## THE HALLUCINOGENIC DRUGS

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be have something new hap
be to feel secure, yet at times

be surprised. Too much pre
leads to monotony, but too

lead to anxiety. To establish

between continuity and

a task facing all organisms,

and social, human and non-

things predictable is generalone of the functions of When a person perceives acthinks clearly, plans wisely appropriately—and represses thoughts and emotionsthat his ego is strong. But the is also inventive, open to perceptions that at first may be Research on the personof highly creative individuals that they are particularly are the challenge of the contradicthe unpredictable, and that even court the irrational ewn make-up as a source of and unexpected insight. Indeed, all recorded history and everythe world men have gone to ble lengths to seek unpredictadisrupting the functioning of A change of scene, a change of a change of mind: these are the prescriptions for getting out of

ing "mind" must be reckened the use of intoxicating substances. Alcohol has quite won the day for this purpose in the U.S. and much of the rest of the world. Consumed at a moderate rate and in sensible quantities, it can serve simultaneously as a euphoriant and tranquilizing agent before it finally dulls the faculties and puts one to sleep. In properly disposed individuals it may dissolve sexual inhibitions, relieve fear and anxiety, or stimulate meditation on the meaning of life. In spite of its costliness to individual and social health when it is used immoderately, alcohol retains its rank as first among the substances used by mankind to change mental experience. Its closest rivals in popularity are opium and its derivatives and various preparations of cannabis, such as hashish and marijuana.

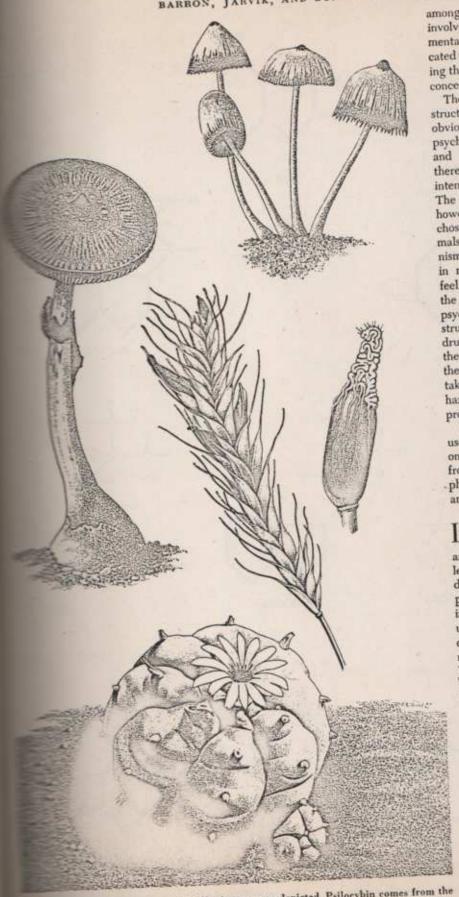
This article deals with another group of such consciousness-altering substances: the "hallucinogens." The most important of these are mescaline, which comes from the peyote cactus Lophophora williamsii; psilocybin and psilocin, from such mushrooms as Psilocybe mexicana and Stropharia cubensis; and d-lysergic acid diethylamide (LSD), which is derived from ergot (Claviceps purpurca), a fungus that grows on rye and wheat. All are alkaloids more or less related to one another in chemical structure.

Various names have been applied to this class of substances. They produce

distinctive changes in perception that are sometimes referred to as hallucinations, although usually the person under the influence of the drug can distinguish his visions from reality, and even when they seem quite compelling he is able to attribute them to the action of the drug. If, therefore, the term "hallucination" is reserved for perceptions that the perceiver himself firmly believes indicate the existence of a corresponding object or event, but for which other observers can find no objective basis, then the "hallucinogens" only rarely produce hallucinations. There are several other names for this class of drugs. They have been called "psychotomimetic" because in some cases the effects seem to mimic psychosis [see "Experimental Psychoses," by Six Staff Members of the Boston Psychopathic Hospital; Scientific American, June, 1955]. Some observers prefer to use the term "psychedelic" to suggest that unsuspected capacities of the imagination are sometimes revealed in the perceptual changes.

