THE COMPLICATIONS OF LSD: A REVIEW OF THE LITERATURE

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While some would insist that all the symptoms of lysergic acid diethylamide (LSD) are in fact complications in that they involve an alteration of the mental state from normal, the present paper will restrict itself to a more limited definition. A complication is defined as an unplanned sequel to administration of the drug, having deleterious effects on the mental or physical health of the subject or those around him.

The material will be presented in as strict chronological order as possible, and this will involve some degree of repetition. The review is felt to be extensive, but by no means exhaustive. It has been achieved by following up specific medical references to the complications of LSD and by culling from that portion of the literature which has come to attention in the course of reading about the drug.

In retrospect, the first person to suggest dangers in the use of LSD appears to have been Hofman (1943) (42). After accidentally ingesting some of the drug while manufacturing it in his laboratory, he experienced a variety of peculiar mental phenomena which led him to fear at one point that he was going insane.

Over the next 12 years, about 80 papers were published on the subject of LSD, mainly dealing with animal and biochemical studies. However, even after only limited human experimentation, the first serious warning about the drug was given in 1955 by Elkes, Elkes and Mayer-Gross (15). Basing their observations on use of the drug with normal volunteers and on reliable reports from colleagues, these authors pointed out that the subject under the influence of LSD could be a danger to himself and others and that early psychotic conditions might be aggravated by it. They also stated that a "delayed and exceptionally severe response may take place and be followed by serious after effects lasting several days" (15, p. 719). They urged that until more was known about the drug its use should be restricted to inpatients and even then only when constant supervision by trained personnel was available.

Cooper (1955) followed this up with a letter to the same journal citing his observations on eight patients. He reported that in the acute phase "sometimes dream-like situations were acted out violently" (11, p. 1078). He described in detail some of the reactions which occurred more than 24 hours after administration of LSD. These included mood swings occurring 2 or 3 days later, childish regression 1 week later, and preoccupation and absent-mindedness persisting for weeks afterwards. Insomnia was described as "a great difficulty" and it was pointed out that adverse reactions were particularly likely to occur when the individual was relaxing for sleep. He also noted that the reactions could begin again after an apparent return to normal behavior.

The first mention of the dangers of extramedical administration was made by Savage (1956), who referred to a woman who became suicidal after taking the drug informally. He also stated that "the average subject was unable to judge when the
effect of the drug had terminated. After he considered himself recovered, he might get a renewed or secondary effect of the drug" (37, p. 38).

Martin (1957), reporting on a series of 50 patients attending a day hospital for LSD treatments, mentioned that two of these had "a violent reaction on their first and second treatments, thus rendering them unsuitable for day-patient treatment" (32, p. 189), but no further details were given.

Savage (1957) was the first to describe a suicide in connection with LSD. This occurred in a schizophrenic girl who had been sick for 10 years and who was being treated with LSD weekly. The treatment apparently "mobilized tremendous rage and resentment against both her parents and myself. At this time, unfortunately, she was allowed to go home on a visit, where she borrowed the family ear and threw herself under a train. While LSD mobilized feelings and affects which had been successfully handled by nihilistic delusions, it also mobilized the supreme resistance: suicide" (38, p. 436). In the same paper, Savage described another case of a woman outpatient who required 4 days of hospitalization for depression during her course of LSD treatment, which she subsequently discontinued.

Lewis and Sloane (1958) reported a "catastrophic breakdown of defences with fear of impending ego dissolution" (25, p. 24) in two of their normal volunteer controls who also happened to be psychiatrists. Both of them had moderately severe paranoid reactions which were only partially responsive to intravenous amobarbital. One of them felt out of touch with reality for several days afterwards. The authors also reported the recurrence of LSD experiences for some time after the administration, and they felt that "the severity of some reactions precludes that use of the drug in out-patient work". Rather prophetically, they concluded "the use of such a drug might seem to raise almost as many problems as it solves" (25, p. 30).

