irrelevance to adolescent and young adult use, etc. Other foreign studies in Egypt and India have suggested some impairment in intellectual and psychomotor performance in chronic users, but they can be faulted on several grounds casting the findings in some doubt. Adverse psychological consequences related to American patterns of use continue to

be relatively uncommon but appear more likely in individuals with pre-existing serious pathology and in response to unexpectedly potent materials. A cannabis psychosis has been discussed in the foreign literature, but if it occurs, it is apparently rare under conditions of American use. There is good evidence that marihuana intoxication impairs psychomotor performance and that driving, piloting an aircraft or operating potentially hazardous machinery are all ill advised while marihuana intoxicated. Use of marihuana in combination with alcohol and other drugs may pose greater hazards than the use of either alone. Finally, as indicated in previous years, tolerance--a diminished response to a given repeated dose of marihuana--has now been demonstrated as have withdrawal symptoms following repeated administration in humans of unusually high doses atypical of social marihuana use in the United States.

① THERAPEUTIC ASPECTS

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

While there have been few new applications reported in the past year, work has continued on a number of applications that were reported as promising in previous years.

One of the most promising applications has been the use of marihuana or THC as an antiemetic agent for cancer patients receiving chemotherapy (75). Unfortunately, one of the undesirable side effects of these powerful chemotherapeutic drugs is that they often produce pronounced nausea and vomiting which may cause continued weight loss in the patient or the patient to discontinue treatment because of the ensuing distress. Since most of the available antiemetics are often unsuccessful in controlling these symptoms, a new drug would be of considerable value. At present a major research project under Federal aegis is underway to determine more definitely whether marihuana is useful for this purpose and under what circumstances.

Another area in which marihuana has potential value is in the treatment of glaucoma, a major cause of blindness. This use is based on an earlier observation that in normals marihuana use reduces intraocular pressure (33). Since mounting intraocular pressure ultimately can destroy the retina in glaucoma patients, the drug was tried on an experimental basis with a small group of such patients with some success. An eye drop preparation has now been developed and has undergone preliminary trials in animals with subsequent human research planned.

A third area of potential therapeutic usefulness is in the treatment of asthmatic patients. Although marihuana smoke has a lung irritant effect, it also results in a temporary increase in the size of air conducting passages (i.e., functions as a bronchodilator). The dilatation produced is desirable in asthmatics since it relieves their symptoms. Despite this desirable property, marihuana or THC has a formidable array of undesirable side effects. However, as several of the pioneer investigators in this area have recently pointed out (77) the drug has some equally significant potential advantages over currently available preparations. Its mode of action is different from that of other drugs with similar therapeutic effects which means it may work when they cannot be used. As pharmaceutical agents, marihuana and its derivatives have unusually low toxicity. As a result it is unusually safe for medical use. Finally, it is quite possible that one or more of marihuana's ingredients or some synthesized variant on them may preserve its desired bronchodilating property free of the undesired side effects of the natural material. Indeed, there is preliminary evidence that that may be true of some of the compounds now being explored (77).

A still highly speculative therapeutic use of marihuana derivatives is their possible value as tumor growth inhibitors. To date it should again be emphasized that there is no evidence that marihuana or any related material has therapeutic usefulness in inhibiting tumor cancer growth. However, work on the mechanism of action of THC and related synthesized materials in inhibiting cell growth under laboratory conditions is continuing.

Although the use of cannabis or its derivatives as analgesics has not thus far proven too promising, at least one study of the past year suggests that a synthetic chemically related substance to THC may have potential value as an analgesic possibly free of the abuse and dependence liability of more traditional potent analgesics (71). This work must be regarded as quite preliminary.

Despite some promise that marihuana and/or its synthesized constituents have shown as potential therapeutic agents, it should again be emphasized that much additional work is necessary before such agents become generally approved as standard medications.

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

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

pharmaceuticals showing initial promise are ultimately discarded as unanticipated drawbacks and limitations in their use arise.

Summary -- Therapeutic Aspects

While there have been few new developments of significance since last year in the therapeutic application of marihuana or its derivatives, it continues to show promise as an antiemetic with cancer patients experiencing nausea from chemotherapy, in the treatment of glaucoma and for other possible purposes as well. A major well controlled study of marihuana's antiemetic properties with cancer patients is currently underway and an eyedrop dosage form of THC for use with glaucoma patients has undergone preliminary work in animals. Because of its different mode of action from other bronchodilators used in the treatment of asthma, THC may also be useful in that context. Other therapeutic applications appear more tenuous at this time. Materials that are ultimately used therapeutically may represent synthesized variants on one or another of marihuana's ingredients chosen to retain the therapeutic benefits while minimizing other undesirable side effects.

FUTURE DIRECTIONS

Cannabis research has made significant strides since the inception of the Federal priority emphasis. This began in the late 1960's with our emerging concern with the rapid increase in marihuana use among youth. Our understanding of the basic chemistry of the substance, its mode of action in the body and some of the acute and chronic implications of American use patterns have all been greatly expanded. Based on the limited evidence to date, some have argued that there is little hazard to use, especially as compared to the better known hazards of such widely accepted drugs as alcohol and tobacco. Others, more mindful of the fact that it often requires many person-years of use of a drug for its true use implications to become understood, are more thoughtfully cautious. As has been pointed out in previous editions, American use has been most heavily concentrated in the healthiest segment of our population, young adults between 18 and 25. Even in this group, typical use remains infrequent and limited to relatively small quantities of the drug, as compared to countries in which use has been widespread for many decades. Comparatively little is known about the potentially disruptive effects of regular marihuana use on children and younger adolescents, a group that may be especially vulnerable because of undergoing rapid physical and psychological growth and development. It is also worth reminding ourselves that widespread use among even young Americans is little more than a decade old.

