

LYSERGIC ACID DIETHYLAMIDE: SIDE EFFECTS AND COMPLICATIONS

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Psychotomimetic agents are coming into more widespread use both as investigative tools and as an aid in psychotherapy. The rationale for the induction of reversible psychotic-like phenomena cannot be considered in detail here. It can be mentioned, however, that such techniques offer a further understanding of the determinants of the naturally occurring psychoses. With these chemical devices, study of isolated elements of normal and abnormal mental function, for example, perception or hallucinations, becomes a laboratory possibility. The state may be employed to screen drugs for clinical use. A subjective appreciation of psychotic symptomatology for personnel in contact with disturbed patients is now available. An important feature of the psychotherapeutic application is that, without impairing mental clarity, defensiveness is reduced and significant unconscious material might be uncovered. Lysergic acid diethylamide (LSD) and mescaline are currently the most dependable drugs capable of producing transient dissociation states for these purposes.

Reports of untoward events occurring in connection with the experimental or therapeutic use of the hallucinogens have been surprisingly infrequent. Agents which call forth such profound alterations of ego structure, awareness, cognition and affect might be occasionally expected to induce adverse reactions.

In order to ascertain whether such incidents were occurring but not being reported, a questionnaire was sent to 62 investigators who had experience with either LSD or mescaline in normal subjects or patients. Most of these physicians had published on their work with the hallucinogens. Others

were referred to us as actively involved in the study of these agents either as a therapeutic adjunct or as a research instrument in human investigations. They were asked for the following information:

1. The number of individuals who had received either LSD or mescaline.
2. The average number of times these drugs were given to each person.
3. The number of major complications encountered. Specific inquiry about suicides, suicide attempts, prolonged psychotic reactions and prolonged depressive reactions was made. When mention of such a complication occurred a summary of the case was requested.
4. The precautions taken by the respondent prior to administration of these drugs.
5. The diagnostic groups excluded from LSD or mescaline administration.

Replies from 44 of the 62 inquiries were received. It cannot be assumed that the responses are necessarily representative, but it should be noted that this yield represents data on almost five thousand individuals who had received either LSD or mescaline on more than 25,000 occasions. The number of times these agents were administered to a single person varied from one to 80. Dosages for LSD ranged from 25–1500 mcg., mescaline was given in 200–1200 mg. amounts. Although this report will deal with LSD, information concerning mescaline is included because the psychic activity of both agents is considered similar.

Adverse responses tended to occur at the higher dosage levels (above 75 mcg. LSD or 400 mg. mescaline) but this was by no means invariable. No instance of serious, prolonged physical side effects was found either in the literature or in the answers to the question-

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naire. When major untoward reactions occurred they were almost always due to psychological factors.

REVIEW OF LITERATURE

Elkes, Elkes and Mayer-Gross (6) have expressed their concern that an occasional experimental subject may be a danger to himself and others. Even normal volunteers might have delayed or severe responses to LSD lasting several days. An early psychotic condition could be aggravated by exposure to such an experience. For these reasons these investigators recommend that the hallucinogenic drugs be used in hospital situations where constant supervision by trained personnel is available.

Savage (9) has noted the completed suicide of a depressed, chronically schizophrenic girl who had been given LSD. Her defensive pattern changed from one of nihilistic delusions of being dead and having no body to that of rage and resentment against parents and therapist. A few weeks later she was allowed to go home for a visit and used this opportunity to throw herself under a train. He also records a depressive reaction lasting for a day which occurred after the ingestion of 150 gamma of LSD. The patient had taken the drug without the therapist's knowledge, but called him after four hours. She later said "I would have died if you hadn't been there." In another instance where the drug (100 mcg.) was taken alone the subject became overwhelmed with intense fears, delusional ideas and complete loss of contact. Recovery was gradual over the next week.

Savage found that conversation or performance tests act to diminish the intensity of the reaction whereas anxiety, isolation or stress increases it. The dosage factor appears important with the larger doses permitting a greater likelihood of becoming overwhelmed by paranoid thinking, suspicion and acting out. Self-experiments without invigilators or neglect of the subject can be dangerous.

In a patient with a lifelong pattern of day dreaming, Stevenson (10) witnessed a psychotic-like state that lasted for a week. The actual experience had been a profound one with considerable depersonalization. Three days later delusional thinking and considerable hypochondriasis was observed. The patient was seen in therapeutic interviews and made a complete recovery.