Eisner and Cohen (1958) (13) reported that they had also noted a "spontaneous occurrence" of LSD-like phenomena at varying intervals following treatment. In commenting on the danger of suicide, they stated that this appeared to be restricted to the higher dosage levels above 75 gamma and to an unfamiliarity with the drug. In this paper they reported that Stoll, who had been involved in the early investigation of LSD with Hofman, had in a personal communication to them reported two suicides in Europe, one of these occurring in a woman who was given the drug without her knowledge. They also noted that transient depressions could occur after LSD and they themselves had "indirectly observed" one case of "treatment precipitated phychosis." They also described an impairment of coordination, and one of their rules in using this drug was that patients should not drive immediately after the treatment. While they generally felt that the drug was safe in the proper hands, they insisted "It is self-evident that the drug should be administered only under medical supervision."

Klee and Weintraub (1953) described four cases of paranoid reactions lasting a few days in "normal" subjects given LSD. They linked these reactions with the previous personalities and emphasized the need for careful screening and handling of volunteers "since paranoid reactions following LSD may become prolonged" (22, p. 460).

Cohen (1960) (7) received replies from 44 out of 62 LSD researchers whom he questioned about the incidence of complications. He estimated that the replies referred to a total of about 25,000 LSD treatments administered to 5,000 individuals. Combining the replies to the questionnaire with a survey of the literature, Cohen reported the following:

1) Adverse reactions during the LSD
treatment included unmanageability, disrobing, accidental self-injury, panic episodes, frightening dissociation, acute hyperactive paranoid state, severe physical complaints and severe catatonic states.

2) During the immediate post-LSD period, there could be a prolongation of the LSD state, with the persistence of anxiety or visual apparitions for another day or two in wavelike undulations. Short-lived depressions were also described during the immediate post-LSD period.

3) Suicide attempts were reported on five occasions by Sandison (two attempted drownings) and by Gilberti et al. (one each).

4) Completed suicides were also reported in five cases by Savage, Hoff (after two 30 gamma sessions), Janiger, Hartman (after one 50 gamma session), and Stoll. This seems to include only one of the two patients referred to by Stoll in the previous paper by Eisner and Cohen. However, Janiger's patient was not considered to be directly linked to LSD administration, since his death occurred 6 months afterwards and was due to nitrous oxide inhalation, to which the subject had been habituated for many years.

5) Prolonged psychosis was reported in eight cases by Hoch and Malitz, van Rhijn, Hoff, Cameron (who also reported a suicide attempt in the same patient), Janiger and Cohen (all one each) and by Sandison (two). All of these psychoses lasted over 48 hours.

6) One grand mal seizure was reported.

In a table in his article, Cohen gives the estimated rates of the major complications associated with LSD, but in a personal communication2 he has indicated that this table was not related to the cases described in the text but utilized additional suicides and attempts, where details of dosage and circumstances were not given. Using this data, he estimated the rate of completed suicide after LSD was given in medical settings to be 0.4 per 1,000 patients. No suicides or attempts were reported in control volunteers given LSD, but psychotic reactions over 48 hours were estimated to occur in 0.8 per 1,000 control subjects, as opposed to 1.8 per 1,000 in patients.

Chandler and Hartman (1960) reported that "fluctuating feelings of well-being, mild euphoria, depression and anxiety can be uncomfortably pronounced for several hours to several weeks" (4, p. 289) after LSD sessions. They also reported one suicide in a woman after her first treatment with the drug. She had had a long history of alcoholism and narcotic addiction and had made three previous attempts at suicide. She had had extensive treatment previously, including 50 electroconvulsive therapy sessions, and even prior to taking LSD she confided to the therapist that she intended to end her life that night anyway. Over the weekend following the LSD treatment, after an argument, her husband walked out of the house, leaving her alone all night. When he returned she was dead from a lethal dose of suil poison. These authors also reported one temporary psychosis lasting about 24 hours.

Ling and Buckman (1960), while insisting that the drug could be safely used on an outpatient basis in selected cases, reported one suicide attempt in a male patient "who discovered while feeling about two years old that his mother was a prostitute" (27, p. 45). They also report that the effects of the drug sometimes recurred during the 2 or 3 days following treatment, but their report is somewhat complicated by the fact that they used methedrine in combination with LSD. They warned that "people under 18 are usually too immature" (27, p. 43) for exposure to this drug.