The hallucinogens are currently a subject of intense debate and concern in medical and psychological circles. At issue is the degree of danger they present to the psychological health of the person who uses them. This has become an important question because of a rapidly increasing interest in the drugs among laymen. The recent controversy at Harvard University, stemming at first from methodological disagreements

the common ways of chang-



Sources of the main hallucinogens are depicted. Psilocybin comes from the Scropharia cubensis (top left) and Psilocybe mexicana (top right). LSD is synthem an alkaloid in ergot (Clariceps purpurea), a fungus that grows on cereal ergot-infested rye seed head is shown (center) together with a larger-scale draw-ergot fungus. Mescaline is from the peyote cactus Lophophora williamsii (bottom).

among investigators but subsequently involving the issue of protection of the mental health of the student body, indicated the scope of popular interest in taking the drugs and the consequent public concern over their possible misuse.

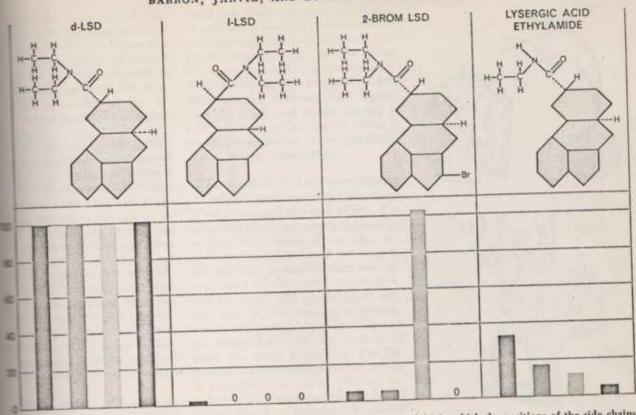
There are, on the other hand, constructive uses of the drugs. In spite of obvious differences between the "model psychoses" produced by these drugs and naturally occurring psychoses, there are enough similarities to warrant intensive investigation along these lines. The drugs also provide the only link, however tenuous, between human psychoses and aberrant behavior in animals, in which physiological mechanisms can be studied more readily than in man. Beyond this many therapists feel that there is a specialized role for the hallucinogens in the treatment of psychoneuroses. Other investigators are struck by the possibility of using the drugs to facilitate meditation and aesthetic discrimination and to stimulate the imagination. These possibilities, taken in conjunction with the known hazards, are the bases for the current professional concern and controversy.

In evaluating potential uses and misuses of the hallucinogens, one can draw on a considerable body of knowledge from such disciplines as anthropology, pharmacology, biochemistry, psychology and psychiatry.

In some primitive societies the plants from which the major hallucinogens are derived have been known for millenniums and have been utilized for divination, curing, communion with supernatural powers and meditation to improve self-understanding or social unity; they have also served such mundane purposes as allaying hunger and relieving discomfort or boredom. In the Western Hemisphere the ingestion of hallucinogenic plants in pre-Columbian times was limited to a zone extending from what is now the southwestern U.S. to the northwestern basin of the Amazon. Among the Aztecs there were professional diviners who achieved inspiration by eating either peyote, hallucinogenic mushrooms (which the Aztecs called teo-nanacatyl, or "god's flesh") or other hallucinogenic plants. Teonanacatyl was said to have been distributed at the coronation of Montezuma to make the ceremony seem more spectacular. In the years following the conquest of Mexico there were reports of communal mushroom rites among the Aztecs and other Indians of southern Mexico. The communal use has almost died out today, but in several

RELATIONS among several of the hallucinogens and are indicated by these structural diagrams. The lim color at top) is a basic structural unit; it appears, the the colored shapes, in serotonin, LSD, psilocybin

and psilocin. Mescaline does not have an indole ring but, as shown by the light color, can be represented so as to suggest its relation to the ring. The close relation between mescaline and the two catechol amines epinephrine and norepinephrine is also apparent here.



CHANGES in LSD molecule produce large changes in its

Here LSD (left) is used as a standard, with a "relative" of 100 in toxicity (dark gray bar), fever-producing effect

Type, ability to antagonize serotonin (light color) and sychotomimetic effects (dark color). The stereoisomer of

LSD (second from left) in which the positions of the side chains are reversed, shows almost no activity; the substitution of a bromine atom (third from left) reduces the psychotomimetic effect but not the serotonin antagonism; the removal of one of the two ethyl groups (right) sharply reduces activity in each of the areas.

