Prolonged Adverse Reactions to Lysergic Acid Diethylamide

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Recently the authors[1] briefly reported complications and misuses associated with hallucinogenic drugs, such as D-lysergic acid diethylamide (LSD). Recently, an increasing number of adverse reactions to these drugs have occurred, and a discussion of the nature of the complications appears indicated. It is not our intention to minimize the potential value of these agents. Rather, we wish to emphasize the importance of continued research with this group of compounds, so that their advantages and limitations are eventually understood. We have already reported on certain aspects of their therapeutic properties.[2,3] However, the question of their therapeutic value remains unsettled since no definitive study has been reported. It is our impression that they are unique tools in the study of altered states of awareness, perception, and ideation.

The nomenclature of these compounds poses problems. "Hallucinogen" is a poor name for this group since true hallucinations occur infrequently. "Illusinogen"[4,5] would be more appropriate, for almost invariably distortions of perception elaborated from sensory cues are noted. The term "psychotomimetic" has been popular, but only delineates a segment of the reaction forms, for many subjects do not experience a psychotic-like state at all. Osmond's term[6] "psychedelic," meaning mind manifesting, has the advantage of being nonjudgmental, but may be too general, since psychic stimulants and sedatives could logically be included under the phrase "mind manifesting." Other

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names for this group of drugs have been: phantastica, deliriants, psychotogens, and psychodysleptics.

An impressive list of botanicals and synthetic chemicals with hallucinogenic properties has been found as a result of assiduous searches by modern psychopharmacologists and primitive man. Chemically, they may be subclassified according to the inclusion or the absence of an indole ring in their structure.

A. The principal indole hallucinogens are:

1. D-Lysergic acid diethylamide (LSD) and its many congeners. LSD is a semisynthetic diethylamide from lysergic acid, a naturally occurring consituent of the fungus, ergot. A recent development is Hofmann's[7] isolation of D-lysergic acid monoethylamide and D-isolysergic acid from ololiuqui. For the first time a lysergic acid derivative with hallucinogenic activity has been found in nature.

2. Psilocybine (4-hydroxy-N-dimethyltryptamine orthophosphate) and psilocin (4-hydroxydimethyltryptamine). These were isolated by Hofmann[8] from the Mexican mushrooms of the *Psilocybe mexicana* group.

3. Bufotenine (5-hydroxy-N-dimethyltryptamine). This is an hallucinogen with marked autonomic properties which has been separated from both the skin of certain toads and from cohaba snuff.

B. The principal nonindolic psychotogens are:

1. Mescaline (3,4,5,-trimethoxyphenethylamine) obtained from the peyote cactus. The buttons of the plant have been used for centuries by Mexican and Southwestern Indians as part of their religious rituals.

2. Hashish (marihuana, cannabis indica). This is also a drug with a long and intriguing history. Yogis found it useful as an aid in meditation. The Thug and Hashishin (assassin) sects employed it for more nefarious purposes. A series of cannabinols have been extracted from hashish and need further investigation.

From a review of the literature and a survey of investigators three years ago, one of us[9] reported on a number of difficulties encountered with the use of LSD. Results of this study are enumerated below:

1. Complications were more apt to occur in patients undergoing psychotherapy with the drug than in experimental subjects.

2. The LSD experience was so dramatic that subsequent illness might be attributed to the drug exposure by either patient or physician.

3. Physical disturbances attributable to the drug were extremely rare and did not cluster about any single organ system.

4. Psychological complications, although infrequent, were the main problems arising from the use of LSD. They consisted of attempted or completed suicides and prolonged psychotic reactions.

5. No instance of physiologic addiction to LSD was encountered.

6. Precautions in selection of patients and subjects and their protection during and after the LSD state were proposed.

More recently, additional untoward effects to LSD have come to our attention; some of them have not been adequately described in previous communications.

I. *Prolonged Psychotic Decompensation.*

A single, or a series of, LSD treatments can produce a psychotic break presumably by releasing overwhelming conflictual material which cannot be handled by the patient's established defenses. It is possible that LSD disrupts psychic homeostatic mechanisms and permits reinforcement of latent delusional or paranoid ideas. Presumably, this occurs when the normal aversive and critical functions of the ego are impaired under LSD.

CASE 1.—The patient, a 36-year-old, married legal secretary appeared requesting psychiatric treatment. At the time of the interview, two years after a single LSD experience, she was preoccupied with pseudophilosophic abstractions about truth, beauty, love, and life. She was flamboyant, under considerable pressure of speech, and easily distractible. Her associations were loose, and her thinking processes were tangential. She stated that under her LSD relevation, "I saw the awful truth: what I am, and how to love people."