Bierer and Browne (1960) reported "no accidents, except for one girl who committed suicide, not under the influence of LSD but impulsively in reaction to an un-
happy love affair” (3, p. 931). No other details are given of this case. The authors, who were using LSD at times in combination with methedrine in a night hospital setting, felt in fact that they had “successfully supported a number of suicidal patients, including one who was a hopeless drug addict” (3, p. 931). This patient did eventually commit suicide a considerable time after LSD treatment had been discontinued.

By 1960, even the treatment of the complications seemed to be raising the possibility of further problems. Abramson et al. reported that oral chlorpromazine, the most commonly used antidote for LSD, produced in some instances “an apparently enhanced reaction to LSD” (1, p. 307). They reported that this effect was not produced by the parenteral administration of chlorpromazine.

Tenenbaum (1961) (43), reporting on electrocardiogram readings on 10 male character disorder patients who were in LSD group therapy, noted abnormalities consisting of T wave regression and S-T segment depression at times occurring without any increase in the heart rate.

Cohen and Ditman (1962), after referring to the 1960 survey, stated “recently we have encountered an increasing number of untoward events in connection with LSD 25 administration” (8, p. 161). They were now able to report on five individual cases of prolonged psychotic reaction in persons who had taken LSD in nonmedical settings or who had been unskilfully handled in therapy. They also reported some acting out behavior and commented on the illicit trafficking which was occurring in relation to the drug. They then went on to describe a “new but not rare entity” (8, p. 162), which they called multihabituation, referring to the frequent indulgence in a variety of stimulants, narcotics, sedatives and hallucinogens.

Linton and Langs (1962) (28), using a subjective questionnaire on the day following LSD administration, reported the frequent occurrence of depression sufficiently severe to indicate the need for continued supervision of the subjects.

Malitz et al. (1962) noted “increased motor restlessness, mounting anxiety and brief intensification of visual hallucinations” (31, p. 190) following intravenous administration of chlorpromazine to terminate the LSD experience in experimental subjects.

Elkes (1963) pointed out that “delayed reactions may last for days or even weeks” (14, p. 196) after taking LSD. Such reactions included “changes in mood (predominantly depressive), perceptual distortions, depersonalization, confusional states, phobias and acting out on ideas of reference.

Grinker (1963) in an editorial expressed some of the growing concern about the illicit use of LSD in the following terms: “Latent psychotics are disintegrating under the influence of even single doses: long continued LSD experiences are subtly creating a psychopathology. Psychic addiction is being developed... This editorial is a warning to the psychiatric profession that greater morbidity and even mortality is in store for its patients unless controls are developed against the unwise use of LSD-25... The affective release interested many psychiatrists, who administered the drug to themselves and some who became enamoured with the mystical hallucinatory state eventually in the ‘mystique’ became disqualified as competent investigators” (20, p. 425).

Cohen and Ditman (1963) (9) provided more detailed information about complications they had previously reported. Their cases of prolonged psychotic decompensation included one woman who was ill for 2 years after a single LSD treatment, a man ill for 2 years after eight treatments, and a man ill for 7 months after 25 treatments. In addition, they reported one case of a 10-year-old boy ill for 1 month after ac-
cidentally ingesting a sugar cube coated with LSD, and another case of a man resistant to treatment after 200 to 300 illicit self-administrations. They also gave a case illustration of an 8-month agitated depression in a psychoanalyst who had taken one dose of LSD and a paranoid reaction in a psychologist who had taken three doses. The authors still felt, however, that "when properly employed, LSD is a relatively safe and important research tool," but they warned that "the imprudent, cursory use of LSD and allied drugs is unsafe and the complications that sometimes result retard their proper scientific study" (9, p. 480).

Ling and Buckman (1963) (26) reporting on their 4 years' experience with combined LSD and Ritalin in the treatment of 350 neurotics also felt the drug was safe if carefully used. In their series there was one suicide attempt, three patients were taken out of treatment because of the danger of suicide, and three patients were hospitalized for unspecified complications.

Sandison (1964) pointed out that "one of the principal dangers of treatment lies in the production of a drug-addicted psychopathic individual," but he felt that "this state of affairs can only occur when the treatment is not carefully and conscientiously supervised" (36, p. 35).

