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The National Institute of Mental Health is continuing support of several studies designed to measure trends in the use of hallucinogens. Indications are that the evidence for persisting psychological and birth defect damage from chronic LSD use is minimal. Though they are a continuing problem, admissions to psychiatric units of persons with "bad trips" are declining. About five percent of those college students polled admitted using LSD. While a minority of these users suffer severe psychiatric problems from drug abuse, there is a decline in admissions to college health services of students with LSD reactions. Marihuana use among students is, on the other hand, on the rise. Of immediate concern is the potential effect of any reality-distorting agent on the future psychological development of the adolescent user. To understand the problem of drug abuse, it is necessary to look beyond specific agents to the underlying causes of students reliance on drugs. Today's alienated youth reject society and its institutions as being irrelevant and seek to alter their own world through drug use. Such societal rejection makes urgent the development of new approaches to bridge the generation gap. (CJ)

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STATEMENT

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BEFORE THE

SUBCOMMITTEE ON JUVENILE DELINQUENCY

OF THE

COMMITTEE ON THE JUDICIARY, U.S. SENATE

ON

RECENT RESEARCH ON LSD, MARIHUANA, AND OTHER  
DANGEROUS DRUGS

(Reproduced by the NASPA Drug Education Project)

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Mr. Chairman:

I am happy to appear today in behalf of the Public Health Service to discuss recent research on LSD, marihuana, and other dangerous drugs, supported by the National Institute of Mental Health.

There has been considerable progress in elucidating the nature and extent of the LSD problem. Intensive research efforts have enabled us to obtain a better understanding of the short- and long-term implications of LSD use, particularly in regard to its psychologic and biologic effects.

The scope of research either funded by the NIMH, or utilizing LSD from the NIMH supplies, covers a wide range of activity from surveys and epidemiologic studies through basic biochemical and experimental psychopharmacologic research. Currently the NIMH is supporting a total of 58 studies and will have expended over \$3.4 million in FY 1968 for research in the area of LSD and related hallucinogenic agents. This represents an increase of 20 projects and \$1.7 million over the level of support in FY 1966.

During early 1967 there was considerable concern regarding the extent of the LSD problem in the United States, particularly in light of reports that the number of users was increasing at a very rapid rate. NIMH is continuing to support several studies designed to measure the extent and trends of LSD and other hallucinogenic use. Preliminary findings from these studies indicate that we have witnessed in the past year a significant decline in LSD use in the United States.

I am sure that there are a number of factors associated with this decline. Our evidence would indicate that a key factor in explaining this decline has been the availability of factual scientific information based on research findings which suggest that LSD can cause severe psychotic reactions and may cause chromosomal changes not only in the cells of the user but also, for women, in her children.

#### CONFERENCE ON TOXIC EFFECTS OF LSD

Five months ago, the NIMH convened a meeting of the country's leading research experts to evaluate the information then available regarding the toxic effects of LSD.

I would like to submit a summary report of this conference for the record. The final report of the proceedings is being completed. I would like to discuss briefly some of the highlights of this conference.

The discussion indicated that with several exceptions the evidence for persisting psychologic damage from chronic LSD administration is minimal. One exception is the observation that chronic users (when not on LSD) showed uniformly lower thresholds to auditory stimuli. This suggests the possibility that sensory overload may be a problem for the chronic LSD user even when he is not ingesting this drug. In other words, these persons are more sensitive to sounds and might have difficulty in discriminating between low and high intensity sounds.

Several workers have described the phenomenon of recurring hallucinogenic experience without recurrent ingestion of the drug. In some instances users of LSD without taking the drug have recurrent paranoid episodes, at times accompanied by vivid hallucinations. The significance and extent of these reactions are not as yet fully known.

Though a continuing problem, admissions to psychiatric units of persons with so-called "bad trips" are declining. Dr. William Frosch, who reported in 1966 that there was a rapidly rising rate of such admissions to Bellevue Hospital in New York City, now informs us that the admission rate for such cases at his hospital has declined.

Some investigators in the past year had expressed concern about possible outbreaks of new forms of acute and/or chronic organic psychoses related to hallucinogenic drug use. The consensus of those present at the meeting was that there is not sufficient evidence to justify this concern. However, modification of the usual therapy for acute hallucinogen caused psychoses is indicated. The results in terms of terminating the acute psychotic reactions are in most instances good.

#### CHROMOSOME DAMAGE

Considerable public attention has recently been focused on the relationship between LSD and chromosome damage. These reports are particularly alarming because of the association of chromosomal damage with leukemia-type syndromes and birth defects. The types of chromosomal changes noted in some LSD users have also been observed in survivors of the Hiroshima atomic blast and other persons exposed to high doses of ionizing radiation, all of whom have an increased likelihood of developing leukemia-type syndromes.