the medicine men or women deros) still partake of Psilocybe

arid region between the Rio and central Mexico, where the eactus grows, the dried tops of "peyote buttons") were eaten shamans, or medicine men, and in tribal rituals. During the 19th the Mescalero Apaches acquired and developed a peyote rite. a protism of the Mescaleros (whence mescaline) spread to the Coand Kiowas, who transformed a religion with a doctrine and well as ritual. Peyotism, which rapidly through the Plains became fused with Christianits adherents worship God great spirit who controls the and put some of his power perote, and Jesus as the man who be plant to the Indians in a and need. Saturday-night meetings, held in a traditional tepee, begin eating of the sacramental peythe night is spent in prayer, enging and introspective contemand in the morning there is a ion breakfast of corn, game and

Recognizing the need for an effective organization to protect their form of worship, several peyote churches joined in 1918 to form the Native American Church, which now has about 225,000 members in tribes from Nevada to the East Coast and from the Mexican border to Saskatchewan. It preaches brotherly love, care of the family, self-reliance and abstinence from alcohol. The church has been able to defeat attempts, chiefly by the missionaries of other churches, to outlaw peyote by Federal legislation, and it has recently brought about the repeal of antipeyote legislation in several states.

The hallucinogens began to attract scholarly interest in the last decade of the 19th century, when the investigations and conceptions of such men as Francis Galton, J. M. Charcot, Sigmund Freud and William James introduced a new spirit of serious inquiry into such subjects as hallucination, mystical experience and other "paranormal" psychic phenomena. Havelock Ellis and the psychiatrist Silas Weir Mitchell wrote accounts of the subjective effects of peyote, or Anhalonium, as it was then called. Such essays in turn stimulated

the interest of pharmacologists. The active principle of peyote, the alkaloid called mescaline, was isolated in 1896; in 1919 it was recognized that the molecular structure of mescaline was related to the structure of the adrenal hormone epinephrine.

This was an important turning point, because the interest in the hallucinogens as a possible key to naturally occurring psychoses is based on the chemical relations between the drugs and the neurohumors: substances that chemically transmit impulses across synapses between two neurons, or nerve cells, or between a neuron and an effector such as a muscle cell. Acetylcholine and the catechol amines epinephrine and norepinephrine have been shown to act in this manner in the peripheral nervous system of vertebrates; serotonin has the same effect in some invertebrates. It is frequently assumed that these substances also act as neurohumors in the central nervous system; at least they are present there, and injecting them into various parts of the brain seems to affect nervous activity.

The structural resemblance of mescaline and epinephrine suggested a possible link between the drug and mental Might the early, excited stage phrenia be produced or at least at by an error in metabolism that a mescaline-like substance?

The produced of at least at le

LSD was discovered in 1943, ardinary potency again aroused in the possibility of finding a elemical activator of the schizoprocess. The M-substance hywas revived on the basis of reat hallucinogenic effects were by adrenochrome and other products of epinephrine, and thesis appeared to be strengththe isolation from human urine close analogues of hallucino-Adrenochrome has not, however, etected in significant amounts in body, and it seems unlikely analogues could be produced seient quantity to effect mental

melation between LSD and serogiven rise to the hypothesis that renia is caused by an imbalance etabolism of serotonin, with exand hallucinations resulting excess of serotonin in certain and of the brain, and depressive and states resulting from a deficienacrotonin. The idea arose in part - Se observation that in some laborasiological preparations LSD acts he scrotonin but in other preparaa powerful antagonist of sero-LSD might facilitate or block searchumoral action of serotonin benin.

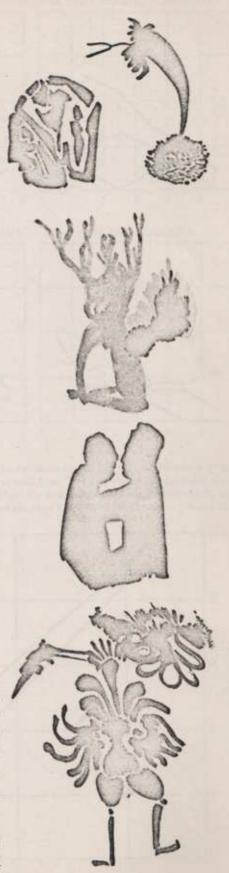
The broad objection to the serotonin of schizophrenia is that it rean oversimplified view of the pattern of symptoms. Moremany congeners, or close anaof LSD, such as 2-brom lysergic equally effective or more effecegonists of serotonin without grificantly active psychological-This does not disprove the however. In man 2-brom blocks the mental effects of a subdose of LSD, and in the heart it blocks the action of both and serotonin. Perhaps there are at the sites where neuroact; in the case of those for it may be that LSD fits the opens the lock, whereas the legically inactive analogues merethe keyhole, blocking the of serotonin or LSD without their effects. Certainly the re-

semblance of most of the hallucinogens to serotonin is marked, and the correlations between chemical structure and pharmacological action deserve intensive investigation. The serotonin theory of schizophrenia is far from proved, but there is strong evidence for an organic factor of some kind in the disease; it may yet turn out to involve either a specific neurohumor or an imbalance among several neurohumors.