Geert-Jørgensen et al. (1964) (18) reported on a 3-year follow-up of 129 patients who had severe character disorders and for whom LSD was considered a "last chance" treatment. They stated that the "complications have been few and it seems absurd to tabulate them" (18, p. 375). However, they described one suicide several hours after administration of LSD and another patient who shot himself 6 months after his final treatment. The latter patient had seemed to be doing very well in the interval and the authors were convinced that his suicide had no immediate connection with the LSD treatment. Four patients who attempted suicide during the course of treatment were mentioned, but the authors felt that only one of these could be considered as a serious suicidal attempt. They stated "It is our impression that these suicidal reactions did not occur at times when the patients had been in states attributable to the LSD after-effects repercussions" (18, p. 376). This series included a case of homicide, which will be described in more detail shortly. The authors also reported "a few patients had brief episodes of after-effects repercussion several months after treatment, either in the form of a revival of the LSD seance or as a groundless fear involving no particular inconvenience" (18, p. 375).

Knudsen (1964) (23) described in detail the case of homicide mentioned above. The patient was a 25-year-old woman who had no family history of mental illness and who appeared to be normally adjusted up until about the age of 20, when she left Denmark to work in Norway as a domestic servant. While there, she apparently became involved with a psychopathic individual who influenced her toward heavy indulgence in drugs, alcohol and sex. She received several hospitalizations during the next few years and was finally given five LSD treatments at spaced intervals. On the morning after her last treatment she left the hospital and fatally stabbed the psychopath, who had intermittently continued to influence her adversely during the previous 5 years. She had no recollection of the actual stabbing itself, but recalled events before and after. The report of the Medicolegal Council which ruled on her case stated "It must be assumed that the treatment...decisively influenced the faculty of the accused for self-control and control of aggressive impulses" (23, p. 394) and she was committed to a mental hospital for further treatment.

Rosenthal (1964) (35) reported a case of "persistent hallucinoses" following re-
peated administration of hallucinogenic drugs. This occurred in a 23-year-old married female artist who had been briefly hospitalized at the age of 18 with hysterical seizures. She later had one therapy session with LSD and subsequently went on to administer LSD, mescaline and psilocybin to herself on about 10 or 12 occasions. She developed increasing anxiety and “lost interest in life, in her marriage and in her work, in which she ‘could not hope to approach’ the experiences which she had had under the influence of the drugs” (35, p. 240). For 5 months after her last exposure to hallucinogenic drugs she experienced spontaneous hallucinations. She had some control over the pleasant ones, but not over the unpleasant ones, which included “terrifying involuntary illusions of people decomposing in the street in front of her” (35, 240). For 5 months after her last exposure and the fact that she had to be hospitalized for treatment of them, she still considered further use of these drugs. Rosenthal stated “It is likely that many adverse reactions are unreported.... More cases of this condition will occur because of the current fad of unsupervised consumption of hallucinogenic drugs in repeated doses” (35, p. 243).

Cole and Katz (1964) interpreted the state of the LSD controversy at that time as follows: “Rather than being the subject of careful scientific enquiry, these agents have become invested with an aura of magic offering creativity to the uninspired, ‘kicks’ to the jaded, emotional warmth to the cold and inhibited and total personality reconstruction to the alcoholic or the psychotherapy-resistant chronic neurotic” (10, p. 758). They went on to point out that “indiscriminate, unsupervised use is clearly dangerous” and stated that there were “reports of insidious personality changes in individuals who have indulged in repeated self-administration” (10, p. 761). They also expressed concern over the possibility that “investigators who have embarked on serious scientific work in this area may have been subject to the deleterious and seductive effects of these agents” (10, p. 761).

Grinker (1964) in another editorial stated “From experimental subjects there are increasing numbers of reports indicating that temporary or even permanent harm may be induced despite apparently careful pre-therapeutic screening of latent psychoses and careful precautions during the artificial psychoses” and he concluded “The drugs are indeed dangerous even when used under the best of precautions and conditions” (19, p. 768).