The initial report of chromosome damage possible attributable to LSD by Dr. Maimon Cohen of the University of Buffalo School of Medicine sparked a flurry of research activity around the effects of hallucinogenic drugs on chromosomes in vivo and in vitro and upon the offspring of exposed human and animal subjects.

The NIMH is currently supplying LSD to 20 investigators engaged in research of this type. The initial report of Cohen referred to the production of chromosomal abnormalities in human white blood cells (lymphocytes) cultured with LSD. These changes were not observed when LSD was not present in the medium (although similar changes have now been observed when such cultures have been made with thiorazine, aspirin and caffeine).

Dr. Cohen's findings were confirmed nearly immediately by Drs. Irwin and Egozcue of the University of Oregon School of Medicine. They additionally reported chromosomal abnormalities in the circulating lymphocytes of several "hippies" in the Portland area. Dr. Herman Lisco of Harvard University has reported identical changes in persons who had been exposed to psilocybin, another hallucinogen.

Similar human in vivo reports about LSD were made by Drs. Cohen,



Frosch and Hirshhorn. Their findings, however, were not confirmed by several investigators at the University of California, by Dr. David Hungerford of the Cancer Research Institute in Philadelphia or by Dr. Albert Kurland's group at Spring Grove State Hospital. In the several studies where chromosomes were examined before and after LSD administration in man, the Irwin and Cohen findings could not be replicated.

If LSD does in fact cause chromosomal abnormalities in man, the significance can only be learned over time. Similar changes occur after certain viral illnesses; but in these conditions the effects are short-term and are not associated with serious pathological consequences. Long lasting chromosomal damage of this type has, however, been reported in persons exposed to atomic radiation and other individuals considered highly vulnerable to leukemia. In considering the leukemia causing potential of LSD we must consider that longitudinal studies in identified individuals are mandatory to determine whether such changes are long-term and a prelude to leukemia. Short-term chromosomal changes may not have any pathological significance.

#### BIRTH DEFECTS

Observations of chromosomal abnormalities also led to several studies to determine the effects of LSD on offspring in several animal species. In the mouse and the hamster, when LSD was administered early in pregnancy, there was a significant increase in the number of spontaneous abortions and birth defects. Contradictory reports have appeared about such findings in the rat. Experts in this field tell us that it is impossible to generalize from one species to another with regard to drug effects upon the fetus. Thalidomide, for example, failed in several animal studies to present birth defects across species lines although it did produce birth defects in man.

There have been a number of newspaper articles which have attempted to relate LSD to reported birth defects. One report in the New York Times of February 10 quotes Dr. William Frosch of New York University describing one child with retarded mental development. This investigator pointed out that there was no direct evidence that the drug was to blame. There has been one report from the University of Iowa which was reported in LANCET and purported to show that an offspring who had been exposed to the drug during the mother's 45th day of pregnancy showed findings similar to that of Thalidomide exposed infants. Dr. Hirshhorn has reported chromosomal breaks in 50 percent of infants exposed to LSD in utero. There have been two reports of encephalocele, an unusual defect in which the brain herniated through an incompletely fused skull in fetuses who had been exposed to LSD early in the pregnancy and then were spontaneously aborted.

Evidence that hallucinogenic drugs can cause birth defects in exposed humans is at best presumptive at this time. Reports from animal studies and in utero chromosomal investigations suggest a possible link between some of the birth defects reported and maternal ingestion of LSD. These investigators themselves would be the first to argue that their findings are not definitive and that a reasoned and deliberate response is indicated.

At this time our information about the biologic hazards of LSD and other hallucinogenic drugs must be considered incomplete. However, in light of the preliminary findings, one should add to the usual warnings about LSD use particular emphasis on the possible hazards for women in the childbearing ages.

Additionally, the advisory committee was strongly supportive of continuing, refining and integrating research into the mechanism of action and the biological and psychological effects of LSD, because of its abuse, its unique nature, and its possible therapeutic potential.

#### SURVEYS OF LSD USE IN COLLEGES

I would now like to turn to a discussion of findings from several surveys of LSD use in college populations. Five percent of the college students polled admitted to using LSD with a range among individual colleges of 2-9 percent. LSD users are much more likely to have also used marihuana as well as other drugs such as amphetamine and barbiturates. Conversely, only a small percentage of those who have used marihuana also use LSD. LSD users tended to be "experimenters" with only 30 percent of the sample "serious" LSD users.