Three interesting delayed reactions to mescaline are related by Harley-Mason, *et al.* (7). In each instance these were associated with either excessive fatigue or stress. For example, one patient two weeks after exposure to 400 mg. of mescaline became physically and mentally exhausted. She saw dark, moving objects, and with her eyes closed, dull colored, hypnagogic imagery.

Cooper (3) has also noted the recrudescence of LSD-like effects weeks or months afterwards. This consists of brief episodes of inappropriate mood swings, spatial and temporal distortions, changes in body image and occasional auditory and visual illusions or hallucinations.

The potential dangers in the use of LSD were reviewed by Eisner and Cohen (5). The possibilities of treatment precipitated depression, suicide and psychosis were discussed. Some speculations about the post-LSD reappearance of transient dissociative phenomena in an occasional patient was offered. It was suggested that if this drug did make unconscious fantasy material more available, it might also lower the threshold for subsequent similar experiences. Favorable conditions for the spontaneous re-emergence of primary process elements seem to be extreme tension, meditation and states of relative restriction of sensory inflow. The patient should be made aware of this remote contingency for it is the inability to account for the event that makes it frightening and potentially hazardous.

In summary, the literature directly records only one suicide and that in a schizophrenic patient, and a small number of short,

self-limited psychotic reactions and other lesser side effects. Turning to the questionnaire additional information of assistance to the investigator using LSD becomes available.

IMMEDIATE ADVERSE REACTIONS

Although data on untoward events during the LSD state was not requested, a number of fleeting but impressive incidents were related in response to our inquiry. Osmond² has seen an epinephrine-like reaction with anxiety, pallor, a cold sweat, thready pulse and dilated pupils. The only convulsion noted was described by Sandison. The incidence of seizures is so low that one wonders whether coincidence might explain the single convulsion reported. The most common, but still infrequent, immediate problem was one of unmanageability. This apparently occurs when insight into the situation is lost and the individual acts upon delusory, usually paranoid, ideas. Instances of running away from the tester, disrobing, or accidental self injury were described. For example, a medical student given 125 mcg. developed an acute, hyperactive paranoid state which required restraints for three hours.

Panic episodes were likewise mentioned. When these develop early they seem to represent the terror involved with the loss of ego controls. At the height of the reaction panic may be precipitated by the mobilization of aggressive impulses or by the upsurge of considerable guilt-laden material. Finally, after many hours of frightening dissociation the subject could develop an intense fear that he will not be able to get back to his ordinary state.

Severe physical complaints can dominate the entire experience. Those subjects whose major defensive response is somatization have been able to fight off the psychic effects of the drug at the cost of suffering a variety of aches and pains for six hours. Osmond

warns of the occasional appearance of a severe catatonic state. We have reported one which was impressive to observe (2).

In this regard it may be well to consider which groups are more likely to have unpleasant, painful reactions to LSD. Those with excessive initial apprehension, rigid but brittle defensive structures, or considerable subsurface guilt and conflict could have difficulties. Although there are exceptions, people who find that the implications posed by the LSD experience are contrary to their basic philosophies become dysphoric. Invariably, those who take hallucinogenic agents to demonstrate that they have no value in psychiatric exploration have an unhappy time of it. In a small series of four psychoanalysts who took 100 gamma of LSD, all had dysphoric responses. Two Zen Buddhists were given LSD in order to compare the drug state with the transcendent state achieved through meditation. Both Zen teachers became so uncomfortable that termination with chlorpromazine became necessary.

In the immediate post-LSD period certain undesirable occurrences have been mentioned and it is well to be aware of these possibilities. The first is a simple prolongation of the LSD state. Ordinarily, after a night's rest it is to be expected that complete cessation of the drug effect will have occurred. However, the persistence of anxiety or the visual aberrations for another day or two in wavelike undulations has been described. Isbell reports five such instances in drug addicts given 1-3 mcg/kilo. Feld speaks of a psychology trainee who took the drug for experiential purposes and had to be given phenothiazines and kept on a locked ward for a day because of excitement. An almost identical case was seen by Mayer-Gross. A psychology student was given 120 mcg. as part of an experiment in the biochemistry laboratory. She remained in a state of agitation and motor restlessness for two days. She recovered and has remained well during a seven-year followup.