Levine and Ludwig (1964) (24) presented a plea for balanced objectivity in relation to the claims for and warnings against LSD. They stated, “The impression one tends to gain from reading many of the articles concerning LSD use is that the drug is fairly dangerous with rather serious complications, most of a mental nature.” However, they feel that “in most of the reported cases no direct cause or relationship was established between LSD therapy and subsequent psychotic deterioration or suicide attempts,” and they concluded that “It would seem that the incidence statistics better support a statement that the drug is exceptionally safe rather than dangerous” (24, p. 318).

Cohen (1964) (5) discussed the increased incidence of complications as a result of the illicit use of LSD. He also considered in some detail the dangers to the therapist who becomes overly enthused about the beneficial effects of the drug. He referred to therapists who have themselves suffered depressions and psychotic breakdowns, or have developed megalomaniacal ideas of grandeur, and he also mentioned one who committed suicide. He suggested that the causes of this “impressive morbidity in view of the relatively small number of American practitioners using the hallucinogens” (5, p. 218) might be related to preexisting dis-
turbances in personality or to adverse reactions due to self-administration of LSD.

Incidentally, Cohen in his book mentioned that during his 1960 survey of researchers using LSD there was one report of coronary occlusion occurring a few days after LSD. This was regarded as coincidental and it was pointed out that no physical complications had been observed in using the drug on debilitated alcoholics.

Downing (1964) (12) reported on his observations on 29 persons who attended the International Federation for Internal Freedom (IFIF) Psychedelic Training Center at Zihuatenejo, Mexico, during the last 2 weeks before its enforced closure in June, 1963. Despite the claim of Leary, the leader of this group, that there had been no problems in using psychedelic drugs in this type of setting, Downing reported that 1 of the 29 persons required psychiatric hospitalization directly from the Center, and that another was hospitalized for treatment of self-inflicted injuries.

Ludwig and Levine (1965) (30) presented information on the general patterns of hallucinogenic drug abuse obtained from intensive interviews of 27 narcotic drug addict inpatients who were being treated at the U.S. Public Health Service Hospital in Lexington, Kentucky. All of them had used hallucinogenic agents at one time or another. One of these patients became so frightened after his first exposure that he “ran his head into the wall to stop the experience, asked a friend to knock him out (the friend tried to co-operate) and later, on his way to the hospital, experienced homicidal impulses towards the cab-driver” (30, p. 96). The authors obtained undocumented reports of people acting out homosexual impulses or becoming more withdrawn, depressed and paranoid when under the influence of these drugs. One patient reported that an acquaintance of his “tied to stab himself, since he believed himself to be invincible” (30, p. 96). Another tried to jump out of a window, believing that his body was weightless. There were also reports of people trying to walk on the sea and two of the patients themselves reported near accidents while driving under the influence of the drugs. One of the patients described the difference between heroin and the hallucinogens as follows: “You addict yourself with the hallucinogens, whereas heroin addicts you” (30, p. 95).

Savage and Stolaroff (1965) pointed out that “by far the greatest damage has been caused by the illicit use of the hallucinogens” (39, p. 220). They felt that the complications of these drugs arose from improper use due to 1) inadequate preparation of the subject; 2) improper support to the subject; 3) too frequent use of LSD; 4) improper handling of patients; 5) improper dosage; and 6) over-enthusiastic response.

Frosch et al. (1965) described in detail 12 out of 27 patients admitted to Bellevue Hospital with the complications of LSD during a 4-month period. They categorized the complications as being panic reactions with a good prognosis, usually resulting in discharge in 1 to 3 days, reappearance of symptoms up to 1 year after multiple exposures to the drug, and extended psychosis in long standing schizophrenics who had taken the drug illicitly. The last two categories had a poor prognosis and all 6 patients in these categories “showed some impairment of performance at the time of our last contact with them” (17, p. 1238). One of their patients jumped out of a window and they emphasized the danger of bodily injury under the influence of the drug, because a person may believe himself to be invulnerable to harm and take unwarranted risks, as several of the patients with panic reactions did.