We now have some data about the characteristics of the student drug user. The academic standing of the occasional user was better than average, while the heavily involved drug users had lower than average scholastic grades. There is a relatively small group, perhaps 3-4 percent of student drug users, for whom taking drugs is no longer a question of "just being in," but whose problem of drug abuse represents a complicated and severe psychiatric problem. There is a decline in the number of admissions to college health services of students with psychotic reactions secondary to LSD use paralleling the decrease at Bellevue noted earlier.

#### ONGOING RESEARCH

Research continues on the possible therapeutic usefulness of LSD particularly in the treatment of alcoholism and psychoneurosis. We currently have 12 studies and are spending this year over \$1 million in this area.

I have already indicated what research results there are and I would now like to describe briefly some of the other research going on in this area and what we are hoping to find out.

There are currently a total of 93 studies being conducted which are using LSD supplied by this Institute. All requests for this drug are reviewed by a joint FDA-NIMH committee to establish the soundness of research designed and to guarantee that all necessary precautions are observed. A large number of these studies are devoted to elucidating the mechanism of action of LSD. This agent has been of great interest to neuropharmacologists and others studying the central nervous system because its actions appear to be related to the levels of serotonin and perhaps to catecholamine levels in the brain (serotonin and catecholamines are naturally

occurring substances which appear to play a key role in the biochemical transactions of the brain.

Sixty percent of studies are in animals, 16% in humans and 24% in isolated tissues. Most of the animal and tissue culture studies are devoted to elucidating the mechanisms of action of LSD. Recent reports by Dr. George Agahanjian and Dr. Daniel Freedman suggest that LSD may exert subtle chemical and/or electrical effects on the very area of the midbrain which is believed responsible for phase I R.E.M. sleep. This is particularly intriguing in view of reports of temporary psychosis in individuals who are specifically deprived of this type of sleep. Additionally, many psychotropic drugs specifically inhibit this phase of the sleep cycle.

Other investigators are studying the metabolism of hallucinogenic drugs. Research is also proceeding on the effects of LSD upon brain protein metabolism and nucleic acid synthesis in order to better understand the biochemical basis of learning and memory. These studies are all correlated with behavioral and learning studies in various animal species. It is clear that LSD is an extremely valuable research tool which has opened up broad vistas for basic research that would be impossible to develop without its ready availability to the research community.

Human studies are designed to test the therapeutic potential of LSD in alcoholism, psychoneurosis and other treatment resistant psychiatric conditions. Additionally, LSD has some behavioral and subjective effects in man which cannot be derived from animal studies. As a tool to study perception, sensory integration and basic emotional mechanisms, LSD and other hallucinogenic drugs should continue to be available for human pharmacological studies.

#### MARIHUANA

I shall now turn to the subject of marihuana. The official name of the drug is cannabis. Basic research to uncover knowledge about the pharmacology and physiological activity of cannabis has been severely hampered by the lack of availability of adequate legitimate sources of a standardized natural product. The little research that has been done has utilized marihuana seized by the Federal Bureau of Narcotics and supplied to researchers. Unfortunately this material was relatively old and had lost much of its original potency.

#### PROBLEMS OF RESEARCH

A key problem in the field of research on cannabis is the lack of a standard product. For results of scientific investigation to be reproducible, researchers must have available agents whose chemical constituents and potency are identical. There is tremendous variability in black market cannabis. Seized materials may be adulterated with other plant or chemical materials, or maybe mixtures of different varieties of cannabis. We know that the potency of cannabis varies according to its age and where it is grown. Until recently the only solution to this problem appears to be the development of a special facility for growing a standardized variety of cannabis.



While this project still has high priority to facilitate scientific studies of natural cannabis the recent synthesis of a number of tetrahydrocannabinols, the chemically active constituents of cannabis, shows great promise in expediting research in the field.

The synthesis of the tetrahydrocannabinols and their increasing availability for research purposes now makes it possible for us finally to perform the vitally needed pharmacologic, biochemical, genetic, and behavioral research necessary to answer our questions about the mode of action and toxicity of cannabis. While there have been reports over the year from foreign countries about irreversible psychoses associated with marihuana use, in recent years responsible scientists in this and other countries have raised considerable question about the validity of these conclusions. For instance, many of these foreign studies were done on chronic institutionalized persons. We are well aware from our own research on institutionalized schizophrenics that after several years it is extremely difficult, if not impossible, to distinguish between the effects of the disease and the effects of institutionalization. Additionally, these foreign studies have dealt with populations with chronic physical diseases, malnutrition, etc. which make it extremely difficult to delineate which symptoms are due to chronic marihuana use and which are due to other factors.

