

Treatment of Alcoholism Using Psychedelic Drugs: A Review of the Program of Research†

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- **Abstract**—Following Albert Hofmann's discovery of LSD's psychoactive properties in 1943, and previous to their scheduling as controlled substances, the psychedelic drugs were widely studied—
○ six international conferences and hundreds of papers discussed their potential therapeutic usefulness.
→ The observation that the frightening experience of delirium tremens sometimes led alcoholics to moderate their alcohol intake suggested to early psychedelic researchers that the “psychotomimetic” experience thought to be produced by LSD could be used to treat alcoholism. A number of hypothesis-generating studies employing a variety of research designs to examine this premise were completed, but relatively few controlled trials attempted hypothesis testing. After twenty-five years of study, a combination of flawed methodology, uneven results and social reprehension led to the abandonment of research on the therapeutic use of psychedelic drugs, leaving many avenues of inquiry unexplored and many questions unanswered. Today, after a thirty-year hiatus, this research is gradually being resumed, and there is renewed interest in the findings of previous studies. This article explores the history of one branch of psychedelic research, the therapeutic use of LSD in the treatment of alcoholism, and of the events that led to the relabeling of the “hallucinogens” as drugs of abuse.

Keywords—alcoholism, hallucinogens, lysergic acid diethylamide, psychedelic drugs, psychotherapy

- Through our great good fortune, in our youth our hearts were touched with fire. It was given to us to learn from the outset that life is a profound and passionate thing.

Oliver Wendell Holmes

- It is therefore necessary that memorable things should be committed to writing, and not wholly be taken to slippery memory which seldom yields a certain reckoning.

Sir Edward Coke

†Research on this article was supported by the University of California Regents Fellowship. The author gratefully acknowledges the support of the Library of the University of California at San Francisco in the completion of this research.

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- Since Albert Hofmann's discovery of lysergic acid diethylamide's (LSD) psychoactive properties in 1943, the therapeutic potential of this drug has been the subject of speculation, study and controversy. Its exceptionally high potency, corresponding to that of endogenous trace substances that are thought to affect mental states, suggested the possibility of psychotherapeutic use to its earliest researchers. Hofmann's reports of his self-experiments with LSD and Stoll's original systematic description of LSD-induced mental states in healthy volunteers and in schizophrenic patients were followed in the next three decades by more than 1,000 reports of therapeutic experimentation with LSD and related substances (Stoll 1947).

○ After 25 years of study, a combination of flawed methodology, uneven results and social reprehension led to the abandonment of this program of research, leaving many

avenues of inquiry unexplored and many questions unanswered. Today, after a 30-year hiatus, research on the therapeutic potential of the psychedelic drugs is gradually being resumed, and there is renewed interest in the findings of previous studies. This article will explore the history of one branch of psychedelic research: the therapeutic use of LSD in the treatment of alcoholism.

EARLY THERAPEUTIC USE OF LSD

The Model Psychosis Hypothesis

In 1953, Humphry Osmond and other researchers in Saskatchewan in western Canada were engaged in a series of studies on schizophrenia involving the use of mescaline and lysergic acid diethylamide. Their aim was to "start with the signs and symptoms and natural history of schizophrenia, and ask how these could be produced" (Osmond & Smythies 1952). Compounds that were thought to produce mental disturbances similar to schizophrenia were administered to volunteers in order to construct biochemical and psychological models of psychoses. In an early report of this research, Humphry Osmond stated that it had "been known for fifty years that mescaline . . . produces symptoms almost identical with schizophrenia" (Osmond & Smythies 1952).

At that time three divergent theories were held by researchers concerning the effects of mescaline and LSD-25. They were variously described as "deliriant" which provoked a toxic delirium, "psychotomimetics" which caused an artificial psychosis which was similar to the experience of a psychotic break (Hoffer 1967), or "psycholytics" which produced psychic states in which the subject recalled repressed memories and other unconscious material in a setting of clear consciousness (Sandison & Spencer 1954). Mayer-Gross (1951), another early researcher in this area, had noted the differences between schizophrenia and the effects of mescaline in 1951: "The symptoms of mescaline intoxication have been compared to those of schizophrenia, but it is much more the strangeness experienced by the patient suffering from schizophrenia and the difficulties of describing what is happening in the two conditions which is similar. Many typical schizophrenic symptoms are never seen in mescaline intoxication." ^{?? More similar than dissimilar}

In a search for a naturally occurring trace substance which could induce a schizophrenic-like reaction, Osmond and Abram Hoffer had studied the "schizogenic" properties of a group of materials, and had coined for them the name "hallucinogens": they included mescaline, lysergic acid diethylamide, harmine, ibogaine, and hashish (Hoffer, Osmond & Smythies 1954). Based upon speculation that the LSD experience could be akin to that of delirium tremens, a disorder involving visual and auditory hallucinations found in habitual and excessive users of alcoholic beverages, they began a series of studies of lysergide in the treatment of alcoholism at Saskatchewan Hospital in Weyburn,

Saskatchewan, where the first two alcoholic patients were treated in 1953 (Thomas 1977; Hoffer 1967).

Attempts to Simulate *Delirium Tremens*

The experience of *delirium tremens* is unpredictable, overwhelming and frightening. First described in 1813, it is sometimes referred to as "the horrors," and may be accompanied by "rum fits" or seizures (Sutton 1813). It is the last in a continuum of alcohol withdrawal symptoms which may begin soon after the cessation of drinking as the blood level of alcohol begins to drop. It progresses erratically from agitation and autonomic hyperactivity, to mental confusion, disorientation, delusions and vivid hallucinations of colored shapes, snakes, dragons, and other fantastic objects. The patient may be amnesic for the experience. (Adriani 1976). *Delirium tremens* occurs in about 4% to 5% of patients withdrawing from alcohol; in the early 1950s, it was fatal in about 10% to 15% of patients (Osmond 1969). Advances in treatment have reduced mortality today to less than 5% (Yost 1996).

Hoffer and Osmond were familiar with the testimonies about "rapid abolition of ancient impulses and propensities" (Osmond 1969: 218) collected by William James from the reformed drunkards of the Jerry McAuley Water Street Temperance Mission in 1902, and with James' observation that the only radical remedy known to medicine " . . . for dipsomania is religiomania" (James 1982). They were aware that "a very remarkable experience" of some kind had been the cause of Bill W's beginning to build Alcoholics Anonymous (AA) (Osmond 1969: 217). They knew that some kind of "hitting bottom" experience was at the heart of the Wesleyan Methodist sect's success in converting alcoholics and helping them to stop drinking by catching them in the remorseful time after a drinking bout, scaring them thoroughly with the potential consequences of continued drinking, and then offering hope for improvement in a program of abstinence (Osmond 1969).

Because of these accounts concerning alcoholics who had experienced delirium tremens and sometimes were noted to "hit bottom" (an experience of surrender that is often considered to be the key to beginning recovery from alcoholism), Hoffer and Osmond wondered if a similar experience, therapeutically induced, would help alcoholics stay sober (Hoffer 1967). They understood the LSD reaction to be similar in character to delirium tremens, but capable of being initiated at a time and place that could be directed and controlled. Hoffer and Osmond speculated that one could inspire an alcoholic patient to "mend his ways" by inducing such an experience (Osmond 1969).