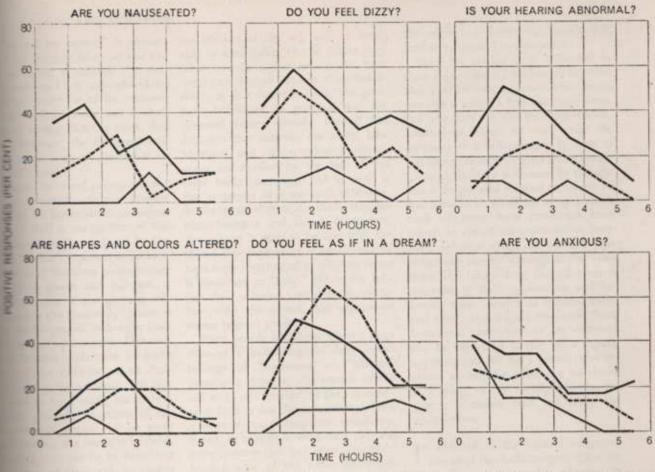
The ingestion of LSD, mescaline or psilocybin can produce a wide range of subjective and objective effects. The subjective effects apparently depend on at least three kinds of variable: the properties and potency of the drug itself; the basic personality traits and current mood of the person ingesting it, and the social and psychological context, including the meaning to the individual of his act in taking the drug and his interpretation of the motives of those who made it available. The discussion of subjective effects that follows is compiled from many different accounts of the drug experience; it should be considered an inventory of possible effects rather than a description of a typical episode.

One subjective experience that is frequently reported is a change in visual perception. When the eyes are open, the perception of light and space is affected: colors become more vivid and seem to glow; the space between objects becomes more apparent, as though space itself had become "real," and surface details appear to be more sharply defined. Many people feel a new awareness of the physical beauty of the world, particularly of visual harmonies, colors, the play of light and the exquisiteness of

The visual effects are even more striking when the eyes are closed. A constantly changing display appears, its content ranging from abstract forms to dramatic scenes involving imagined people or animals, sometimes in exotic lands or ancient times. Different individuals have recalled seeing wavy lines, cobweb or chessboard designs, gratings, mosaics, carpets, floral designs, gems, windmills, mausoleums, landscapes, "arabesques spiraling into eternity," statuesque men of the past, chariots, sequences of dramatic action, the face of Buddha, the face of Christ, the Crucifixion, "the mythical dwelling places of the gods," the immensity and blackness of space. After taking peyote Silas Weir Mitchell wrote: "To give the faintest idea of the perfectly satisfying intensity and purity of these gorgeous color fruits



WATER COLORS were done, while under the influence of a relatively large dose of a hallucinogenic drug, by a person with no art training. Originals are bright yellow, purple, green and red as well as black.



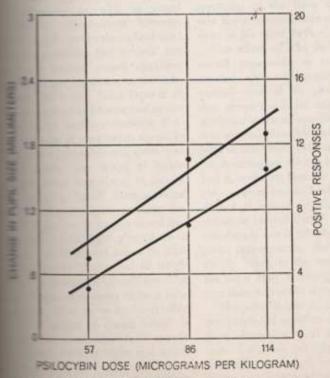
ECTIVE REPORT on physiological and perceptual effects

LSD was obtained by means of a questionnaire containing 47

the results for six of which are presented. Volunteers were

sound at one-hour intervals beginning half an hour after they

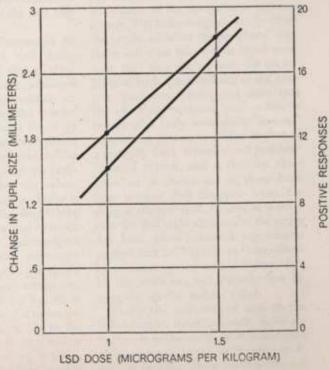
took the drug. The curves show the per cent of the group giving positive answers at each time. The gray curves are for those given an inactive substance, the broken black curves for between 25 and 75 micrograms and the solid black curves for between 100 and 225.