Despite the emphasis that marihuana research has received, our knowledge remains incomplete. The reasons for this are many. Because there are marked species differences in cannabis effects, animal models are in some respects less useful with this drug than they are with some other substances. For example, while marihuana produces a dose-related increase in heart rate in humans, in most animal species heart action is slowed. And because it is characteristically

smoked in America, for many purposes this would be the preferred mode of administration in animal testing. Yet animal experiments in which the animals smoke in a manner resembling humans are much more difficult to create than other, more traditional modes of pharmacological administration.

Even when cannabis is studied in cultures with more traditional use, as has been pointed out, such cultures differ significantly from our own in many ways as do the patterns of cannabis use in them. Our own use patterns are decidedly changing. Not only has use overall markedly increased over the past decade, so have the numbers who are using on a daily basis, alone and in conjunction with other drugs. While marihuana use was once clearly deviant behavior indulged in by a small minority, it has now achieved some measure of majority acceptability among young people. With this increase in social acceptability has come a diffusion of use to both younger and older groups in which use may have quite different implications than the more limited use of the '60s. It should also be emphasized that "street" marihuana varies from inert, or nearly so, to relatively high potency materials of highly variable composition as compared to the standardized materials used in laboratory experimentation.

As part of a continuing effort to modify and improve the Federal cannabis research program, the National Institute on Drug Abuse created a task force of non-government experts to consider the research evidence and to make substantive recommendations on future research directions. In May 1977, the work of this task force culminated in a report reviewing methodological and conceptual considerations in marihuana research and making substantive recommendations for future directions (79).

One of the central questions considered by this group was the advisability of initiating a single, very large, long-term longitudinal study of the effects of marihuana analogous to some of the studies that have been done on cigarette smoking. For a variety of reasons (e.g., the relatively low level of use in any general population sample, even one confined to users in the age range 18-25 and the high cost relative to the likely research "pay off"), the task force concluded that a number of more limited studies of a diversity of smaller populations would be more cost effective.

Among the specific recommendations of this expert advisory group with a brief discussion of their rationale are the following:

- a. Emphasize studies of pulmonary effects, transient, and enduring central nervous system effects, effects on psychosocial and physical development and on participation in adult social roles, susceptibility to infection and disease (among users) and the effects of use on individuals with pre-existing disease states.

All of these are areas in which there is some evidence or theoretical basis for concern about marihuana's effects.

- b. Emphasize wide ranging exploratory studies. This recommendation is based on the present limitations of our knowledge regarding the enduring effects of cannabis. By diversifying our approach, the advantages and disadvantages of various research strategies can be to some extent balanced, increasing the likelihood of more useful research findings.
- c. Emphasize the study of long term, heavy marihuana use. Since it is likely the effects of marihuana, like those of other drugs, are dose-related, adverse effects are most likely to be found by studying relatively long term heavy users.
- d. Emphasize periods of maximum sensitivity. The task force consensus was that the individual is most likely to be adversely affected by marihuana use during such stages of rapid growth and change as fetal development, late childhood and adolescence. Therefore, research priority should be given to study of use during those stages of presumed maximum sensitivity.
- e. Take advantage of cost-effective opportunities to supplement existing data bases. A number of health care delivery systems (health maintenance organizations providing group medical care and the military are examples), other existing studies of child health and development and various ongoing research studies have potential for collecting data on marihuana use and its possible effects. Utilization of these sources wherever possible may well permit the accumulation of highly useful information quickly and economically.

Other recommendations of the task force concerned specific technical matters such as the desirability of developing a standardized pool of questionnaire items for assessing marihuana effects and providing a mechanism for continued input by experts in the field concerning long range marihuana planning.

A start has been made on carrying out these recommendations through solicitation of grant applications to carry out high priority research and developing access to suitable study populations. More active implementation is being planned for next fiscal year, when additional funds are programmed for these projects.

It is again worth emphasizing that many of the important, outstanding questions about marihuana are not likely to be easily answered in the immediate future. Indeed, many of them may require many years before they are satisfactorily answered. While laboratory experimentation with animals and humans can provide important data on marihuana's acute and chronic effects and study of chronically using overseas populations can be helpful, it is probably only through study of a diversity of age groups under a variety of actual use conditions here in the United States that we will be able to accurately gauge present

and future implications of American cannabis use. The fact that marihuana is now the third most frequently used psychoactive substance (next to alcohol and tobacco) makes it imperative that its public health implications be adequately explored and the problems it may produce anticipated. Our present program of research has that objective.

Summary -- Future Directions

Despite significant advances in our knowledge of the health implications of marihuana use, much remains to be learned especially about the implications of chronic use and the possible effects on users who may be especially vulnerable to its effects (e.g., children and younger adolescents). A report from a task force of non-government experts in marihuana research, advisory to the National Institute on Drug Abuse, recommended several directions for future research, viz. emphasize studies in such areas as pulmonary effects, effects on psychosocial and physical development, especially of younger users, emphasize research on long term chronic use and on such periods of potential maximum sensitivity to marihuana's effects as fetal development, late childhood and early adolescence. The Task Force also recommended that existing data bases such as health maintenance organizations be used where appropriate as a means of developing data on large numbers of users on a highly cost-effective basis. Plans for actively carrying out the Task Force's recommendations are underway.

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DHEW Publication No. (ADM) 79-700

Printed 1979

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Public Health Service

ALCOHOL, DRUG ABUSE, AND MENTAL HEALTH ADMINISTRATION

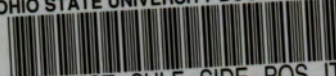


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