A valuable point is illustrated by Merlis'

² Where bibliographic reference numbers are not used, the quoted material derives from the questionnaire.

three patients who were left alone after the interview period was completed. The drug effects were declining and it was assumed that they were recovering uneventfully. Instead, they became increasingly tense and confused and required further therapeutic support. This exemplifies the importance of constant attendance even during the waning phase of the psychotomimetic experience.

More frequently remarked upon were short-lived depressions. These have been seen by a number of the correspondents as well as by the writer. A variety of possible causative factors are evident. The depression may simply be the letdown after the drug induced hyperphoria and feeling of self transcendence. If the experience was characterized by an emergence of considerable shame or guilt, an inability to integrate or re-repress the released memories may induce a brief depressive reaction. In the therapeutic situation when the insights acquired during the drug sessions are not translated into altered patterns of behavior and of dealing with people then aggressions may be turned inward (5).

SUICIDE

An analysis of the data on successful and unsuccessful suicide attempts reveals that in only a very few instances a direct connection between the LSD experience and the movement toward self-destruction could be discerned. Some of the reports stated that the suicidal incident was mentioned for completeness rather than because of a conviction that a causal relationship existed. On the other hand, genuine efforts to end one's life have apparently also been seen.

SUICIDE ATTEMPTS

Drowning is considered to be preferred by suicidal LSD patients according to Sandison. Two of his patients attempted to drown themselves and other patients reported drowning fantasies. Although drowning as a preferential mode of destruction is not noted by others, it is interesting to speculate that

death in the grand manner could be considered by those who have achieved a state of complete ego dissolution.

Gilberti treated an obsessive compulsive with a depersonalization syndrome with average amounts of LSD combined with psychotherapy. There was no improvement. A month or two later the patient attempted suicide, was hospitalized and improved after insulin coma therapy.

Ling's case is an example of a devastating insight which overwhelmed the defensive position. Under the drug the patient vividly relieved a period at age two when his father had been in the Navy and his mother had given her "love" indiscriminately and promiscuously to all men except the patient. This uncovered information in a markedly disturbed person produced a depression and attempt at suicide. With intensive psychotherapy he recovered from the depression.

A psychiatric resident in our hospital wanted to see what LSD would do for one of his patients that had not been moving in psychotherapy. The diagnosis was chronic anxiety in a schizoid personality. Twenty-five micrograms were given; during the next few hours the patient kept repeating "I see it all now," but refused to communicate with the therapist. Three days later he scratched his wrists with a razor blade. The depression lifted slowly and he was eventually discharged from the hospital essentially unimproved.

COMPLETED SUICIDES

Consummated suicides attributable to LSD are indeed rare. Savage's case (1) has been referred to already. Stoll, during a visit to this country, spoke of a woman who had been given the drug without her knowledge. The devastating effects of a completely unexplicable psychic disruption were seemingly too much for this person to endure and she took her life.

In response to our questionnaire Hoff related that after two 30 mcg. sessions a patient became depressed for three weeks and

then committed suicide. No further details were given.

A physician who had habitually inhaled nitrous oxide for many years was given 150 mcg. of LSD. Six months afterwards he was found dead in his room with the NO₂ mask on his face. The respondent (Janiger) does not consider that this suicide was the result of LSD administration, rather the occurrence was mentioned "for the record." From the circumstances it may be questioned that suicide had even been contemplated.

A 44 year old suicidally depressed female who was addicted to Demerol was given 50 mcg. of LSD by Hartman. Three previous suicidal attempts had been made and 50 electroshock treatments had been administered in the past. Hospitalization was refused by the patient because of her fear of further shock treatments. The LSD session was marked by the ventilation of some hostility. Five days later she became involved in an argument with her husband who then left her alone against the orders of her physician. She swallowed a lethal amount of snail poison.

It is noteworthy that all the suicidal acts have been in disturbed patients rather than normal subjects. In addition, their response to psychotherapy with LSD had been poor. From the information available these were a seriously disturbed group prior to treatment with LSD. The establishment of improved criteria for the selection of patients and increased attention to the patient who is not progressing under LSD therapy can reduce even further the remote possibility of suicide. There are no reports that LSD itself has been used as a method for committing suicide.

