DOCUMENT RESUME

ED 216 264 CG 015 878

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TITLE Marijuana and Health. Eighth Annual Report to the U.S. Congress from the Secretary of Health and Human Services 1980.
INSTITUTION National Inst. on Drug Abuse (DHHS/PHS), Rockville, Md.
REPORT NO DHHS-ADM-81-945
PUB DATE 80
NOTE 56p.; For related documents, see ED 123 224, ED 120 624, and ED 138 553.
AVAILABLE FROM Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402.

EDRS PRICE MF01/PC03 Plus Postage.
DESCRIPTORS Attitude Measures; *Drug Abuse; *Drug Education; *Drug Therapy; *Marihuana; Physical Health; *Physiology; Psychopathology; *Public Health; State of the Art Reviews; Trend Analysis

ABSTRACT

This edition, the eighth in the series of annual reports, is a nontechnical summary of recent developments in marihuana research with a summary of research through the end of 1979 concerning possible health implications, which cannot be reported with great certainty because of the brief duration of the American marihuana experience. Areas of discussion include: (1) the possible effects on reproduction and pulmonary function; (2) the nature and extent of marihuana use and its chemistry; (3) acute effects on memory and intellectual tasks including driving; (4) long-term effects; (5) psychopathological effects; (6) therapeutic uses in treating cancer chemo-therapy patients; (7) the effects of marihuana in combination with alcohol and other drugs; and (8) the hazards of marihuana as a recreational drug. Future research directions and a references section are also included. (JAC)

MARIJUANA AND HEALTH

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

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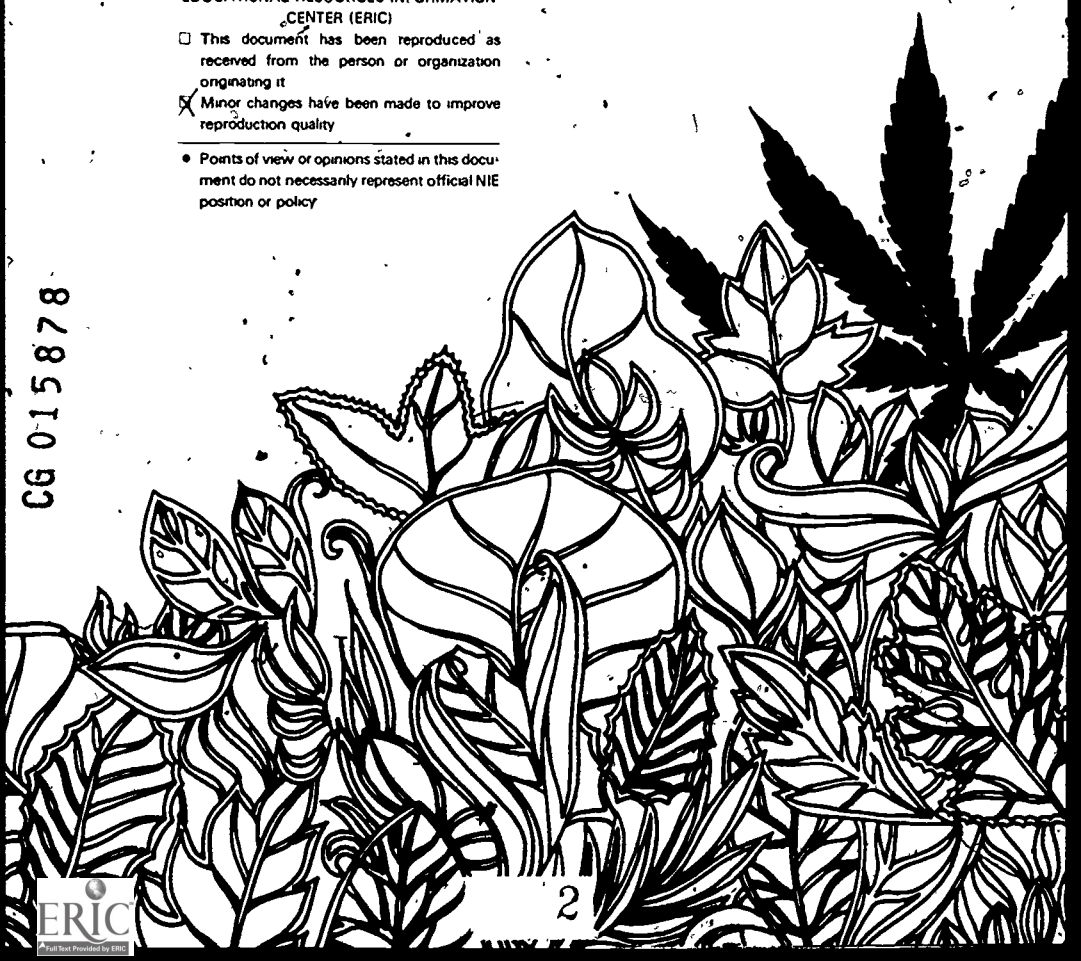