Cohen (1966) felt that “complications to the extra-legal use of LSD have increased so rapidly that it is now possible to propose a more complete classification of untoward reactions” (6, p. 182). Case descriptions ac-
accompanied most of the categories, which are as follows:

A) **Psychotic disorders**
   1) Accidental LSD intoxication in children characterized by anxiety and visual illusions lasting several weeks.
   2) Chronic LSD intoxication with ataxia, slurred speech and incoordination.
   3) Schizophrenic reactions occurring in schizophrenic individuals or ambulatory schizophrenics.
   4) Paranoia with relatively appropriate thought processes, except in the area of megalomania or delusions.
   5) Acute paranoid states usually occurring during the LSD experience itself and involving danger to the subject or to others around him. One death is reported in a young man who stepped into the traffic and tried to stop it and another death in an individual who drowned. Another man drove through traffic convinced that he could change the red lights by concentrating on them. In another case two men took LSD together; one of them was beaten up by the other, subsequently jumped or was thrown out of a fourth floor window and suffered multiple injuries.
   6) Prolonged or intermittent LSD-like psychoses.
   7) Psychotic depressions usually associated with agitation and anxiety.

B) **Nonpsychotic disorders**
   1) Chronic anxiety reactions associated with depression, somatic symptoms, difficulty in functioning and a recurrence of LSD-like symptoms such as time distortion, visual alterations and body image changes for weeks or months.
   2) Acute panic states with a potential to self-injury.
   3) Dysthymic behavior, involving a complete loss of previously held values and ideas, loss of motivation to study or work and indulgence in "sociopathological jargon."
   4) Antisocial behavior, involving obliteration of cultural values of good and bad and society's rules of right and wrong, especially in individuals with a previously attenuated moral code.

C) **Neurological reactions**
   1) Convulsions, not observed by Cohen but reported by Sandison (one case) and by Baker (five convulsions in 150 patients).
   2) Permanent brain damage. This has not yet been demonstrated, but in a personal communication to Cohen, Adey reported prolonged electroencephalographic changes in cats given large amounts of LSD. Cohen suggested that a number of human beings have ingested massive amounts and some of these may in future show brain damage. He also pointed out that the "purity of the illicit LSD is open to question and nothing is known about the toxicity of possible contaminants" (6).

Cohen concluded that "It must be explicitly stated that some individuals should never take drugs of this category and that one's friends are not suitable judges of suitable candidates. Furthermore, a secure environment is essential for the patient or the subject who takes LSD, since he is now vulnerable, hypersuggestible and emotionally labile" (6, p. 186).

Rinkel (1966), who had introduced LSD to the United States in 1949, stated that the "dangers are many times multiplied by their illegitimate use. Persons who have taken LSD obtained on the black market become psychotic often weeks or months after the ingestion of LSD. They are being admitted to hospital in an ever-increasing number" (34, p. 1415). He also pointed out that "the cult aspect of the LSD movement has rendered serious damage to the scientific study of this group of drugs" (34, p. 1416).

Pos (1966), reporting on 24 patients treated over a 3-year period with a total of 56 LSD sessions, felt that "the events of the LSD-25 sessions could not be predicted on the basis of pre-LSD-25 experience with the patient" (33, p. 341), even though the patient had been in intensive psychotherapy. He reported one questionable suicidal attempt during an LSD session and one attempt by jumping out of a window 6 hours after LSD administration.

The American Psychiatric Association produced a position statement on LSD at the meeting of the Council on June 12th, 1966, in which it stated "The indiscriminate consumption of this hazardous drug
can and not infrequently does lead to destructive physiological and personality changes" (2, p. 333).

Ungerleider et al. (1966) pointed out that "some preparations claimed to be LSD contain impurities, particularly atropine-like compounds" (45, p. 389). They presented a study of 70 patients attending the emergency room at one of the Los Angeles hospitals during a 7-month period. All were showing complications after having taken illicit LSD. The commonest presenting symptoms were hallucinations (29 per cent), anxiety (24 per cent), depression (21 per cent) and confusion (20 per cent). A number had exposed themselves to a variety of hallucinogenic agents, but 40 per cent had taken only LSD and 29 per cent had taken it only once. A total of 66 per cent had taken the drug over 1 week before admission to the hospital. Of these 70 patients, 25 required psychiatric hospitalization and 17 were in the hospital over 1 month. The authors raised a question about chlorpromazine being able to reverse the symptoms and described in detail one case which was resistant to up to 2,000 mg of chlorpromazine daily, together with trifluoperazine. They concluded that their findings seemed to contradict statements implying that the complications of LSD are infrequent.