Hoffer and Osmond soon noted, however, that substances such as LSD and mescaline, which they had understood to produce hallucinations, could also produce "a particularly vivid and intense awareness of personality problems" which seemed to make the alcoholic more amenable to psychotherapy (Smith 1958). For many patients,

this was also an "admonitory" experience, in which they were profoundly shocked and frightened by their vision of themselves and how alcohol was affecting them. Hoffer and Osmond abandoned the idea of provoking a simulacrum of the *delirium tremens* in favor of encouraging patients' self examination of personality problems, and the development of insight into their "dismal present and appalling future" (Osmond 1969). They made no deliberate attempt to produce fear in their patients, since they had noted early in their investigations that making alcoholics afraid "often produces a desperate resolution to go on drinking" (Osmond 1969), and seemed to lead to severe anxiety and poor communication (Smith 1958).

In 1956 Humphry Osmond presented a paper at the New York Academy of Sciences conference entitled: "The Pharmacology of Psychotomimetic and Psychotherapeutic Drugs." In this paper, which was "a review of the clinical effects of psychotomimetic agents," Osmond described the major uses of this class of drugs. Some of these uses were the subject of ongoing research: the study of psychopathology through the production of "model psychoses," the experiential training and education of psychiatrists and psychologists, and use as an adjunct to conventional psychotherapy. Two of the potential uses that he proposed were less well known: exploration of the normal mind under unusual conditions, and discoveries with social, philosophical and religious implications made while using LSD and other drugs of this class (Osmond 1957). Osmond pointed out that to continue to consider these agents to be primarily "psychotomimetic" begged the question of their other potential uses. To prevent this, he proposed a new name for the class of drugs that would include their capacity to enrich the mind and enlarge the vision: *psychedelic*, a term coined from Greek roots indicating "manifesting the mind." Research on the potential therapeutic benefits of psychedelic drugs in the treatment of the alcoholic continued for the next 12 years, producing innumerable areas of controversy.

MAJOR TREATMENT STYLES

Psychedelic Therapy

The focus of the Saskatchewan Hospital program changed as the researchers came to believe that, although their patients benefited from their treatments, it was not the psychotomimetic effect that was beneficial to them. The literature on alcohol treatment acknowledges that "clients who make successful recoveries often attribute their success to a spiritual experience or enlightenment" (Longabaugh et al. 1994). Clinebell (1963: 487) has suggested that "one of the significant factors in the etiology of alcoholism is the vain attempt of the person to satisfy deep religious needs by means of alcohol." Included among these needs are experiences of the transcendent and numinous; a sense of meaning, purpose and value in one's life; and a feeling of unity, trust and relatedness.

The Saskatchewan Hospital program found that LSD and mescaline could address such needs in the alcoholic patient by inducing an experience "so profound and impressive that his life experience in the months and years to follow becomes a continuing growth process" (Sherwood, Stolaroff & Harman 1962). This emphasis on a transcendent, overwhelming, conversion-like experience evoked by a high dose (200 or more micrograms) came to characterize "psychedelic" therapy as one of the two approaches to the therapeutic use of LSD.

Psycholytic Therapy

In the other major therapeutic approach, *psycholytic* therapy, LSD is viewed as a facilitator of psychotherapy, and is used to produce insight, recall, reliving and abreaction (Savage et al. 1969; Terrill 1962). Psycholytic therapy has been primarily practiced in Europe. The term *psycholytic* was coined in 1960 at a small European symposium on the use of LSD in psychotherapy in Göttingen, Germany; it was intended to suggest dissolving or releasing of tensions and conflicts in the human mind (Grof & Grof 1975). In this form of therapy the remembering and reliving of childhood experiences are particularly prominent (Sandison & Spencer 1954). The goal is to solve present neurotic complexes in order to allow restructuring and maturation of the entire personality (Leuner 1967). Low to moderate doses (usually less than 150 micrograms) are repeated at intervals of at least one week to facilitate conventional psychoanalytically-oriented psychotherapy for neuroses and psychosomatic disorders (Grinspoon & Bakalar 1979). By the mid-1960s, the European Medical Society for Psycholytic Therapy included eighteen affiliated treatment centers in Holland, Denmark, Great Britain, Germany and Czechoslovakia (Grinspoon & Bakalar 1979).

DEVELOPMENT OF PSYCHEDELIC THERAPY TECHNIQUES

The First Report of Studies at Saskatchewan Hospital

According to Hoffer (1967), early in the Saskatchewan Hospital research "... no special effort was made to control the environment of the patient undergoing therapy. Hospital rooms or psychiatrists' offices were used and there were many environmental distractions which interfered with the patient's experience." By 1957, when Hoffer and Osmond turned the Saskatchewan Hospital treatment program over to Colin Smith in order to continue their research on schizophrenia, the researchers had recognized that the environment, and especially the attitudes of the people around the LSD subject, influenced his experience profoundly. Reports of volunteers and patients also suggested that the drugs produced a "marked loosening of repression and greater facility in recognizing conflicts" (Chwelow et al. 1959). "Attitudes of love, faith and optimism" were desirable, as it appeared that the more intensely the patient

experienced self-surrender and self-acceptance, the better the results (Chwelos et al. 1959: 585).

The first report of this treatment, which was published in 1958, discussed 24 of "the most difficult alcoholics obtainable, those who had already failed to respond to other treatments and who, in the opinion of their own therapists, had a very bad prognosis" (Hoffer 1967). There was no attempt to use a control group receiving an alternative treatment or a placebo because, as Hoffer (1967) described it, . . . "it would have been a trivial procedure to use placebo since both subject and therapist with any experience with LSD would know the difference."

After an initial two- to four-week course of inpatient therapy which included attempts to develop therapeutic rapport, patients were given either a single dose of 200 to 400µg. of LSD or 500 mg. of mescaline. The patients were interviewed while under the influence of the drug, and strong suggestions to discontinue the use of alcohol were made. The content of this interview was then discussed during a further few days of inpatient therapy, and the patients were discharged. The average duration of follow-up was one year (range two months to three years). Twelve of the patients were abstinent or drinking only very small amounts at follow-up, and an additional six had substantially reduced their alcohol intake. Six were unchanged (Smith 1958).

Smith's report (published in 1958 in the *Quarterly Journal of Studies on Alcohol*) emphasized that the effect of the drugs used was not separable from the treatment program as a whole. In addition, he pointed out that "exhortation, persuasion and suggestion" provided by the therapist during the drug session would be likely to enhance the effect of the technique, although this practice did not come easily to him personally (Smith 1958: 415).

The Influence of A. M. Hubbard

In 1957 the Saskatchewan Hospital research group became aware of the work of A. M. Hubbard, "the unpublicized father of the American psychedelic therapy movement" (Caldwell 1968). Osmond traveled to British Columbia to examine some of the alcoholics who had been treated with LSD using Hubbard's techniques, which were said to be particularly effective (Hoffer 1967). Hubbard, who had accumulated a large series of unpublished cases while working with "gravely ill alcoholics" (Osmond 1957), used music, flowers, and evocative symbols and pictures to enhance and direct the drug experience. The goal was to promote increased self-acceptance and spontaneity by encouraging alcoholics to reflect on themselves and their lives. In addition, Hubbard favored the "single overwhelming experience that produces drastic and permanent change" (Grinspoon & Bakalar 1979). This format came to be identified as psychedelic therapy.

The research group accepted the idea that an exact adherence to Hubbard's techniques was needed to properly evaluate his claims and the accounts of successful

treatment that Osmond had obtained from Hubbard's patients in Vancouver. Hubbard was invited to conduct demonstrations of his methods for the Saskatchewan Hospital research group during a two-week visit to Saskatoon. Three therapists from Saskatchewan Hospital, Hoffer, Smith and N. Chwelos, observed Hubbard's sessions; they were favorably impressed by Hubbard's skill and sensitivity and, beginning in January 1958, they began to modify their treatment techniques on the basis of Hubbard's methods (Hoffer 1967).