PROLONGED PSYCHOTIC REACTIONS

A number of psychotic breakdowns in association with LSD were reported to us. Hoch and Malitz relate the interesting story of two 30 year old identical twins who were given 180 mcg. of LSD intravenously. One was schizophrenic; he became more autistic,

affectively disordered and in poorer contact. The other twin was brought in as a "normal" control. He reacted with somatic and perceptual disturbances but had recovered by evening and left the hospital. Two days later he developed nausea, tension, a feeling of immobilization, anxiety, depersonalization and preoccupation with a "dream" he had under LSD. He was admitted to the hospital where mild barbiturate sedation was given. Five days later he was discharged and returned to work.

A 25 year old preschizophrenic latent homosexual with many neurotic fixations was mentioned by van Rhijn. He received 200 gamma of LSD with the result that the schizophrenic features became more obvious. His behavior became bizarre and he required hospitalization. The final outcome was not reported.

Hoff reports one and Sandison two cases of prolonged psychotic reactions in patients with dosages in the 100-200 mcg. range. Recovery was incomplete in one of these patients.

Cameron tells of a 23 year old withdrawn, depressed male patient who had had hallucinatory experiences in the past. After the administration of 100 mcg. and the completion of the therapeutic interview he barricaded himself into a room and made an abortive suicidal attempt. The psychotic manifestations persisted for a fortnight and was terminated with 48 hours of deep sleep therapy.

A patient of Janiger's had taken peyote clandestinely before and shortly after two treatments with 125 and 150 mcg. of LSD. He went into what might be described as a chronic LSD state for weeks, culminating in an undifferentiated schizophrenic reaction for which he was hospitalized and treated with phenothiazines. Over a period of six months he made a slow but complete recovery.

A patient at the Metropolitan State Hospital³ was recently brought to our attention.

³ Permission to examine the case record and

He is a 31 year old, divorced male. Since 1951 when he had been a participant observer at the atomic explosion at Eniwietok, he had noted increasing anxiety. It was during this voyage that he received a "Dear John" letter from his wife. Subsequently, the blast was interpreted by him as a manifestation of God's power, at other times it was the serpent in the Garden of Eden.

He developed an intolerance to noise, shakiness especially when around people, fears of heights and elevators, and a phobia about getting his hair cut. There was preoccupation with the significance of his bowel movements. Help was sought from various religious groups and finally he entered the Catholic church. His priest recommended psychiatric care and for two years a therapist saw him two or three times weekly. Apparently he was exposed to an unusual variety of treatments including dream analysis, spiritual readings, reincarnation discussions, a novel sort of group therapy and hypnosis. When no particular response to these procedures took place the therapist gave him LSD in 75, 125 and 175 mcg. doses at weekly intervals. The technique used was rather unconventional. The patient was blindfolded; occasionally the therapist would come into the room and ask him to describe his sensations. After the first session he was depressed for two or three days. The second treatment was the most significant. During it, he clearly saw in great detail, how as a child of four he had smothered his baby brother in order to keep him from crying. He had no previous conscious awareness of the "murder," but has always had a feeling that something bad had happened when he was very young. This material was tape-recorded, as the therapist was not present during parts of this session.

After termination of the interview the memory was so strong and convincing that he went to the police and "confessed."

interview the patient was granted by Dr. Robert Wyers, Superintendent, Metropolitan State Hospital, Norwalk, California..

Whether this incident was fact or fancy could not be established. He was not detained by the police. However, there was an upsurge of agitation, confusion and depression which was not changed by the final LSD interview.

Shortly thereafter, he voluntarily committed himself to Metropolitan State Hospital. At the time of admission poor insight, ideas of reference, flattened affect, circumstantiality and moderate anxiety were described. Psychological testing indicated that the patient was a decompensating schizophrenic who was desperately struggling to reestablish his shattered defenses. He improved slowly over the next half-year without specific therapy.

This case is described in some detail because it illustrates a number of correctible deficiencies which entered into the patient's management.

1. The therapist was possibly a rather disturbed person himself who favored unconventional methods of treatment. His personal experience with LSD as a therapeutic agent was limited.

2. The therapist did not deal with the highly traumatic material as it arose, resolving the guilt feelings, giving support, etc. Instead of a disaster, the second session may well have been highly therapeutic.

3. The patient was blindfolded and left alone for long periods. This in itself might well evoke panic. There should have been constant contact with the therapist or other trained person.

4. It may be that LSD was relatively contraindicated for the patient. Incipient schizophrenics are considered increased risks for this type of therapy.