Following the experience she complained of an inability to control her thoughts. A belief that she was in the Garden of Eden, preoccupation with religious themes, and socially unacceptable behavior such as appearing nude in public became manifest. Ten days after her LSD treatment her husband placed her in a mental hospital and she was given a series of electroshock treatments. Despite partial improvement she has had long periods when she was unable to work because of emotional lability and uninhibited speech and behavior. Several subsequent hospitalizations have been necessary.

The diagnostic impression was one of an affective schizophrenia. Although a schizophrenic process may have antedated the LSD treatment, the patient functioned well and held responsible positions prior to her breakdown. She was recently given a course of thioridazine medication with definite improvement.

CASE 2.—The patient was a 32-year-old secretary to a psychotherapist who had a large "LSD practice." She states that she had taken LSD 200-300 times within a three-year period in dose of 25μg-400μg. In addition, other hallucinogens, sedatives, and stimulants had been tried singly and in various combinations. Most of these drug experiences were pleasant, but more recently they had become dysphoric. She stated that the LSD changed her from an inhibited, blocked person to a "freer" individual, but it had left her without control over her emotions.

When first seen she was in a panic-like state, loose in verbal associations, fearful of being alone, and expressing a strong desire for sedation. Frightening, spontaneous recurrences of the hallucinatory phenomena which had been seen under LSD were almost daily events. These consisted of skulls of familiar faces moving on the wall and feelings of accompanying horror.

Despite some initial improvement on chlordiazepoxide, she remained anxious, depressed, and overdependent.

In this patient the extraordinary frequent ingestion of LSD and other psychochemicals resulted in a borderline panic state with spontaneous visual hallucinatory phenomena.

CASE 3.—The patient was a 41-year-old white female office manager who was referred by her therapist. Since her last LSD treatment, two years ago, she had been panicky, agitated, depressed, and obsessed about going crazy or killing herself.

Her early life had been very chaotic. The only relationship between the mother and father was one of bickering, assaultiveness, and reprisal. From the time she was 11 and until she was 14 her alcoholic father had sexually played with her. When the patient was 17 the father killed her mother and himself. For a short period she was a prostitute. During this time she became pregnant and bore an illegitimate female child. She has had two brief marriages and is now divorced.

Two years ago she made an unsuccessful suicide attempt with sleeping pills. After this she received a course of electroshock therapy for depression. Two months later, she was given eight LSD therapy sessions. The eighth session was so frightening that she fled to another part of the country to avoid further treatment.

Since that time she has been confused, agitated, and preoccupied with guilt feelings about her life. Copious weeping and occasional screams interrupted the interview. She told her story quite dramatically. She claimed to be unable to be in crowds or alone, unable to sleep, eat, or work. Hospitalization was recommended but refused. A short time later another suicide attempt with barbiturates was made. After recovery she was kept in the hospital for a three-month course of psychotherapy with partial improvement and was discharged to outpatient group therapy.

This patient represented a poor candidate for LSD therapy. She was a tenuously adjusted person who had never formed any meaningful relationships. During her LSD interviews unconscious material became available to her which she could neither accept nor repress. As a result her defenses appeared to disintegrate. An array of hysterical, obsessive-compulsive, and hypochondriacal, fragmented coping efforts were made. Extreme anxiety culminating in panic-like episodes was recurrent. Her emotional disturbance was so great that she was considered to be psychotic by some examiners. Others believed that she was an hysterical personality in an extreme anxiety and depressive reaction.

CASE 4.—(This case was seen in consultation with Dr. Sherman Little, Children's Hospital, Los Angeles.) A 10-year-old male accidentally ingested a sugar cube containing 100μg of LSD which his father, a detective, had confiscated from a "pusher." The child had a severe reaction with colored visual distortions, hallucinations, and anxiety. These became less distressing during the next three days but did not subside.

Chlorpromazine did not completely control the phenomena but did diminish "the pain of the checkerboards passing through my body."

When the boy returned to school a week later the pages wavered and interfered with his reading. While looking at the TV screen he would become upset because he saw movements without the set being on. A lump would form in his throat, and he clung to his father at these times. Some days might be completely uneventful; on others he re-experienced the visual illusions and became anxious.

One month after the incident he still saw light halos with closed eyes. Hospitalization at this time resulted in a gradual but complete improvement.

CASE 5.—The patient was a white, married male who teaches hypnosis. He complained of episodic anxiety, a variety of pains, depression, and visual distortions for seven months since taking LSD about 25 times for psychotherapeutic purposes. At present he has feelings of impending doom, at times he "wants to climb the walls." The periodic illusions and emotional upsets come on when he is under stress. During these episodes he sees animals and faces moving on the wall.