A Further Report from Saskatchewan Hospital

In 1958, Colin Smith (1959) wrote a follow-up article to his earlier report of the Saskatchewan Hospital pilot study entitled "Some Reflections on the Possible Therapeutic Effects of the Hallucinogens, with Special Reference to Alcohol." It introduced some interesting topics that other researchers would later elaborate upon: he offered a thoughtful appraisal of some of the deficiencies in the existing research on LSD and mescaline and of their "putative therapeutic effects" (Smith 1959); and he attempted to address how the psychological effects of these drugs were understood in differing ways by different researchers.

The article outlined the technique then being used by the Saskatchewan Hospital group. Patients were first asked to freely give consent after a full discussion of the nature of the drug. After receiving their doses of LSD they were ". . . encouraged to relax by listening to music and by examining paintings." According to Smith, "It was hoped by this method to make the experience a thought-provoking one rather than a frightening one. At present, I avoid the use of suggestion during the experience, with one exception: I do suggest strongly to the patient that he discontinue drinking" (Smith 1958). Patients frequently were not asked to describe their experiences until the following day, and the overall tone produced was one of psychological safety and helpful friendliness (Smith 1959).

Treatment had been described in the original report of the pilot study as "LSD and mescaline used as adjuncts to treatment consisting of superficial psychotherapy supplemented by occupational and recreational therapy" (Smith 1958). In the follow-up article, Smith noted the well-known difficulty of estimating the effect of treatment in psychiatry. He recognized the way in which personal factors such as the style, training, and orientation of the therapist influence the psychological situation created in LSD therapy. In an attempt to standardize the "dose" of therapy, the Saskatchewan Hospital research group duplicated as exactly as possible the techniques that they had learned from Hubbard, and developed a treatment manual of individual and group procedures for the use of LSD (Blewett & Chwelos 1959). No objective measures of the therapeutic alliance of patient and therapist nor of primary patterns of the therapeutic relationship were used (as they would not be developed for almost 20 years).

As described by Smith, the group selected for LSD or mescaline treatment consisted of "particularly refractory alcoholics" (Smith 1959: 292). The original report of the pilot study had attempted to provide some measure of the severity of their alcoholism by assessing the number of years of uncontrolled drinking, previous occurrence of *delirium tremens*, and the existence of other complications of alcoholism (including blackouts, hepatitis, and peripheral neuropathy). Specific diagnoses of the study participants were provided, but did not delimit a homogeneous group. Subgroups of patients had clinical diagnoses of character disorder, psychopathy, borderline or actual psychoses and concomitant use of drugs other than alcohol. These diagnoses were assigned by the patients' own therapists, who were not involved in the LSD and mescaline treatment (Smith 1958).

Smith addressed the importance of follow-up in estimating the effectiveness of new treatment, and pointed out that it is not unusual for a new treatment to enjoy a "honeymoon" period of great enthusiasm for the method, followed by disillusionment and skepticism as patients who were judged to have been helped or even cured by the treatment begin to relapse (Smith 1959).

In his original report of the results of the pilot study, Smith had concluded that in view of the refractory nature of the patient group, the results appear sufficiently encouraging to merit more extensive and preferably controlled trials (Smith 1958). In his follow-up to the publication of the results of the pilot study, he reiterated that "initial results seem encouraging enough to justify further carefully controlled clinical trials" (Smith 1959).

METHODOLOGY IN STUDIES OF TREATMENT EFFECTIVENESS

The characteristics of an adequate study of psychotherapeutic use of LSD or similar drugs were delineated by O'Brien and Jones (1994) in their presentation at the Swiss Academy of Medical Sciences symposium celebrating the 50th anniversary of the discovery of the psychotropic action of LSD. They pointed out that clearly defined objectives and an adequate sample size should be present in a hypothesis testing study, and that research should be influenced neither by the enthusiasm, nor by the skepticism, of the researcher toward the treatment being evaluated. In addition, they described eight essential features of an adequate study of treatment effectiveness:

- *Specific diagnosis* of patients before treatment
- *Random assignment* of patients to treatment options
- Use of *severity measures* to assess patients
- *Standardized therapy*
- *Informed consent*, specifying risks versus benefits
- Use of objective "*blind*" raters to assess diagnostic category or patient improvement

- Use of *placebo control* groups
- Acknowledging *importance of follow-up*

Methodology of the Saskatchewan Hospital Study

Of these requirements, the Saskatchewan Hospital pilot study made no provision for *random assignment*, and evidently dismissed *placebo control* as an impossibility. *Severity measures* were employed, but were unsophisticated by comparison with today's assessments. The pilot study did not methodically use *blind raters* to assess diagnostic category or patient improvement, but did employ diagnoses determined by the patients' own therapists, who were not members of the research team. The patient population was not homogeneous, nor was treatment directed at patients with a *specific diagnosis*. Although all were designated as refractory alcoholics, the treated group also contained subgroups with other psychiatric diagnoses and abusers of other drugs. No attempt was made to conceal the nature of the drug from the patients, and *informed consent* was obtained. Although the duration of follow-up varied widely from patient to patient, confirmation of the patients' estimates of their posttreatment drinking was sought from other observers, and the use of AA to obtain follow-up data suggests that the *importance of follow-up* was understood by the researchers. *Standardized psychotherapy* was attempted for the technique used in LSD sessions, and a treatment manual was developed, but no description of the content of this manual nor of therapist supervision was provided. Smith recognized the methodologic imperfections of the pilot study, and called for carefully controlled clinical trials to further investigate encouraging preliminary results (Smith 1959, 1958).

Theory Development in the Saskatchewan Hospital Study

There is a well-documented tendency for proponents of various psychotherapeutic theoretical orientations to find their concepts of the psyche confirmed in psychedelic drug sessions (McCabe & Hanlon 1977; Grof & Grof 1975; Ditman & Whittlesey 1959; Whitelaw 1957; Sandison & Spencer 1954; Katzenelbogen & Fang 1953). In the work of the Saskatchewan Hospital research group, some of these core concepts were derived from the work of William James and of Harry M. Tiebout (James 1982; Tiebout 1954, 1953, 1949). Hoffer and Osmond were influenced by James' stories of conversion as a turning point in the alcoholic career, and by Tiebout's formulation of the conversion experience (Osmond 1957). According to Tiebout, conversion is a psychological event in which a person who is governed by a set of hostile, negative attitudes shifts to predominantly positive and affirmative ones (Tiebout 1949). This is catalyzed by what Tiebout (1949) describes as an act of surrender:

We can now be more precise in our definition of an act of surrender. It is to be viewed as a moment when the unconscious forces of defiance and grandiosity actually cease to function

effectively. When that happens the individual is wide open to reality; he can listen and learn without conflict and fighting back. He is receptive to life, not antagonistic. He senses relatedness and an at-oneness which become the sources of an inner peace and serenity, the possession of which frees the individual from his compulsion to drink. In other words, an act of surrender is an occasion when the individual no longer fights life but accepts it.

This moment arrives when the "force of circumstance or reality" (Tiebout 1949: 58) renders the alcoholic completely powerless. It was this force of circumstance that Osmond and Hoffer speculated might be found in the experience of *delirium tremens*. Contrary to their expectations, the high doses used for their presumably refractory alcoholic subjects propelled many of them, not into a frightening and aversive delirium, but into an experience of transcendence and conversion.

THE PSYCHEDELIC EXPERIENCE AS DISTINGUISHED FROM THE *DELIRIUM TREMENS*

In May of 1958, Ditman and Whittelsey presented their report of a card sort test designed to compare *delirium tremens* and the LSD experience. They concluded that: "The delirium tremens experience was predominantly characterized by hallucinations that seemed real, anxiety, horror, depression, irritation, and paranoid thoughts. The LSD experience, in contrast, was typified by euphoria, humor, relaxation, and a nebulous sense of wonderment" (Ditman & Whittlesley 1959).