Fink et al. (1966) (16) estimated that 40 per cent of the prolonged reactions reported in the literature had not improved at the time of the reports, some of which extended up to 2 years after exposure. In their own series of 158 administrations to 65 chronic hospitalized psychotics, they reported prolonged reactions lasting up to 3 months in 3 patients (2 per cent). These reactions occurred in patients who had a phasic history of a schizoaffective type of illness before LSD. The post-LSD picture was one of exacerbation and exaggeration of previous symptoms, with a superimposed confusional, delirious state. One of these patients made a suicidal attempt and 2 of the cases were unresponsive to high doses of chlorpromazine.

Scher (1966), in an interesting if somewhat anecdotal review of patterns and profiles of addiction and drug abuse in Chicago, pointed out that "the abuser of LSD will, in the course of time, tend to develop paranoid ideas. One of the most frequent paranoid impressions is that everyone around the user except himself is homosexual" (40, p. 547). He also pointed out that the illicit synthesis of LSD may be "dangerous to the manufacturers, who are usually in a semi-stupor from the very process of manufacture" (40, p. 547).

Louria (1966) stated that LSD "must be listed as one of the most dangerous drugs in the pharmacopeia of man" (29, p. 47). He referred to one case of homicide in which a former medical student killed his mother-in-law while under the influence of the drug and had no recollection of his action. He described various types of disturbed behavior in approximately 100 patients admitted to one New York hospital in a 13-month period. He also stated, "There is no doubt that even apparently well-adjusted persons can be thrown into an acute psychosis requiring days or weeks of hospitalization. This is true even in the hands of an experienced physician who carefully selects his patients” (29, p. 49).

Keeler and Reifler (1967) (21) described in detail a case of suicide under the influence of LSD which they felt would not have occurred in this particular individual had he not been in a toxic state. The case was that of a 20-year-old college undergraduate, who disrobed and jumped out of a window to his death while under the influence of self-administered LSD, taken when in the company of several other people who were also taking LSD. The young man had been a part of the LSD subculture for several months, during which he had become preoccupied about
the homosexual feelings which were frequently brought out and discussed in the group meetings. He seemed to withdraw somewhat and his academic work deteriorated, with irregular class attendance. However, a few days prior to his death he discussed plans for the immediate and distant future with his friends. He “took LSD in the company of others, was observed to pace in and out of the room in which the others were and, without explanation, while by himself disrobed and took his life” (21, p. 885). The authors concluded “The circumstances strongly suggest that he would not have died at the time he did if he were not in a state of LSD intoxication” (21, p. 885).

Ungerleider and Fisher (1967) (44) reported on a wide range of complications observed by themselves. These included grand mal seizures in a previously nonepileptic person and persistence of episodic recurrences up to 1 year after ingestion. They described one young man who was prevented from throwing his girlfriend off a hotel roof under the delusion that he had to offer a human sacrifice after having taken his first LSD trip. They also commented on researchers, themselves LSD users, who “become so enthusiastic that they even refused to consider psychosis and suicide as bad results” (44, p. 51). They pointed out that the occurrence of either acute or chronic side effects cannot be predicted by psychiatric interviews and psychological testing and stated, “Some of the worst reactions have been in persons, often physicians and other professionals, who appeared stable by every indicator” (44, p. 51). These authors also gave several instances of marked changes in personality and values in relation to current societal standards.

Schwarz (1967) (41) reported two cases of paradoxical responses to chlorpromazine after LSD. In one case, intravenous chlorpromazine given to terminate an LSD-25 session precipitated a subjective and objective exacerbation of the LSD phenomena. This patient showed a milder but similar response to oral chlorpromazine the day after. In the other case, a student who had been experiencing spontaneous recurrences for 3 weeks after taking LSD illicitly reported that oral chlorpromazine given to counteract these seemed to precipitate them again. The author discussed possible psychological and biochemical explanations of this phenomenon and suggested that it raises the suspicion that LSD or some metabolite might be present in the brain some time after ingestion of the drug.