ACKNOWLEDGMENTS

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

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

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

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

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

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Washington, D.C. 20402

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EXECUTIVE SUMMARY

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

Nature and Extent of Use

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

Chemistry

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

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

Acute Effects

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

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

Long Term Effects

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

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

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

Psychopathological Effects

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

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

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

Therapeutic Uses

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

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

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

INTRODUCTION

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

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

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

NATURE AND EXTENT OF MARIJUANA USE IN THE UNITED STATES

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

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

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

*see ADDENDUM, pages 37-38

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

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

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

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

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

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

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

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

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

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

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

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

Summary--Nature and Extent of Marijuana Use

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

Current Attitudes and Beliefs About Marijuana

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

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

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

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

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

HUMAN EFFECTS

Chemistry and Metabolism of Cannabis

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

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

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

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

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

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

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

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

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

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

Acute Effects of Marijuana

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

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

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

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

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

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

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

Acute Marijuana Intoxication and Complex Psychomotor Performance in Driving and Flying

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

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

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

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

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

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

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

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

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

Pulmonary Effects

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

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

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

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

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

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

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

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

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

Reproductive Effects of Marijuana

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

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

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

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

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

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

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

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

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

Cardiovascular Effects

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

Marijuana and the Immune Response

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

Chromosome Abnormalities

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

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

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

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

Alterations in Cell Metabolism

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

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

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

Brain Damage Research

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

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

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

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

A researcher who used electrodes implanted deep within the brains of monkeys instead of more conventional scalp recording techniques has found persistent changes related to chronic use (72). This same investigator has reported that rhesus monkeys administered marijuana smoke from one joint daily for five days per week for six months show persistent microscopic changes in brain cellular structure following this treatment (73). While both these experiments demonstrate the possibility that more subtle changes in brain functioning or structure may occur as a result of marijuana smoking in animals, the implications of these changes for subsequent human or animal behavior are at present unknown. Other studies, using more conventional EEG techniques to measure brain electrical activity, have found changes temporarily associated with acute use, but no evidence of persistently abnormal EEG findings related to chronic cannabis use (74,75).

Psychopathology

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Effects of Chronic Use on Intellectual Functioning

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

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

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

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

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

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

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

Tolerance and Dependence

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

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

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

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

THERAPEUTIC ASPECTS

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

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

Control of Nausea in Cancer Chemotherapy

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

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

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

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

Glaucoma

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

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

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

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

Other Therapeutic Uses

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

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

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

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

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

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

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

EFFECTS OF MARIJUANA IN COMBINATION WITH ALCOHOL AND OTHER DRUGS

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

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

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

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

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

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

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

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

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

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

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

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

THE HAZARDS OF MARIJUANA VERSUS OTHER RECREATIONAL DRUGS

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

Any consideration of the hazard a drug poses must take into account not only its present use, but also use that might be reasonably expected in the future. At present, this involves many imponderables such as the parameters of risk for various groups in our society at different levels of use, the likely circumstances of use, effects on user functioning and motivation of heavier use patterns, degree of use restriction possible, combined use with other drugs--to name but a few. As the history of the introduction of alcohol demonstrates, it is very difficult to anticipate the problems which will arise in a given society in advance. Thus, any attempt to compare the health impact of marijuana with that of alcohol and tobacco at current levels of use is certain to minimize the hazards of marijuana. But any comparison at levels of anticipated use involves many assumptions that are at best dubious and at worst may be dangerouly misleading. Such a comparison seems, therefore, useless and undesirable until such time as the parameters of risk are better specified than they can be at present.

FUTURE DIRECTIONS

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

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

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

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

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

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

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

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

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

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

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

ADDENDUM

The 1979 National Survey--A Marijuana Use Update

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

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

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

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

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

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

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