Of the eight instances of psychotic reactions lasting more than 48 hours that were reported in response to our questionnaire, only one was in an experimental subject and that subsided within a few days. It is to be recalled that he was the identical twin of a schizophrenic. The remaining seven cases occurred in patients undergoing therapy. Two of these went into a remission within a

TABLE 1
*Estimated Rates of Major Complications
Associated with LSD*

	Attempted Suicide	Completed Suicide	Psychotic reaction over 48 hours
Experimental subjects	0/1000	0/1000	0.8/1000
Patients under- going therapy	1.2/1000	0.4/1000	1.8/1000

few weeks and the other five had either prolonged courses or the details were insufficient to establish the outcome.

A tabulation of the material supplied in the survey indicates the approximate incidence of the important complications encountered (Table 1).

ADDICTION

No instance of addiction to LSD was reported. Physiological addiction is unlikely because of the extremely rapid onset of tolerance (1). Psychological habituation is conceivable but the groups prone to addiction, the immature dependent or the acting out psychopath, are more likely to have an unpleasant than an euphoric response to LSD. None of the respondents indicate that the individuals who achieve a mystical state with the assistance of this drug have become habituated. As an investigative drug the controlled supply of LSD does not permit a final answer to the question of addiction. If it should become generally available we will obtain confirmation or denial of our opinions concerning its nonaddictability.

PRECAUTIONS

SCREENING

Many investigators insist upon a preliminary physical and psychiatric examination of subjects. A family or personal history of nervous breakdown is sufficient to exclude volunteers from some studies. Occasionally, a liver panel, electrocardiogram, MMPI or other psychologic screening test is required. Most commonly, a psychiatric interview

with the prospective candidate is considered sufficient for selection of experimental subjects. The interview is also used for orientation, to establish rapport and to answer questions which may be bothering the volunteer. In some institutions signed releases are obtained.

The patient considered for LSD is probably fairly well known to the therapist. His selection is an individualized problem, and certain relative contraindications will be discussed later. His briefing is a matter of some importance, with the value of the drug interview sometimes depending on the preliminary instructions. Something of the nature of the experience and the expectations for the session are communicated at this time. Misconceptions are corrected and necessary reassurances are given.

DURING THE SESSION

That the person under the influence of LSD should not be left alone is universally agreed. Human contact is comforting and serves as a pivot between every day reality and the strange world of LSD. Without it the patient can readily lose all orientation. Personnel in contact with the subject should be experienced and sympathetic. Control of the subject through continuous observation by trained and understanding workers is one of the more important preventative measures that can be taken.

The significance of personnel attitudes and of the setting for the therapeutic application of LSD should be mentioned. The state is a highly suggestive one with the patient responding strongly to environmental cues. He can sense the therapist's unspoken feelings with phenomenal accuracy. Impersonality, coldness and disinterest is the equivalent of being left alone.

Although rarely needed, LSD antagonists should be available. Chlorpromazine is the most satisfactory agent for termination. When a rapid effect is desired 25-50 mg parenterally is given, 50 mg orally acts slower but is effective in a half hour. These

amounts can be repeated if necessary. The other phenothiazines have not been used as frequently and those with a piperazine ring in the side chain may not equal chlorpromazine in reversing the LSD state. The action of azacyclonal is dubious. Reserpine has occasionally intensified the reaction. Nicotinic acid is successfully used by one group. Intravenous or intramuscular sodium amytal in 0.375–0.75 Gm. amounts is an effective agent in aborting LSD activity.

POST-LSD CONSIDERATIONS

Normal volunteers are ordinarily allowed to leave the hospital eight hours after an average dose has been ingested. However, they are not permitted to drive and they should spend the evening quietly at home with someone who knows the approximate nature of their experience. The opportunity for telephonic contact with the investigator ought to be possible. Sometimes a sedative is routinely prescribed at bedtime.

The outpatient receiving LSD is required to stay in the hospital overnight by many therapists. He remains in a room with a nurse or attendant in the adjacent area. Sleeping medicine is available if needed. Nondrug interviews shortly afterwards are recommended to re-order and re-evaluate the emotional and intellectual elements of the LSD experience. Sandison suggests more followup care be given those who have had 150 mcg. or more.