**DISCUSSION**

It should be emphasized that this review of the complications of LSD covers only the medical literature on the subject. Many other reports of adverse reactions are available in the lay press, particularly in relation to the informal use of the drug.

It should be obvious that the total number of incidents mentioned in this paper cannot be taken to indicate any kind of absolute figures. It can be assumed that additional complicated cases, including fatalities, have occurred but have not been reported in either the medical or lay press. No statistical analysis can be attempted, but some general impressions appear justified from the above review.

1) The acute intoxicated state carries risk of acting out in a manner dangerous to the subject or others.

2) For several days after ingestion of LSD, anxiety, depression or paranoid thinking can occur even in normal control subjects.

3) Spontaneous recurrences some time after ingestion are often mentioned and appear to constitute a common complication of LSD. These phenomena still require explanation, but the apparent precipitation of a similar recurrence by the ad-
ministration of another chemical compound (chlorpromazine), if supported by observation, should encourage further investigation of the possibility of a continuing process with a biochemical basis.

4) Prolonged mental illnesses, including persistent anxiety, depression, psychosis and personality deterioration toward a nonactivist role in society have all been reported.

5) Definite physical effects from LSD have not been proven, but there are several slight indices of suspicion in this area. Prolonged electroencephalogram changes have been reported in cats. Epileptic convulsions have been observed in humans. Mildly significant electrocardiogram changes suggestive of coronary insufficiency have been recorded in the only study which could be found using this test. One coronary occlusion has been reported several days after LSD.

In view of the reported complications which might arise in the use of LSD, steps to prevent these are given frequent emphasis in the literature. The recommendations generally follow the classical lines of 1) careful selection of subjects, 2) attention to the setting, 3) safe dosage and 4) follow-up of subjects. Taken in isolation, each of these criteria appears to harbor some as yet undefined aspect in relation to this particular drug.

Careful selection of the subjects, including detailed knowledge of their backgrounds, psychological testing and even psychotherapy interviews, does not appear to guarantee freedom from complications.

Attention to the setting does not seem to eliminate the dangers entirely, and complications are reported in a wide variety of medical, research and informal situations. The setting, however, would appear to be an important factor in the management of adverse reactions when these do arise.

Dosage criteria are also questionable, since one suicide has been reported after two 30-µg sessions, and one after one 50-µg session.

Careful follow-up appears to have loopholes in that spontaneous recurrences have an out-of-the-blue character which makes their prediction well nigh impossible.

Certainly careful attention to all four criteria, i.e., subject, setting, dosage and after-care, will minimize the risks, but the use of LSD would appear to carry an innate unpredictability which makes it a difficult drug to use even in medical settings. This does not make its medical use unjustifiable, since, in the first place, trained personnel and appropriate facilities are available to deal with complications and, secondly, any medical procedure carries a certain risk of morbidity and even mortality. Thus a suicide rate of 0.4 per 1,000 psychiatric patients given LSD, even though it is four times the average suicide rate in the U.S.A. (46), might not be unexpected, particularly in view of the severity of the cases treated.

Such a figure does, however, assume graver significance when it is realized that a number of severely disturbed people and borderline psychiatric patients find self-medication with LSD attractive. In addition to the rejection of the first criterion of control (careful subject selection), the other three criteria (setting, dosage and after-care) often receive only ineffectual lip service. Finally, there is often a refusal on the part of the user to acknowledge the unpredictability of his own reaction to a substance which he has never ingested before and of which he has only the scantiest knowledge. There is a blind faith in whatever the LSD pusher says about the reliability of an illicitly manufactured chemical which is offered around in a wide variety of sizes, forms and colors. It is interesting to note that one of the chief characteristics of the LSD reaction, suggestibility, is so obvious in some individ-
uals even before they have purchased the drug.

In conclusion, while the therapeutic value of LSD-25 must remain a subject of debate for the time being, there would appear to be little doubt that the informal use of this drug is dangerous.

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