Smith was aware of the varying and contradictory descriptions of the phenomena produced by drugs with supposed hallucinogenic properties even before he began to work with them in therapy. In his follow-up article to the Saskatchewan Hospital pilot study, he reported three different kinds of observed effects of LSD and mescaline: experiences similar to those of *delirium tremens*; enhancement of access to previously repressed material for psychoanalysis; and effects resembling religious conversion experiences (Smith 1958). Other investigators would subsequently describe these phenomena as stages in a continuum of experience (Savage 1962; Sherwood, Stolaroff & Harman 1962). Smith had noted that the patients who had an intense reaction to LSD had improved more than those having a mild one (Smith 1958). Ditman's work and his own experience convinced Smith that the similarity between the effects of LSD and *delirium tremens* was superficial.

In September 1959, the Saskatchewan Hospital research group published a further follow-up to Smith's two previous reports, including results of the treatment of an additional 16 patients using the modifications in technique that had been implemented after the group's contact with A. M. Hubbard. This report pointed out that the experience obtained resulted from a combination of the patient's

attitude, the effect of the drug on the individual, and the surroundings of the patient during the drug experience; and that it was "impossible to state categorically what the effect of the drug alone [might be]" (Chwelos et al. 1959).

Self-Surrender as a Factor in Treatment Effectiveness

The Saskatchewan researchers attempted to list the most common changes in perceptions, emotions and understanding reported by patients and volunteers who had LSD sessions. These effects were then grouped into six types or levels of experience: this represented a continuum determined by the degree to which the subject experienced surrender of his usual patterns of emotions and perceptions, and changed his self-concept in favor of complete self-acceptance. They concluded that the therapeutic importance of the LSD experience lay in its ability to disrupt habitual patterns of thinking and feeling to create an opportunity for this change in self-concept to occur.

The differences in the phenomena reported by different researchers to be caused by psychedelic drugs were understood to be the product of patients' differing levels of experienced self-surrender. This level in turn was influenced by the extent to which the therapeutic atmosphere reflected complete acceptance of the patient. The researchers proposed that psychotic manifestations seen in the drug experience were produced by the person's trying to maintain his usual perceptions and self-concept. Confrontation with repressed unconscious material was understood as a preliminary stage in the process of gaining complete self-understanding and self-acceptance (Chwelos et al. 1959).

Given this understanding of the importance of surrender in psychedelic therapy, the Saskatchewan research group emphasized the need for a safe and supportive environment and empathetic staff. They pointed out that "unsympathetic, hostile, and unfeeling personnel bring about fear and hostility with a marked increase in the psychotic aspect of the experience" (Chwelos et al. 1959). These views reflected the influence of A. M. Hubbard on the Saskatchewan Hospital research group.

The Hollywood Hospital Studies

This shared perspective was described by the first report of the research group at Hollywood Hospital in Vancouver, where Hubbard was the Director of Psychological Research (MacLean et al. 1961). Hubbard's work, which "has never been widely reported in the scholarly and professional journals," influenced many of the earliest researchers, self-experimenters and therapists to use psychedelic drugs (Caldwell 1968: 45). The Hollywood Hospital report is the only one that bears his name; however, his practice of arranging the emotional and physical surroundings of the drug experience to encourage a profound experience of ego-transcendence became a crucial ingredient of successful psychedelic therapy (McCabe & Hanlon 1977; Caldwell 1968; Terrill 1962). The Hollywood

Hospital group provided an articulate description of the effects of LSD as they were understood by these two groups of researchers:

The ingestion of a therapeutic dose of LSD-25 produces profound alterations in perception, e.g., visually colors become brighter and patterns become more clearly defined. These changes occur within an hour and become more marked during the ensuing two or three hours. All perceptual modalities show parallel changes.

Because an individual's concept of reality is based upon his sense experience it follows that if these sense experiences be altered, his reality ties are lost to him. This includes his self-concept. A state is induced in which the unifying aspects of the individual's personality cease to function. In an uncontrolled setting, this reduction of self-concept to the point of depersonalization often results in confusion and panic. This is why LSD-25 was initially classed as an hallucinogenic or psychotomimetic (psychosis mimicking) agent. But if the same process can be controlled, an experience can be developed in which the usual screen of rationalization is much reduced and may even be almost eliminated. The therapeutically controlled situation permits and helps the person to find meaning, reality and structure in the unusual experience. When the unhabitual perceptions are organized the individual undergoes what Osmond has referred to as a psychedelic (mind-manifesting) experience. It is this experience with its increased insight, its expanded awareness, and its altered frames of reference, that is the therapeutic vehicle. LSD-25 is not a medication in the usual sense. It is simply a triggering mechanism that initiates an experience lasting 12 hours or more. . . . Since it is, therefore, the experience and not the medication that is therapeutic, the treatment situation or milieu becomes the overwhelmingly important factor. It must permit the person to find new reference points, and it becomes the function of the therapist to provide these in such a way that they will be understandable to the patient and conducive to his emotional growth. . . . In guiding such an experience the therapist must refrain from projecting his own solutions to problems upon his patient. On the other hand, if he is to help the patient find any structure in the experience he must in some way assist in the provision of a new frame of reference. A way of accomplishing this without projection, developed by one of our group, is to provide universal symbols to which the subject may attach his own meaning. Through these symbols he may become aware of those archetypal or universal meanings which underlie all human feeling and thinking. The symbols provide intermediate points of reference, creating a bridge between the habitual self-concept and a new concept based on self understanding and self-acceptance. . . . As this new self-concept develops, the need for habitual inappropriate defense mechanisms is reduced and the patient can now relate to another person more directly, with less defensive screening (MacLean et al. 1961).

MacLean and his colleagues used a large initial dose of 400µg. They reported on a total of 61 alcoholics (50 men and 11 women), with an average period of uncontrolled drinking of 14.36 years. Pretreatment status was assessed using an autobiography, psychiatric history, and therapists' notes from preparatory sessions. These cases were considered to have an unfavorable prognosis because of failure in AA, numerous previous hospital admissions, and a history

of *delirium tremens*. Follow-up data were collected using interviews and questionnaires; patients were scored on interpersonal relationships, work habits, self-appraisal and the appraisal of close associates. Drinking patterns and signs and symptoms of psychosis were scored if applicable. A composite score was obtained by combining these data. Weighting given to the various measures was not specified. After a median of 9.09 months of follow-up, 30 patients (49%) were "much improved." This was defined as complete abstinence or a "marked improvement" in drinking pattern compared to the 12 months preceding therapy, as well as marked improvement in interpersonal relationships, work habits, self-acceptance and family relations. The criteria for improvement in these areas were not specified. Sixteen patients (26%) were "improved" in the rated areas, including a "definite reduction in alcohol intake"; 15 (25%) were unchanged (MacLean et al. 1961: 38). The researchers concluded that "LSD-25, *used with the described treatment method* [italics added], is effective in the treatment of alcoholism. . . ." (MacLean et al. 1961: 45).

Methodology in the Hollywood Hospital Studies

Many of the criteria for an adequate study described by O'Brien and Jones were not met by this report. *Specific diagnoses* were established only to the extent of grouping the patients into four diagnostic categories based on coexisting problems. Years of uncontrolled drinking and history of alcohol complications were the only assessments used to determine *severity*. Only four of the total of 61 patients were "uncomplicated alcoholics" (MacLean et al. 1961). *Informed consent* was not mentioned, but patients were counseled about what might occur during their LSD sessions during the preparatory period. *Placebo control* was not attempted, and patients were not *randomly selected*, instead being targeted for selection as particularly difficult cases with an unfavorable prognosis. The treatment environment, and the composition, experience and attitude of the treatment group were identified as significant factors, and were specified in detail; and a treatment manual was developed, but was not described in the report (Blewett & Chwelos 1959). *Objective raters* were not used. The period of *follow-up* varied from three to 18 months (median 9.09 months). The Hollywood Hospital research group planned this study as a large-scale follow-up to the exploratory work of the Saskatchewan Hospital group, but no hypothesis was specified for testing in their study (MacLean et al. 1961).