The AND SUBJECTIVE effects vary with dosage as shown

Be data plotted in black are for the increase in size of

mumber of positive responses to questions like the



ones at the top of the page are shown in color. The objective and subjective measures vary in a similar manner. The data are from an experiment done by Harris Isbell of the University of Kentucky.

the waning hours of the efpulocybin as follows: "As the
wore on I felt very content to
and stare out of the window
and the trees, and at that
call feeling that the snow, the
fireplace, the darkened and
droom were so perfect as to

anges in visual perception are pleasant. Aldous Huxley of his books about mescaline - d Hell in recognition of the sensations induced by the "hellish" experiences include on of blackness accompanied of gloom and isolation, a -diffication of the glowing cola wed in the "heavenly" phase, a mekly greens and ugly dark subject's perception of his own become unpleasant; his limbs to be distorted or his flesh decaying; in a mirror his face ear to be a mask, his smile a ess grimace. Sometimes all huements appear to be mere or everyone seems to be dead. experiences can be so disturbing sidue of fear and depression long after the effects of the drug off.

there are complex auditory decinations as well as visual egthy conversations between people, perfectly orchestrated compositions the subject has beard before, voices speaking languages unknown to the subhave also been reports of bory odors and tastes and of visother bodily sensations, Frepatterns of association normally to a single sense will cross over senses: the sound of music visual impression of jets of light, a "cold" human voice subject shiver, pricking the pin produces the visual imof a circle, light glinting on a tree ornament seems to shatto evoke the sound of sleigh time sense is altered too. The of time may seem to be a slow flow or to be intolerably A "sense of timelessness" is souted; the subject feels outside second time, or time and space

individuals one of the most stancies in perception is afthe distinction between subject at. A firm sense of personal depends on knowing accurately

the borders of the self and on being able to distinguish what is inside from what is outside. Paranoia is the most vivid pathological instance of the breakdown of this discrimination; the paranoiae attributes to personal and impersonal forces outside himself the impulses that actually are inside him. Mystical and transcendental experiences are marked by the loss of this same basic constancy. "All is one" is the prototype of a mystical utterance. In the mystical state the distinction between subject and object disappears; the subject is seen to be one with the object. The experience is usually one of rapture or ecstasy and in religious terms is described as "holy." When the subject thus achieves complete identification with the object, the experience seems beyond words.

Some people who have taken a large dose of a hallucinogenie drug report feelings of "emptiness" or "silence," pertaining either to the interior of the self or to an "interior" of the universeor to both as one. Such individuals have a sense of being completely undifferentiated, as though it were their personal consciousness that had been "emptied," leaving none of the usual discriminations on which the functioning of the ego depends. One man who had this experience thought later that it had been an anticipation of death, and that the regaining of the basic discriminations was like a remembrance of the very first days of life after birth.

The effect of the hallucinogens on sexual experience is not well documented. One experiment that is often quoted seemed to provide evidence that mescaline is an anaphrodisiae, an inhibitor of sexual appetite; this conclusion seemed plausible because the drugs have so often been associated with rituals emphasizing asceticism and prayer. The fact is, however, that the drugs are probably neither anaphrodisiacs nor aphrodistacs-if indeed any drug is. There is reason to believe that if the drug-taking situation is one in which sexual relations seem appropriate, the hallucinogens simply bring to the sexual experience the same kind of change in perception that occurs in other areas of experience.

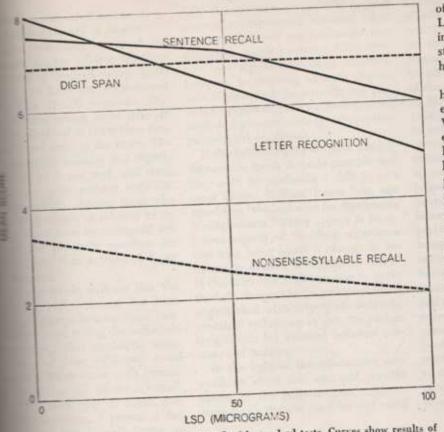
The point is that in all the hallucinogen-produced experiences it is never the drug alone that is at work. As in the case of alcohol, the effects vary widely depending on when the drug is taken, where, in the presence of whom, in what dosage and-perhaps most important of all-by whom. What happens to the individual after he takes the drug, and his changing relations to the setting and

the people in it during the episode, will further influence his experience.