He claims that prior to the LSD treatments he had no anxiety, but was unproductive and "zombie-like." At present he is writing five books and wonders, "Do I have to pay for this higher level of functioning with anxiety and pain?"

There is a flavor of grandiosity to his ideation. For example, he told his mother some of her thoughts before he was born. He speaks of his mental activity as though it has a special potency as when he says, "I have to watch my thoughts, I might think myself dead."

The impression is that of an anxiety and depressive reaction with dissociative features reminiscent of the LSD experience. In our opinion his LSD therapy did not succeed in working through his conflicts, or re-repressing the traumatic material recalled under the drug sessions.

II. *Depressive Reactions.*—When the LSD experience mobilizes considerable feelings of guilt or shame, an extended depression can result. In rigid or overconscientious individuals who undergo the ego dissolution that the hallucinogens can induce, a depression may follow the use of the drug.

CASE 6.—The subject was a psychoanalyst who took 100μg of LSD in order to experience LSD state. Although the visual effects were intriguing, he complained of considerable somatic discomfort during the period of drug activity.

For the next eight months, he presented a picture of an hypochondriacal agitated depression. He complained of weakness, back pain, and leg cramps. For a long time he was convinced that a coronary occlusion had occurred. This was never confirmed by laboratory tests. He was restless, anxious, and unhappy. He ruminated about the possibility that he had revealed damaging unconscious material during the LSD period. He made a slow but complete recovery.

III. *Release of Pre-Existing Psychopathic or Asocial Trends with Acting Out, or Abandonment of Social Responsibilities.*—This is illustrated by the following cases.

CASE 7.—The patient was a married, white female housewife who appeared seeking a diagnosis. It was difficult to say whether she was sober and garrulous, or mildly under the influence of some drug at the first interview.

Her early history included the fact that at 15 years of age she ran away from a reform school and appeared at a Vedanta Center 2,000 miles away, dirty, in rags, and hungry. She was taken in, and she spent a number of months there. Later, while studying in a New York City college as a "psych major" she lived in Greenwich Village, smoked marihuana, and enjoyed the marginal life of that colony. Seven years ago she "settled down" by becoming pregnant and marrying an older man, a "square." They had two children, and she says that she was a model mother.

She has had LSD at least six times. On the first occasion she suddenly realized that her mother wanted a boy when she was born. Subsequent occasions are described as "immensely valuable" and the "opening up a new world" and as "something that one should have every Saturday night."

During the last three occasions the LSD was combined with carbon dioxide inhalations, methylphenidate, and JB-329, an experimental psychotomimetic drug with atropine-like effects. She then became involved in a group who used marihuana, meperidine, and opium, all obtained from Mexico. These drugs, she claimed, helped her write better. She asserts that she was not addicted to any of these, "there were no withdrawal symptoms." In order to obtain her own supplies she ran away to Mexico with her pusher and discovered a "beat" colony at Guadalajara where heroin, barbiturates, and marihuana are apparently items of commerce. This period of sexual and artistic looseness is described with considerable positive affect. She returned to her home eventually because of her children, bringing back a supply of "pot" and heroin. She cannot decide whether to stay with her children or abandon them for the amoral, irresponsible life of the "beat" world.

A role that LSD could have played in this woman's acting out behavior was to release her partially suppressed impulses and reduce any existing counterforces. Her LSD exposures had occurred essentially without therapeutic support or assistance, after which she fell back into an earlier mode of existence which is now too entrancing to relinquish.

The impression is one of antisocial reaction in an emotionally immature personality whose current behavior may have been triggered by haphazard LSD exposure.

The patient also illustrates "multihabituation," the misuse of a variety of sedatives, narcotics, stimulants, and hallucinogens taken in series by borderline individuals. Such individuals claim not to get "hooked" on any one agent. They are certainly habituated to the drugged state. This "offbeat" existence satisfies the need for forbidden or unique experiences and the need to get away from their sober selves.

CASE 8.—The patient is a white male who received four LSD sessions (50μg-150μg) in a state hospital. During his third treatment the patient developed an overwhelming feeling that he was turning into a bad person, a monster. The threatening or unacceptable impulses that emerged aroused intense panic feelings, and intramuscular chlorpromazine was given to abort the episode.

His past history includes the information that he had been arrested over a hundred times for armed robbery. Two months after leaving the hospital he was arrested for grand theft. His defense was that LSD had changed his personality and he was not responsible for his actions. This was unacceptable to the court, and he was convicted and sentenced.

This instance is included, not to illustrate an adverse reaction to LSD, but to demonstrate how a sociopath can try to use the drug experience to excuse his subsequent behavior.