In their report, which was submitted for publication in early April of 1960, the Hollywood Hospital research group took note that fears of "cultism, fanaticism or thrill-seeking" were developing around the use of psychedelic drugs, but deemed such fears overrated (MacLean et al. 1961: 44). In January of 1960, a day-long symposium on LSD was held at Napa State Hospital, and subsequently broadcast on radio station KPFA. The symposium attracted

considerable attention, in part by presenting a "new view" that LSD was more than a facilitator of therapy; it was an entirely new experience. Some of the papers from this symposium, which were later published in the *Journal of Nervous and Mental Disease* (Savage 1962; Terrill 1962), cited the Canadian research groups as the developers of this new view. Although an increasing number of persons outside the research environment were becoming interested in LSD, MacLean and his colleagues took the position that even though the LSD experience might be attractive because of its ability to "amaze and even overwhelm the individual through changes in perception . . . [the] extreme physical and psychological discomfort" that this new experience could produce would act as a built-in control for potential misuse (MacLean et al. 1961: 44).

EARLY CONTROLLED STUDIES

The York County Clinic Studies

The first research group to attempt a controlled study of the use of psychedelic therapy for alcoholism was the York County Mental Health Clinic in Newmarket, Ontario, Canada (Jensen 1963; Jensen & Ramsay 1963). Their treatment was based upon an attempt to instill the motivation to get well in chronic alcoholics who were assumed to be ambivalent about admission to a program of milieu therapy. In their pilot study, published in June 1962, patients were divided into three groups: 58 patients received the full inpatient treatment program, including LSD therapy; 35 received the researchers' standard therapy but no LSD; and 45 others were admitted to the hospital for treatment by other psychiatrists during the same period. The group receiving standard therapy without LSD was composed of patients who were judged to be unfit for LSD therapy, left the hospital early, or refused the LSD treatment. Thirty-eight patients, or 70% of the LSD treatment group, were judged to be improved at six to eight months post-discharge, compared to 47% and 45% of the two control groups (Jensen 1963).

Based on these preliminary findings, further research was conducted using a modification of this design, and a subsequent report was published in June 1963. This report covered a total of 70 patients receiving the full program of milieu therapy, AA group meetings and LSD treatment, and 55 controls who were assigned to psychiatrists not using LSD when no beds were available to them in the experimental unit at the time of their admission. No attempt was made to include those who refused to take LSD, who left the hospital before their LSD session or who were "considered unfit for LSD therapy" in the evaluation (Jensen 1963: 319). Eight of the treatment group and 26 of the controls were not available at follow-up. Of the remainder, 74% (46) of the treatment group, and 41% (12) of the controls were improved at six to 18 months post-discharge (Jensen 1963).

Although Jensen and his colleagues attempted to provide a control or comparison group, the many methodological

difficulties of these studies severely limited their usefulness. In particular, the large number of the controls not found at follow-up creates great difficulty in comparing the results in the two groups. Additional problems with the studies include the variability in the period of follow-up, the lack of a specific diagnosis or severity measure, and uncertainty about how the posttreatment rating was determined.

The Union Hospital Studies

Despite methodologic problems, the reported success of the early Canadian exploratory studies encouraged the expansion of LSD treatment programs for alcoholism in Canada. Beginning in 1959, O'Reilly and Reich, and O'Reilly and Funk conducted a series of LSD treatments of alcoholics at Union Hospital in Moose Jaw, Saskatchewan (O'Reilly & Funk 1964; O'Reilly & Reich 1962). A total of 68 patients were treated with a 200 μ g. dose of LSD. Fifteen of the patients had more than one LSD session. Patients were consecutive admissions to the psychiatric department, and all were chronic alcoholics who had not responded to other forms of treatment. International Classification of Diseases (ICD) diagnoses were assigned for a variety of additional problems. A special nurse was assigned to each patient to explain and discuss all aspects of the LSD treatment. Patients were monitored for two to 34 months, and collateral information on drinking status was obtained from relatives and agencies in addition to patient self-reports. The immediate response to therapy was assessed after two months, and the last two months of the follow-up period were used to indicate recent trends. Thirty-eight percent of the patients were completely abstinent during the two months preceding follow-up. Abstinence was not found to be related to patient demographics, concurrent diagnoses, social circumstances, drinking history, nor to which of eight psychiatrists administered the patients' LSD sessions. Only "the nature of the LSD experience" was independently correlated with future abstinence (O'Reilly & Funk 1964: 260). What the researchers defined as a "transcendental" experience, "a new way of looking at one's life, with a loss of previous defensive meanings or perceptions of oneself" was the only factor found to be related to sobriety (O'Reilly & Funk 1964: 260).

The Union Hospital studies share many of the methodological flaws that were present in other self-described exploratory studies of this period. The patients vary in diagnosis and severity, there is no control group, the period of follow-up is not standardized, and the pre- and posttreatment data obtained are not clearly specified. The second report, by O'Reilly and Funk, which appeared in June of 1964, noted that controversy was arising over the use of LSD-25 in psychiatry. The authors may have been referring to numerous stories that appeared in 1963 and 1964 in the popular press, and to efforts to limit the

accessibility of psychedelic drugs by U.S. and Canadian authorities. The potential impact of such publicity on the willingness of patients to participate in LSD therapy and on the interpretation of reported success rates was mentioned briefly, but deemed to be "outside the scope of this study" (O'Reilly & Funk 1964). In any case, the future of LSD treatment for alcoholism seemed assured in Saskatchewan. In December 1962, the Saskatchewan Bureau on Alcoholism had reported that "such excellent results have been noted by the bureau staff in individual cases, usually with resistance to other forms of therapy, that LSD treatment, which was originally regarded by the bureau as experimental, became a standard form of treatment to be used where indicated" (Bureau on Alcoholism 1962).

RESTRICTION OF ACCESS TO LSD

The Growth of LSD Experimentation

Beside using LSD in the treatment of alcoholism, U. S. researchers had begun to explore the possibility that it might be used to enhance creativity, or to facilitate psychotherapy (Eisner & Cohen 1958). In their enthusiasm, some researchers had begun to share LSD with friends in their homes, and as publicity about the effects of LSD increased, so did the demand for LSD experiences (Abramson 1967: 475). Many prominent persons, including the founder of Alcoholics Anonymous, Bill Wilson, and Chuck Dederich, the founder of Synanon, were having LSD sessions. Television and newspaper coverage depicted LSD as a new wonder drug (Novak 1997). A 1958 report in the *Journal of Nervous and Mental Disease* included "LSD-25 social parties" in a list of ways that LSD might be used (Feld, Goodman & Guido 1958: 176).

Cohen's Survey of Investigators

The first attempt to systematically assess the potential side effects and complications of psychedelic therapy was Sidney Cohen's 1960 survey of 62 investigators using psilocybin or LSD in therapy. The 44 researchers who replied to his questionnaire had administered psychedelics to almost 5,000 individuals on more than 25,000 occasions. Based on the data they supplied, Cohen estimated that psychotic breaks, panic attacks and other psychiatric reactions lasting over 48 hours occurred in 0.8 per 1000 normal volunteers, and 1.8 per 1000 patients undergoing therapy. Suicide was a less frequent complication, occurring in less than 0.4 per 1000 patients. No suicides or suicide attempts were reported in volunteers.