Since the setting is so influential in these experiments, it sometimes happens that a person who is present when someone else is taking a hallucinogenic drug, but who does not take the drug himself, behaves as though he were under the influence of a hallucinogen. In view of this effect one might expect that a person given an inactive substance he thought was a drug would respond as though he had actually received the drug. Indeed, such responses have sometimes been noted. In controlled experiments, however, subjects given an inactive substance are readily distinguishable from those who take a drug; the difference is apparent in their appearance and behavior, their answers to questionnaires and their physiological responses. Such behavioral similarities as are observed can be explained largely by a certain apprehension felt by a person who receives an inactive substance he thinks is a drug, or by anticipation on the part of someone who has taken the drug before.

In addition to the various subjective effects of the hallucinogens there are a number of observable changes in physiological function and in performance that one can measure or at least describe objectively. The basic physiological effects are those typical of a mild excitement of the sympathetic nervous system. The hallucinogens usually dilate the pupils, constrict the peripheral arterioles and raise the systolic blood pressure; they may also increase the excitability of such spinal reflexes as the knee jerk. Electroencephalograms show that the effect on electrical brain waves is usually of a fairly nonspecific "arousal" nature: the pattern is similar to that of a normally alert, attentive and problemoriented subject, and if rhythms characteristic of drowsiness or sleep have been present, they disappear when the drug is administered. (Insomnia is common the first night after one of the drugs has been taken.) Animal experiments suggest that LSD produces these effects by stimulating the reticular formation of the midbrain, not directly but by stepping up the sensory input.

Under the influence of one of the hallucinogens there is usually some reduction in performance on standard tests of reasoning, memory, arithmetic, spelling and drawing. These findings may not indicate an inability to perform well; after taking a drug many people simply refuse to co-operate with the tester. The very fact that someone should want to



OF LSD on memory was determined with standard tests. Curves show results of subjects given an inactive substance, 50 micrograms of the drug and 100 micrograms.

either hostility or amusement.

by one of the authors in which
fattention and concentration were
stered to subjects who had been
different doses of LSD indicated
sotivation was perhaps as impordetermining scores as the sub-

hallucinogenic drugs are not adme-if one means by addiction that and a single of the second of and the drug becomes necessary, usually a loceasing amounts, for satisfactory logical functioning. Some indibecome psychologically dependthe drugs, however, and develop in that sense; indeed, there is melency for those who ingest halluhabitually to make the drug the center of all their activi-LSD, mescaline and psilocybin do physiological tolerance. If the quantity of LSD is administered successive days, for example, not suffice by the third day to prothe same subjective or physiologiefects; tolerance develops more and less completely with mesand psilocybin. When an indibecomes tolerant to a given dos-

age of LSD, the ordinarily equivalent dose of psilocybin produces reduced effects. This phenomenon of cross-tolerance suggests that the two drugs have common pathways of action. Any tolerance established by daily administration of the drugs wears off rather rapidly, generally being dissipated within a few days if the drug is not taken.

The three major hallucinogens differ markedly in potency. The standard human doses-those that will cause the average adult male weighing about 150 pounds to show the full clinical effectsare 500 milligrams of mescaline, 20 milligrams of psilocybin and .1 milligram of LSD. It is assumed that in a large enough dose any of the hallucinogens would be lethal, but there are no documented cases of human deaths from the drugs alone. Death has been brought on in sensitive laboratory animals such as rabbits by LSD doses equivalent to 120 times the standard human dose. Some animals are much less susceptible; white rats have been given doses 1,000 times larger than the standard human dose without lasting harm. The maximum doses known by the authors to have been taken by human beings are 900 milligrams of mescaline, 70 milligrams

of psilocybin and two milligrams of LSD. No permanent effects were noted in these cases, but obviously no decisive studies of the upper limits of dosage have been undertaken.

There are also differences among the hallucinogens in the time of onset of effects and the duration of intoxication. When mescaline is given orally, the effects appear in two or three hours and last for 12 hours or more. LSD acts in less than an hour; some of its effects persist for eight or nine hours, and insomnia can last as long as 16 hours. Psilocybin usually acts within 20 or 30 minutes, and its full effect is felt for about five hours. All these estimates are for the standard dose administered orally; when any of the drugs is given intravenously, the first effects appear within minutes.