IV. *Paranoid Reactions—Confirmation of Latent Ideas of Grandiosity by the Tran-*

scendental Aspects of the LSD Experience.—People who use paranoid mechanisms of denial and projection are relatively poor candidates for LSD. Their rigid, sometimes tenuous, grasp on reality may be disrupted for long periods of time.

They may react with increased suspiciousness and incorporate the drug experience as part of a vast plot. More commonly the chemical ego dissolution results in intense feelings of unity, death and rebirth, salvation and redemption. After the drug effects have worn off, the megalomaniacal belief that the individual has been chosen to convert others to the new faith may be retained. Small LSD sects have been established on this basis. The leaders gain considerable gratification out of their position of omnipotence which includes granting their disciples the LSD experience. Recently one lawsuit brought attention to a pastor who told his congregation that LSD could bring them all closer to God. Without entering into the complex and provocative problem of the drug-induced religious experience at this time, it seems obvious that sweeping recommendations that everyone ought to take LSD is an unsophisticated utterance with dangerous potential.

CASE 9.—A psychologist was given LSD on three occasions (75μg-125μg) and for weeks thereafter acted out grandiose plans. One was to take over Sandoz Laboratories in order to secure the world supply of the drug. He threatened his wife with a gun, then left her, wrote some songs and plays of minor merit, and went off to live in the desert. He recovered gradually after a number of months without specific treatment.

It is not difficult to identify the individuals who openly express their megalomaniacal notions. There are others who are sufficiently aware of the reality situation to keep the knowledge of their own omnipotence hidden. They can become quite successful in controlling people in the role of religious leaders or lay therapists.

Comment

The actual incidence of serious complications following LSD administration is not known. We believe, however, that they are infrequent. It is surprising that such a profound psychological experience leaves adverse residuals so rarely. This may lend support to the impression that psychological homeostatic mechanisms for handling acute stresses are more resilient than is commonly believed.

As the serious complications to LSD are reviewed, certain patterns seem to emerge.

1. The patients who have difficulty tend to be emotionally labile, often hysterical or paranoid personalities. Many are already in treatment, and others seek out LSD therapists hoping that some instantaneous, magical experience will cure them. They are hypersuggestible and, given a drug which reduces critical ego function, can become overwhelmed with a deluge of anxiety and guilt laden "insights."

2. In the majority of the cases who developed complications the drug had been obtained from improper sources. A black market [1] exists in this country, and tablets, ampules, and sugar cubes saturated with LSD have become available in the large cities and on some university campuses. Certain practitioners obtain supplies from Mexico and other foreign countries.

3. It is noteworthy that when a psychotic reaction follows LSD usage, the clinical picture is reminiscent of the drugged condition. Hallucinations tend to be visual with colors and movement of objects characteristic of the LSD state. It is as though the pattern of psychosis mimics the dissociation that precipitated it.

4. Although a number of the patients recognized that the LSD had caused their psychotic or neurotic break, nevertheless they believed that the treatment had been extraordinary and often sought additional drug exposures. Such faith reflects the unusual nature of the experience and the personality of the patients concerned.

5. Therapists who administer hallucinogens should clearly recognize their patients' motivations and the potential hazards of a profound consciousness-changing experience. In view of the psychological potency of these chemicals the therapist should scruti-

nize his own motives in administering them. Until the indications, techniques, and precautions are better understood, LSD therapy should be restricted to investigators in institutions and hospitals where the patient's protection is greater and appropriate countermeasures are available in case of adverse reactions.

6. It appears that antisocial groups have embraced LSD and mescaline in addition to marihuana, the amphetamines, the barbiturates, and the narcotics. Since the LSD state can be a shattering one psychologically, these individuals may sustain severe undesirable reactions. Easy access to the drug will result in its accidental or deliberate administration to people without their knowledge, and this can be a devastating event. We can only repeat[9] that carefully screened, maximally supervised patients given the drug by responsible, experienced investigators will avoid many difficulties in the postdrug period. The imprudent, cursory use of LSD and allied drugs is unsafe, and the complications that sometimes result retard their proper scientific study. When undesirable reactions and sensational publicity become associated with a drug, competent investigators are inclined to avoid participating in the careful, thoughtful studies which are necessary to evaluate it properly.

Summary

Adverse effects can occasionally follow the administration of D-lysergic acid diethylamide (LSD). Complications such as prolonged psychotic reactions, severe depressive and anxiety states, or intensified sociopathic behavior are much more likely to occur after the unsupervised or inexpert use of this drug. When properly employed, LSD is a relatively safe and important research tool.

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