Cohen concluded that untoward events were infrequent, and that the psychedelics were "safe when given to a selected healthy group" if used with proper precautions (Cohen 1960: 39). Recommended precautions included constant supervision, hospitalization if doses greater than 1µg. per kg of body weight were used, provision of trained

and experienced support personnel during the experience, and the availability of consultation in the event of post-treatment symptom development (Cohen 1960).

Despite the relatively benign picture painted by Cohen's survey, by the end of 1961 a "climate of criticism" was developing around psychedelic research (Stevens 1987). Psychopharmacologist Jonathan O. Cole expressed "very mixed feelings" about research with psychedelics, particularly the possibility that they might be used to "establish long-term control over minds" by "altering loyalties or changing moral attitudes or political beliefs" (Cole 1961: 117). Sensational accounts of the LSD experiences of celebrities, the influence of LSD on creativity, and the superiority of LSD treatment to conventional psychotherapy spurred popular demand, and college students began experimenting with psychedelics (Novak 1997; Subcommittee on Executive Reorganization 1966).

The Harvard Experiments

In October 1961, the Harvard Psilocybin Research Project run by Timothy Leary and Richard Alpert had been criticized by its sponsor, the Center for Research in Personality, for failure to adhere to guidelines similar to Cohen's. At a special faculty meeting, David MacClelland, director of the Center, enumerated four "symptoms" he had noticed in the Project's participants, both researchers and experimental subjects. Disassociation and detachment, interpersonal insensitivity, religious and philosophical naïveté, and impulsivity seemed to distinguish those who had taken LSD. MacClelland saw these characteristics as evidence that the chief effects of psilocybin and similar substances were to encourage withdrawal from social reality and concentration on one's inner life (Caldwell 1968; Gordon 1963). The Project was required to surrender its official supply of psilocybin to Dr. Dana Farnsworth, head of the University Health Service, to be released only for experiments approved by an *ad hoc* faculty committee. Reports of the disciplinary action were carried by the *Harvard Crimson* and then picked up by national news wire services.

In the Spring of 1962, when the committee refused to provide psilocybin for Walter Pahnke's (a doctoral student in the History of Philosophy and Religion) carefully designed Marsh Chapel experiment on the ability of psilocybin to provoke mystical experience, supplies that had not been surrendered by Leary and Alpert were used instead (Stevens 1987; Gordon 1963; Pahnke 1963). University authorities protested that this was not the only occasion on which Leary and Alpert had failed to follow the newly agreed-upon procedure. Psychedelic researchers defended their action, pointing out that Pahnke's faculty-appointed doctoral committee had approved the experimental protocol, and that Farnsworth was "in no way equipped as an expert" on the use of psychedelic drugs (Clark 1969: 47). Soon afterward, Timothy Leary left Harvard without notice, and Richard

Alpert became the only Harvard faculty member to be fired in this century.

This highly controversial episode was discussed in a special issue of the *Harvard Alumni Bulletin* on the university's professors and their work. Henry K. Beecher, the Dorr Professor of Research in Anaesthesia, refuted the accusation that University opposition was driving research underground, and maintained that, to the contrary, there was "an abundance of support in this field for the able, responsible investigator, at present more than ever before" (Beecher 1963).

Reports of Adverse Reactions, Untoward Events and Complications

By July of 1962, Sidney Cohen and Keith Ditman had encountered the rapidly growing illicit use of LSD, and had published an article describing "an increasing number of untoward events in connection with LSD-25 administration" (Cohen & Ditman 1962). Although they continued to support the investigational use of LSD for its potential to aid in the study of the mind, they pointed out that the unsupervised use of the drug increased its potential for producing serious consequences. The consequences mentioned included antisocial acting-out behaviors, misuse of LSD as part of a larger pattern of multidrug use and "abuse of [the] euphoriant property" of LSD by marketing it as an item of underworld traffic (Cohen & Ditman 1962: 161).

This was followed by a second report on adverse reactions to LSD, in which Cohen and Ditman foresaw that the problems that could occur after inexpert or casual experimentation could further complicate the research environment (Cohen & Ditman 1963). They reported on nine cases illustrating several types of untoward effects: prolonged psychotic decompensation, depressive reactions, release of preexisting psychopathic antisocial trends, abandonment of social responsibilities, and paranoid reactions in which the transcendental aspects of the LSD experience confirmed latent ideas of grandiosity. They still held that such reactions were infrequent, however, as long as the drug was employed with "carefully screened, maximally supervised patients, given the drug by responsible, experienced investigators" (Cohen & Ditman 1963). With considerable prescience, they noted that: "When undesirable reactions and sensational publicity become associated with a drug, competent investigators are inclined to avoid participating in the careful, thoughtful studies that are necessary to evaluate it properly" (Cohen & Ditman 1963). By December of 1962, when this article was submitted, new legislation had already been passed by the U.S. Congress that would restrict availability of LSD solely to researchers engaged in federally-approved studies.

LSD as an Investigational New Drug

The discovery of the teratogenic properties of thalidomide had focused attention on the need for better regulation

of the use of experimental drugs. In 1962, the Kefauver-Harris amendment to the Cosmetic, Food and Drug Act of 1938, created a class of "investigational new drugs," i.e., drugs that had not yet been marketed, but were undergoing testing to demonstrate their safety and efficacy. These "new drugs" could not be distributed commercially without approval from the Food and Drug Administration (FDA). Despite the fact that they had been studied for almost two decades and had been the subject of more than one thousand English-language articles (Cohen 1968), several of the psychedelics fell under this classification, as the FDA was not satisfied that their safety and efficacy had been established (Subcommittee on Executive Reorganization 1966: 61).

A special investigational new drug (IND) application form for permission to use drugs classified as investigational was instituted in 1963; before that time anyone could order LSD, psilocybin or mescaline by submitting to Sandoz a signed statement that the person ordering had the training and facilities to conduct drug investigations, and that the supplies of the experimental drug obtained would be used only for research purposes (Subcommittee on Executive Reorganization 1966: 60). Researchers and other interested users obtained LSD and psilocybin from Sandoz's branch office in New Jersey. LSD was supplied under the trade name Delysid[®], in the form of small, blue 25µg. tablets or 100µg./cc ampoules for parenteral use (Hollister 1968). Mescaline could be ordered from several chemical supply firms for about \$20 per gram (Weil 1963). These sources had provided material with which therapists in Los Angeles, Vancouver, and the San Francisco Bay Area were providing LSD sessions to paying clients eager for the experience (Stevens 1987; Sherwood, Stolaroff & Hartman 1962; Chandler & Hartman 1960).

Under the new IND regulations, Sandoz technically became the "sponsor" for all investigations of LSD and psilocybin. James Goddard of the FDA testified in 1966 that Sandoz had in 1963 filed a basic investigational plan for testing LSD that indicated that a reasonably safe and rationally conducted program of experimentation would be required of researchers (Subcommittee on Executive Reorganization 1966: 61). There was, as yet, no direct relationship between investigators and the FDA (Lowinger 1966). Sandoz's role in relation to psychedelic researchers was more that of distributor of LSD than as the sponsor of research, and researchers were using LSD from Sandoz in studies that were not designed by Sandoz (Levine 1998). Sandoz's patent on LSD-25 expired in 1963, and manufacturers in Czechoslovakia and Italy soon began commercial production of the drug. Sandoz was becoming uneasy about its ability to continue to control the distribution of LSD (Christen 1966).