#### PROPOSED RESEARCH

With the impending availability of adequate supplies of synthetic tetrahydrocannabinol we have developed and have given high priority to an intensive systematic plan of research to elucidate a number of basic facts. These studies will range from the investigation of long-range toxicity in animals through biochemical research and carefully controlled human studies. Additionally, we will expand on our current program of social and psychological investigations of marihuana users. We have already begun negotiations to perform studies in these foreign countries where the "marihuana psychosis syndrome" has been described.

We estimate that studies of marihuana will cost approximately \$5.25 million over the next three years. Though major gaps in our knowledge do exist, data from ongoing and past research have already given us some answers.

#### SURVEYS OF MARIHUANA USE IN HIGH SCHOOLS AND COLLEGES

Surveys of high school and college drug use indicate that approximately 20 percent of the college students questioned reported some experience with marihuana. It is estimated that about two million high school and college students have had some experience with marihuana. Generally more men students reported involvement. Of those who reported having ever used marihuana, 65 percent had used it less than ten times with "once or twice" the commonest response. It is of great interest that fully 50 percent of those who have tried marihuana experienced no effects. This finding may be a function of at least four factors, (1) the agent may not have been potent, (2) frequently effects are seen only after repeated use, (3) the expectation of the user has a significant effect on what he experiences, (4) the social setting in which use takes place has an effect on the response.



Under NIMH contract support a survey instrument for more accurately assessing the prevalence of drug abuse in high school and college populations has been developed. On the basis of successful pilot studies with this instrument a grant proposal for a five-year study is pending review by the National Advisory Mental Health Council at its meeting next month.

Our evidence would indicate that in contrast to the decreasing use of LSD, use of marihuana has been increasing.

The United Nations estimates that in 1950 there were 200 million users of marihuana in the world, mainly in India and in North Africa. In the United States, we are not quite sure of the exact extent of the problem. Estimates as high as 20 million have been made, but it is much more likely that in the neighborhood of 4 to 5 million persons have used it at least once.

#### EFFECTS OF CANNABIS

Little can be added to previous reports on the toxicity of marihuana. It is considered to be a mild hallucinogen, taken by the usual route of smoking, occasionally by ingestion. It may induce a mild euphoria and lead to heightened suggestibility and a faulty perception, really an exaggerated notion of thinking more clearly, profoundly and creatively. In addition, it is known to cause reddening of the membranes of the eyes, rapid heartbeat, muscular incoordination, unsteadiness, drowsiness, and distortion of time and space perception.

In acute intoxication, especially when ingested, it may also produce visual hallucinations, pronounced anxiety, paranoid reactions and transient psychoses lasting 4 to 6 hours. It generally tends to lessen inhibitions and creates for the user a false reality based on his wants, his motivations, or the set. In this respect it is similar to LSD but its effects are not as potent.

The muscular incoordination and the distortion of space and time perception commonly associated with marihuana use are potentially hazardous since the drug adversely affects one's ability to drive an automobile or perform other skilled tasks.

We still do not know enough about the long-term effects of marihuana use. As in the case of tobacco, it is possible that there are serious consequences of chronic use which will only become apparent through careful longitudinal studies.

One needs to be particularly concerned about the potential effect of a reality distorting agent on the future psychological development of the adolescent user. We know that normal adolescence is a time of great psychological turmoil. Patterns of coping with reality developed during the teenage period are significant in determining adult behavior. Persistent use of an agent which serves to ward off reality during this critical development period is likely to compromise seriously the future ability of the individual to make an adequate adjustment to a complex society.

While we have no data to indicate that marihuana can affect chromosomes, this possibility is being investigated.

### PREVENTION AND EDUCATION

Prevention and education efforts in the area of hallucinogenic agents have a high priority for the NIMH. Efforts in this and other areas related to research are coordinated with the FDA through a mechanism by which the Chief of the FDA's Division of Drug Studies and Statistics has a joint appointment in the NIMH Center for Studies of Narcotic and Drug Abuse.

I would like to point out that prevention and education efforts aimed at the student population demand extremely careful preparation and implementation. Even high school students are extremely sophisticated about drugs. We are constantly impressed at speaking appearances before high school and college audiences about:

1. The extent of accurate knowledge mixed with misinformation about all drugs, not just LSD and marihuana, but barbiturates, amphetamines, etc; and

2. The suspicion with which students approach information supplied by "official sources."

"Scare" techniques are not only ineffectual, but are even detrimental to conveying needed information about the hazards of drug abuse. With the present incidence of marihuana use, many students have either experienced or observed first-hand the effects of this drug. They know that psychoses or other grave consequences are not an inevitable concomitant of smoking one marihuana cigarette.