At the present time LSD and psilocybin are treated by the U.S. Food and Drug Administration like any other "experimental drug," which means that they can be legally distributed only to qualified investigators who will administer them in the course of an approved program of experimentation. In practice the drugs are legally available only to investigators working under a Government grant or for a state or Federal agency.

Nevertheless, there has probably been an increase during the past two or three years in the uncontrolled use of the drugs to satisfy personal curiosity or to experience novel sensations. This has led a number of responsible people in government, law, medicine and psychology to urge the imposition of stricter controls that would make the drugs more difficult to obtain even for basic research. These people emphasize the harmful possibilities of the drugs; citing the known cases of adverse reactions, they conclude that the prudent course is to curtail experimentation with hallucinogens.

Others-primarily those who have worked with the drugs-emphasize the constructive possibilities, insist that the hallucinogens have already opened up important leads in research and conclude that it would be shortsighted as well as contrary to the spirit of free scientific inquiry to restrict the activities of qualified investigators. Some go further, questioning whether citizens should be denied the opportunity of trying the drugs even without medical or psychological supervision and arguing that anyone who is mentally competent should have the right to explore the varieties

experience if he can do so

systematic survey of the of serious adverse reactions gens covered nearly 5,000 which LSD was administered an 25,000 occasions. Psytions lasting more than 48 observed in fewer than twoper cent of the cases. The mpted suicides was slightly of 1 per cent, and these swehiatric patients with hisstability. Among those who as subjects in exthere were no attempted suipsychotic reactions ocsewer than a tenth of 1 per

reports do indicate that the e of bad reactions has been perhaps because more indibeen taking the hallucinothat emphasize sensaor even deliberate social Since under such circumis usually no one in attendknows how to avert danelopments, a person in this may find himself facing an inghtening hallucination with ent who can help him to abere the hallucination ends begins. Yet the question of a proper setting is not a simple the criticisms of the Harments was that some were in private homes rather than or clinical setting. The exdefended this as an attempt a feeling of naturalness and safety." Such a setting, mesized, should reduce the of negative reactions such as and increase the posices. Controlled studies of esis have not been carried

sychiatrists and psychologists alministered hallucinogens in setting claim specific benetreatment of psychoneuroses, and social delinquency. The dies are difficult to evaluate amost none have employed one summary of the statistics on the treatment of does indicate that about 50 of the patients treated with a of psychotherapy and LSD alcohol for at least a year, with 30 per cent of the paby psychotherapy alone. for recent study the results of testing before and after

LSD therapy were comparable in most respects to the results obtained when conventional brief psychotherapy was employed. Single-treatment LSD therapy was significantly more effective, however, in relieving neurotic depression. If replicated, these results may provide an important basis for more directed study of the treatment of specific psychopathological conditions.

If the hallucinogens do have psychotherapeutic merit, it seems possible that they work by producing a shift in personal values. William James long ago noted that "the best cure for dipsomania is religiomania." There appear to be religious aspects of the drug experience that may bring about a change in behavior by causing a "change of heart." If this is so, one might be able to apply the hallucinogens in the service of moral regeneration while relying on more conventional techniques to give the patient insight into his habitual behavior patterns and motives.

In the light of the information now available about the uses and possible abuses of the hallucinogens, common sense surely decrees some form of social control. In considering such control it should always be emphasized that the reaction to these drugs depends not only on their chemical properties and biological activity but also on the context in which they are taken, the meaning of the act and the personality and mood of the individual who takes them. If taking the drug is defined by the group or individual, or by society, as immoral or criminal, one can expect guilt and aggression and further social delinquency to result; if the aim is to help or to be helped, the experience may be therapeutic and strengthening; if the subject fears psychosis, the drug could induce psychosis. The hallucinogens, like so many other discoveries of man, are analogous to fire, which can burn down the house or spread through the house lifesustaining warmth. Purpose, planning and constructive control make the difference. The immediate research challenge presented by the hallucinogens is a practical question: Can ways be found to minimize or eliminate the hazards, and to identify and develop further the constructive potentialities, of these powerful drugs?



NATIVE AMERICAN CHURCH members take part in a peyote ceremony in Saskatchewan, Canada. Under the influence of the drug, they gaze into the fire as they pray and meditate.