CONTRAINDICATIONS

Naturally, detectable neuropsychiatric disease in volunteers and paid subjects is cause for exclusion from experimental work requiring a relatively normal group. It is surprising how often serious psychopathology is found among these people. It is entirely possible that LSD and mescaline attract certain unstable individuals in their search for some magical intervention.

With respect to patient selection, there is general agreement that markedly schizoid personalities or compensated schizophrenics

should be excluded because of the possibility of precipitation into a psychosis. The established schizophrenic also tends to do poorly with the hallucinogens, yet a variable degree of success in their treatment has been reported using special techniques. No one is inclined to consider the organic psychotic as a candidate for LSD therapy. The epileptic is also ordinarily excluded although prudence rather than evidence dictates this restriction. The mentally retarded patient would seem to be a poor choice.

Serious, active physical disease is a contraindication to therapy if only because the stress of an LSD experience can be exhausting. Nevertheless, following Huxley's and Heard's (8) suggestion, we have given LSD to a small number of terminal cancer patients, who had difficulty accepting the idea of their personal death, without untoward effects.

Since these drugs are detoxified in the liver (11), damage of that organ is assumed to be a bar to treatment. This restriction may be more rational with regard to mescaline than LSD because the latter drug was administered to a series of unselected Skid Row alcoholics (4) many of whom had fatty livers or cirrhosis, without unusual sequelae.

Individual therapists would avoid placing obsessive compulsives, hysterical or acutely anxious and agitated patients into the treatment situation. Others feel that these groups are the ones that respond best to LSD therapy. The seriously depressed patient is avoided by some because of the danger of suicide. Although the risk is greater, we are inclined to think that suicide can also be averted with LSD in selected depressed patients. However, they must be kept in a completely controlled situation. The precise contraindications have not yet been worked out for the neurotic patient.

The paranoid personality should be regarded dubiously with respect to LSD. On occasion, one of them will become grandiose as a result of a mystical experience under the drug and will use this as final proof of a

hitherto only suspected omnipotence. In one case that was indirectly observed (5) systematized delusions concerning LSD and religion developed. This happened to be the therapist's first case in which LSD was used and he reacted to the heady and extremely well-structured delusory schemes by going along with them initially. This points up the requirement that the doctor who employs LSD as a psychotherapeutic adjunct be a mature person. It is conceivable that LSD may serve as a gratification for the therapist's own needs for power.

MESCALINE

Although this survey dealt primarily with lysergic acid diethylamide, information with regard to side effects with mescaline was also received. In general these tended to duplicate comments submitted with reference to the former drug.

The well known proclivity for mescaline to produce some nausea and, less frequently, emesis was again noted. Two of Denber's patients sustained a shock-like state ten minutes after receiving 500 mg. intravenously. The blood pressure fell, the pulse became imperceptible, and the skin was ashen and cold. Anxiety and agitation were obvious. Intravenous sodium amytal blocked these effects in one case and chlorpromazine in the other. Denber suspects that a paroxysmal cardiac irregularity may have been causative. A severe panic reaction was witnessed by Smythies requiring termination of the experiment with intravenous sodium amytal.

The fleeting recurrence of the mescaline state after a period of complete recovery was listed by four investigators. One wonders whether this phasic relapse may not be somewhat more frequent with mescaline than with LSD.

Stevenson gave 400 mg. of mescaline to a young girl who proceeded to have auditory hallucinations and doubts about the reality of perceived objects for several days there-

after. She made an uneventful recovery without residuals except for a distaste for mescaline.

DISCUSSION

This report of adverse effects and complications to the more common psychotomimetic drugs is doubtless incomplete. However, it must be generally representative of the gamut of mishaps that might be encountered. By far, the greatest morbidity and mortality occurs in patients rather than experimental subjects. How it compares in this regard to other treatment modalities is quite unknown. A search of the literature for a statistical report on the incidence of suicide during psychoanalysis or other forms of psychotherapy was fruitless.

The hallucinogenic experience is so striking that many subsequent disturbances may be attributed to it without further justification. The highly suggestible or hysterical individual would tend to focus on his LSD experience to explain subsequent illness. Patients have complained to Abramson that their LSD exposure produced migraine headaches and attacks of influenza up to a year later. One Chinese girl became paraplegic and ascribed this catastrophe to LSD. It so happened that these people were all in the control group and had received nothing but tap water.