LSD Coverage in the Popular Press

A flurry of articles about LSD appeared in popular

periodicals during 1963, until, as Abram Hoffer suggested, it was "hardly likely that any literate citizen has not heard something about it" (Hoffer 1967). The *Ladies' Home Journal* quoted Jonathan Cole of the National Institute of Mental Health on LSD in an article on "Instant Happiness": "[LSD] can produce an unstable state varying—within five minutes—from horror to ecstasy" (Goldman 1963). *Time* described spiritual experiences reported by users of psilocybin, LSD and peyote as "instant mysticism" (Anonymous 1963b). *Cosmopolitan* reported that: "Suddenly LSD has become the sophisticated 'fun thing' to try around the smart set, the fast set and the beat set, and if you haven't got a buddy who can run down to his friendly neighborhood LSD bootlegger and buy an ampoule of those little blue pills, you are simply not in, my friend" (Gaines 1963).

As the drug's official sponsor, Sandoz began in 1963 to restrict the U.S. distribution of LSD to National Institute of Mental Health-funded programs, Veteran's Administration-sanctioned programs in VA hospitals, government agencies, and programs in state universities that had approval from state mental health commissioners (Caldwell 1968). In Canada, transportation and sale of LSD were forbidden, and possession was permitted only by researchers with university appointments who were listed with the Ministry of Health (Hoffer 1967). Private therapists without institutional affiliations were not included in the list of approved researchers for whom Sandoz would act as the IND application sponsor. Unlike the "neighborhood bootlegger," most therapists and clinics were unable to obtain the psychedelics, as they could not afford the time and expense the new regulations required them to invest (Janiger 1996). Some therapists continued to do LSD work with their patients, but the patients had to obtain their own drugs on the black market (Abramson 1967). Other therapists were forced to discontinue their work because of problems with funding. The International Foundation for Advanced Study in Menlo Park, California, operated by Robert Mogar, Willis Harmon, Myron Stolaroff and others, closed in 1964 because the fee of \$650 per person per session was not enough to cover costs, and hoped-for federal financial support was not forthcoming (Editor 1964).

THE DEVELOPMENT OF PROFESSIONAL CONTROVERSY

As it was quite difficult to synthesize pure LSD-25, controls on importation and use were originally thought to be adequate for restricting the illicit supply. In the early 1960s, however, a new process for culturing the ergot fungus made the precursor chemicals much more readily available (Osmond 1973). The 1963 White House Conference on Narcotics and Drug Abuse considered the psychedelics to be of only minor importance as drugs of abuse, largely because of their limited availability and high cost (White House Conference on Narcotics and Drug

Abuse 1963). Others foresaw that the publicity that they had received and the possibility of profit would be likely to increase their distribution (Cohen & Ditman 1962).

Theoretical and philosophical speculation about LSD was beginning to appear in the journal literature. Joel Elkes, who had been among the first to call attention to the potential for untoward reactions to LSD (Elkes, Elkes & Mayer-Gross 1954), reiterated concerns about the side effects, complications, and dangers of abuse of the psychedelics that had been noted earlier in Cohen's survey of research (Elkes 1963). In a short editorial, Roy Grinker (the editor of *Archives of General Psychiatry*) claimed that "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 . . ." necessitating greater controls on the use of LSD (Grinker 1963: 425).

This editorial by Grinker, who never published any work on LSD and was, according to Abram Hoffer, "uncontaminated by first-hand experience with it" (Hoffer 1967), appeared in the same issue of the *Archives of General Psychiatry* as Cohen and Ditman's study of prolonged adverse reactions to LSD, and was subsequently cited as a reference on the severity of the LSD problem by a 1963 editorial in the *Journal of the American Medical Association*, among others. The *JAMA* editorial, by Dana Farnsworth of the Harvard University Health Service, admitted that research on the psychedelics was vital and should continue. While he decried the "hysterical attitude that could result in the adoption of unwarranted restrictive legislation," he also suggested that "regular use of the hallucinogens will prepare individuals to 'move up' to other and more powerful drugs such as morphine or heroin" and described psychedelics as "substances which are a real menace to mental and physical health" (Farnsworth 1963).

By March of 1964, *JAMA* described the use and misuse of the psychedelics as "among the touchiest topics of recent months" and provided "a sober look at the present situation" by Jonathan Cole and Martin Katz (1964: 758), two senior psychopharmacologists from the National Institutes of Mental Health (NIMH). Cole and Katz likened the "psychotomimetics" to the broom of the sorcerer's apprentice (in that they had walked out of the laboratory and turned on their researchers) and maintained that "rather than being the subject of careful scientific inquiry, these agents have become invested with an aura of magic. . . ." (p. 758). Nevertheless, Cole and Katz asserted the need for careful study of this class of drugs because of the potential importance of the therapeutic claims made for them in treatment of otherwise treatment-resistant psychiatric conditions.

Cole was the first to publicly favor "the Scotch verdict of 'not proven' [as] . . . a skeptical middle position" on the therapeutic use of psychedelic drugs (Cole & Katz 1964: 759) an assessment that recurs intriguingly in the subsequent

literature (Levine 1968; Ettinger 1967; Smart & Storm 1964). When NIMH set up the Psychopharmacology Service Center to monitor LSD-type drugs, Cole was appointed chief. Cole introduced Sanford Unger and Albert Kurland in early 1963, and encouraged them to start the Alcoholic Rehabilitation Unit at Spring Grove State Hospital in Baltimore, where they could subject the psychedelic approach to therapy to "careful study under closely controlled conditions" (Cole & Katz 1964: 759).

Cole and Katz' *JAMA* article was accompanied by Roy Grinker's second editorial warning of the dangers of the drugs he described as "psychomimetic [sic]" (Grinker 1964: 768). Dr. Grinker complained that the use by therapists of LSD made it "impossible to find an investigator willing to work with LSD-25 who was not himself an 'addict'" (Grinker 1964). This usage is a classic example of a basic misconception described by Fort: "Generally any socially disapproved drug comes to be referred to as narcotics or dope and the user as an addict" (Fort 1968). Nevertheless, Grinker's editorial was widely quoted in the popular press, and used as evidence of the dangers of LSD research by the editors of the *New England Journal of Medicine* (Editor 1966).

Battle lines were being drawn. At the May 1964 convention of the American Psychiatric Association (APA), the controversies about LSD became "a central point of interest, fear, and warnings" (Godfrey 1969: 228). Advertisements announcing the publication of a new journal, the *Psychedelic Review*, were refused by *The Progressive* and by *American Psychologist* (Bunce 1979). Despite the passion with which the psychedelics were discussed by both proponents and opponents, there still seemed to be consensus that what was needed was more and better-designed research (Cole & Katz 1964; Beecher 1963; Cohen & Ditman 1963, 1962; Farnsworth 1963; Grinker 1963). The complex machinery of experimental design and research funding was slowly moving to produce "detailed and carefully controlled studies designed to be free from possible distortions due to either bias or enthusiasm" (Cole & Katz 1964).

CALLS FOR CONTROLLED STUDIES

Smart and Storm's Critique of LSD Research

In June of 1964, the first comprehensive critical assessment of the existing research on the use of LSD in the treatment of alcoholism was published by the *Quarterly Journal of Studies on Alcohol*. Reginald Smart and Thomas Storm of the Addiction Research Foundation in Toronto, Canada outlined some basic requirements for clinical research on treatment efficacy: random assignment of subjects, objective comparison of posttreatment outcomes with pretreatment ratings, a control group receiving placebo or nondrug treatment, and follow-up at fixed post-treatment intervals (Smart & Storm 1964). They acknowledged that failure to use a control group was

common in psychiatric treatment, and pointed out that the exceptional numbers of positive results found in early reports of a new therapy was particularly characteristic of uncontrolled trials. Since none of the studies they examined had employed placebo control, Smart and Storm suggested that "a placebo having some immediate but mild sensory effect" could usefully have been employed because of the highly variable effects expected from LSD administration (Smart & Storm 1964: 335). The follow-up procedures of the five reviewed studies were also criticized for their lack of precise outcome measures, pretreatment comparison measures, and fixed follow-up intervals (MacLean et al. 1961; Chandler & Hartman 1960; Chwelos et al. 1959; Eisner & Cohen 1958; Smith 1958). The overall assessment was that these deficiencies "raised serious questions concerning the scientific warrant for any belief that LSD is a useful adjunct to the treatment of alcoholism" (Smart & Storm 1964). Even so, Smart and Storm also returned the "Scottish verdict of 'not proven'" and called for further study of the therapeutic usefulness of LSD (1964: 337).