It is clear that to be effective, a preventive educational effort must be carefully tailored to specific population groups and must be based on the best educational and scientific footing. The decrease in LSD use is, at least in part, I would suggest, a function of the degree to which users will respond to scientific evidence of potential danger.

Let me give you one example of how we have implemented this approach. In September 1966, the National Association of Student Personnel Administrators joined with FDA, NIMH and the Treasury Department in planning a program to provide student personnel and other college administrators with up-to-date, accurate information which would help them understand and cope with student drug use. Subsequently, FDA funded a contract to implement these plans. Under the direction of Dr. Helen H. Nowlis, Professor of Psychology and former Dean of Students at the University of Rochester, the National Association of Student Personnel Administrators' Drug Education Project was developed. In February and March 1967, over 1400 persons participated in seven regional conferences for the purpose of acquiring and exchanging information about the problems of drug abuse on the campus.

The continuing demand for consulting services for professional groups and colleges planning drug education programs led to a continuation of the project on a part-time basis. I am sure that Dr. Nowlis, who I understand will also appear before the Committee, can provide a detailed discus-

sion of this project.

The NIMH is now developing a variety of materials as part of its education efforts. Films for television as well as small groups, film strips, pamphlets, etc., are being prepared. We have consulted with leading experts in the communications industry as well as educators so that our materials will be instructive, effective and scientifically sound.

#### ALIENATION

Mr. Chairman, I think that it is critical to point out that in trying to understand scientifically the problem of drug abuse, one must look beyond the specific problems of such agents as LSD, marihuana, amphetamines and barbiturates to some of the underlying causes of widespread drug use and abuse. We live in a drug-oriented culture. From aspirin to sleeping pills, from tranquilizers to "the pill," Americans, of all ages, are ingesting drugs in greater variety and greater numbers than ever before. I think that if we are to get to the root of this problem of drug abuse, we must be prepared to investigate and identify the underlying problems which lead people to choose to distort or ward off reality with drugs.

One way of conceptualizing the problem is to view drug abuse in the student population in the broader context of the nature and extent of "casualties" of the educational system. Through our interest in school and college mental health, suicide prevention, and alcoholism, we have become increasingly aware that a fair percentage of our brightest and most competent youth are not "succeeding" in their encounter with the higher educational system.

Behavioral scientists use the term "alienation" in describing the cross-generational disease epitomized by the youth-coined term "don't trust anyone over 30." Alienation has been characterized as: "rebellion without a cause. . . rejection without a program . . . a refusal of what is without a vision of what should be."

Lapses in communication between generations were noted by Greek philosophers over 2,000 years ago, and more recently were manifested in American society by the so-called "lost generation" of the 1920's and the "silent generation" of the 1950's. However, the current problem of alienation in the United States is wider, deeper, and more diffuse than at any previous time in our history. It affects the rich and the poor, the college student and the school drop-out, the urban and the rural youngster. The number of persons, both young and old, beset by alienation is far greater than that ever seen in any previous generation.

Because many alienated youngsters question the relevance of major societal values and institutions, they find themselves unable to learn from the various opportunities that presently are available to them. As Freedman and Brotman point out. . . "To ask one of the youngsters, as one of the authors did, 'Where's the action?' elicits a scornful answer: 'There's only action if you have a high.' The implication is clear; what is meaningful is the subjective state. If an undrugged state is defective, myopic, why not alter perception through drugs and create a

new 'reality?' Some youngsters who feel helpless to accommodate to or change an unacceptable world, consciously choose to alter their own. . . . Their most frequent statement is that life is a 'drag.' It lacks meaning for there is no engagement; the future is unknown but certainly horrible. Since you cannot alter the world or determine the direction in which it will go, you must alter your state of consciousness and perception, that is, see the world and experience the world through a 'high.' Any alteration is acceptable, and thus, the barbiturate user can describe to you the joys of a 'drowsy high' and the amphetamine user will talk about the 'high' he gets on benzedrine - and likewise for the LSD, marihuana, and heroin abuser. All that is important is in one's subjective state. Perceptions and beliefs of the square world or the non-drug world are superficial, distorted, meaningless. . ." This rejection of many goals of the society, the unwillingness to model themselves on any stable adult leaders and the inability to acquire the necessary attitudes and skills for responsible adult behavior, make urgent the development of new and innovative approaches to bridge the intergenerational gap.

If this is not done, there are serious dangers that large proportions of current and future generations will reach adulthood embittered towards the larger society, unequipped to take on parental, vocational and other citizen roles, and involved in some form of socially deviant behavior.

I would propose that if we are ever to solve the problem of drug abuse, it is critical for us to focus on and try to solve the root causes of alienation.