Abramson reports no complications in his large series and is inclined to think that a placebo effect accounts for many of the mishaps observed by others. That this is plausible is demonstrated by Busch's comment that the only suicide attempt he has seen was in his control group. An immediate, severe skin reaction following the ingestion of distilled water as an LSD placebo is mentioned by Ditman.

The physician might likewise be inclined to attribute undesirable incidents that arise to an unique and potent psychochemical. This could lead to an overreporting of side effects. Conversely, serious complications

may sometimes go unreported because the investigator has guilt feelings about the matter.

The precautions which could reduce the incidence of untoward incidents may be briefly summarized.

1. The careful and thoughtful selection of subjects and patients is a necessity. For the psychotherapist not too familiar with this modality, particular care in the choice of patients is desirable. Prepsychotic individuals and those whose major defense is paranoid projection are apt to be aberrant reactors.

2. A sufficient level of control of the patient during and after the experience is necessary. The need for constant attendance during the session has been mentioned. Those who move to either extreme of the emotional scale and those whose reality contact is impaired should be appropriately accompanied even when going to the toilet. Hospitalization for 24 hours is justified for patients especially when more than one mcg/kilo is used. Experimental subjects whose LSD state has subsided may be taken home on the conditions that a friend or relative be available and that decision-making of a major nature be delayed until the next day.

3. The patient may require reassurance and support during the active phase of the drug's activity. The physician need not be constantly present, a trained and sympathetic nurse or attendant may substitute for him.

4. The technique of using LSD as a psychiatric adjunct is a special skill. The therapist himself should probably have experienced the LSD state. It appears that complications are more likely with a therapist who is relatively unfamiliar with the agent. Supervision of the first few interviews by a physician experienced in LSD therapy might be desirable.

5. The therapist must be prepared to handle a sudden upheaval of repressed and

traumatic memories without permitting the patient to be overwhelmed. The preferred technique for doing psychotherapy with LSD is far from settled. The accelerated recall of memories with strong emotional content requires an active, rather than an expectant, participation by the therapist.

6. Personnel in contact with the LSD patient ought to be specifically trained and understanding of the nature of the state.

7. Measures to counteract the effect of the drug should be at hand.

8. In the days following the exposure the physician must be available for consultation should disturbing symptoms develop.

CONCLUSION

From a review of the literature and the communications of 44 physicians who have administered LSD or mescaline, an attempt to categorize and analyze the potential hazards has been made. This inquiry into the adverse effects of the hallucinogenic drugs indicates that with proper precautions they are safe when given to a selected healthy group. Their use in patients has been associated with an occasional complication. An analysis of these incidents suggests that with the application of certain safeguards many of the side effects might have been avoided.

REFERENCES

1. CHOLDEN, L. S., KURLAND, A. AND SAVAGE, C. Clinical reactions and tolerance to LSD in chronic schizophrenia. *J. Nerv. & Ment. Dis.*, 122: 211-221, 1955.
2. COHEN, S., FICHMAN, L. AND EISNER, B. G. Subjective reports of lysergic acid diethylamide in a context of psychological test performance. *Am. J. Psychiat.*, 115: 30-35, 1958.
3. COOPER, H. A. Hallucinogenic drugs. *Lancet*, 268: 1078, 1955.
4. DITMAN, K. Personal communication.
5. EISNER, B. G. AND COHEN, S. Psychotherapy with lysergic acid diethylamide. *J. Nerv. & Ment. Dis.*, 127: 528-539, 1958.
6. ELKES, C., ELKES, J. AND MAYER-GROSS, W. Hallucinogenic drugs. *Lancet*, 268: 719, 1955.
7. HARLEY-MASON, J., LAIRD, A. H. AND SMYTHIES, J. R. The metabolism of mescaline in the human. *Confinia neurol.*, 18: 152-155, 1958.

8. HUXLEY, A. AND HEARD, G. Personal communication.
9. SAVAGE, C. The resolution and subsequent remobilization of resistance by LSD in psychotherapy. *J. Nerv. & Ment. Dis.*, 125: 434-437, 1957.
10. STEVENSON, I. Comments on the psychological effects of mescaline and allied drugs. *J. Nerv. & Ment. Dis.*, 125: 438-441, 1957.
11. STOLL, A., ROTHLIN, E., RUTSCHMANN, J. AND SCHALCH, W. R. Distribution and fate of C^{14} labeled LSD-25 in the animal body. *Experientia*, 11: 396-399, 1955.