Because this review was the beginning of a blizzard of controversy about the earliest published research on LSD as a treatment for alcoholism, two significant details are of interest. The first is the use of "not proven" as an assessment of the usefulness of LSD as an alcoholism treatment. This Scottish expression, infrequently used in U.S. English, has surfaced fairly frequently since then as a description of the status of LSD therapy. It had been employed by Cole and Katz in this context in their March 1964 *JAMA* article. Since Smart and Storm submitted their critique for publication in October 1963, one wonders if they might possibly have influenced Cole and Katz through some kind of prerelease circulation of their critique. In any case, Smart and Storm's critique was circulated in July, one month post-publication, to thousands of U.S. and Canadian physicians in résumé form (Jordy 1964). By August, Colin Smith had already submitted a reply (Smith 1964).

Smith's Reply to Smart and Storm

Smith's reply, which appeared in December 1964, was in part concerned with the second significant detail: Smart and Storm's assertion that there had been no calls from the earliest LSD researchers for controlled clinical trials. He pointed out that he had, in fact, recommended that controlled trials follow the Saskatchewan Hospital group's self-identified exploratory studies, and had further argued that exploratory studies were essential in order to derive a testable hypothesis and to obtain research support for controlled trials. Smith acknowledged that the current methods for evaluating the effectiveness of alcoholism treatment were unsatisfactory, and prophetically suggested that an alliance of methodologists and clinicians was required for improvement (Smith 1964).

In addition, Smith addressed an issue not raised by Smart and Storm's critique: the safety of lysergide treatment. He cited reports by Cohen, and Cohen and Ditman, on the infrequency of adverse LSD reactions (Cohen & Ditman 1963; Cohen & Ditman 1962; Cohen 1960). He pointed out that Hoffer's new and extensive review of the literature on therapeutic use of psychedelics had reached the conclusion that the risk of complications from the use of lysergides in therapy seemed to compare favorably with other psychiatric treatments including those using electroconvulsive therapy, tranquilizers, and insulin coma (Hoffer 1965; Smith 1964).

Hoffer's Review of LSD's History

In March of 1965, Hoffer published a comprehensive review article concerning LSD's history; originally titled "D-Lysergic acid diethylamide (LSD): A review of its present *value*" [italics added], it was retitled "A review of its present *status*" before publication (Smith 1964). Hoffer depicted the entire history of LSD since the discovery of its psychoactive properties as a series of controversies: whether it produced a model of schizophrenia, whether it was therapeutically useful, and whether its unsupervised use could be controlled. He also divided psychedelic research into three stages: the early work of Osmond and others in Canada on psychotomimesis and alcoholism treatment; the expansion, catalyzed by A. L. Hubbard, of psychedelic treatment for "a broad group of behavioral problems and neuroses" by therapists in California; and large-scale trials at Spring Grove Hospital in Maryland and elsewhere (Hoffer 1965). Hoffer pointed out that since most people were unaware of the early studies, they were conducted in an atmosphere free from both harsh criticism and legal restriction. With the publicity that resulted from the activities of Leary and Alpert at Harvard University, the general public had become aware of the use and abuse of the psychedelics, and widespread media interest had led to the imposition of strict legal controls. The result, in Hoffer's estimation, was a research environment pervaded by fear and mistrust (Hoffer 1965).

Ludwig and Levine's Analysis of the LSD Controversy

In October of 1964, Jerome Levine and Arnold Ludwig (who were planning what was to become the most methodologically complex and frequently cited study of psychedelic therapy for alcoholism) published an exceptionally well-balanced analysis of "the LSD Controversy." They pointed out that, in evaluating LSD therapy, "besides the many methodological and conceptual problems which arise in evaluating the usefulness of any form of psychiatric therapy, certain other 'non-scientific' factors tend to cloud the issues" in regard to LSD (Levine & Ludwig 1964). Among these were the aura of sensationalism created by the notorious adventures of Leary and Alpert; the introduction of bias and imprecision by therapists' use of the

substances they were studying; the lack of controls in virtually all early studies of the psychedelics; and the widely varying estimates of the dangers and risks involved in the use of LSD.

Levine and Ludwig (1964) suggested that both popular accounts and journal editorials gave a "misleading and exaggerated" impression of the research data available, by suggesting that LSD was "fairly dangerous, with rather serious complications, mostly of a mental nature." They maintained that "neither advocates nor critics seem[ed] to have enough objective information on which to base their entrenched positions," and called for adequately controlled studies and follow-up evaluations before drawing any final conclusions. Also, two concerns were expressed: that research with LSD would be curtailed because of the accumulation of "erroneous impressions, incomplete case reports, hearsay accounts, and illogical interpretations" about the dangers of LSD, and that the increasing use of LSD outside of a therapeutic or experimental setting might expose unsupervised users to unforeseen dangers.

Adverse Reactions to Unsupervised Use

While FDA commissioner James Goddard later testified that investigations as late as 1963 did not disclose any widespread abuse of LSD, others would claim that by the time the first surveillance of nonmedical and illegal use of LSD was conducted in 1961, there was already more LSD in the community than in the research environment (Novak 1997). In May of 1966, Ungerleider and Fisher (1966) asserted that "far more LSD is bought on the black market (it is either imported illegally from Mexico or produced locally by amateur chemists) than is given experimentally or psychotherapeutically" (Ungerleider & Fisher 1966). Some researchers suggested that the "psychedelic movement" had purposely minimized or suppressed reports of adverse reactions (Robbins et al. 1967; Subcommittee on Executive Reorganization 1966). As hospital admissions became more frequent, they claimed, it had become impossible "to contain many of the psychotic reactions within the LSD movement itself and to keep them from public attention" (Robbins et al. 1967: 997). While the available data on the occurrence of untoward reactions suggested that they were relatively rare in the research setting, wider availability and increased self-experimentation coincided with an increase in the number of hospitalizations following LSD ingestion. Also, physicians in areas where LSD was obtainable for use in unsupervised environments were beginning to see an increase in untoward psychedelic reactions. It was, however, not until December of 1965 that Frosch, Robbins and Stern published the first report on the adverse effects of psychedelics seen in the Bellevue Hospital Emergency Department.

From March through June of 1965, 27 patients were admitted to Bellevue Psychiatric Hospital in New York as a result of taking LSD; this sudden increase prompted the

first published report of adverse psychedelic reactions to drugs taken outside the research environment, which appeared in the December 2, 1966 issue of the *New England Journal of Medicine* (Frosch, Robbins & Stern 1965). The authors of this report found that adverse reactions could be grouped into three syndromes: acute panic reactions, overt psychoses, and what later came to be called "flashbacks," experiences of perceptual distortion and depersonalization similar to the drug state, but occurring without further drug use. Recovery from panic reactions was usually rapid, and no long-range problems had been noted; but for the other two syndromes the prognosis was unclear, since many patients were still experiencing some "impairment of performance" when last contacted (Frosch, Robbins & Stern 1965).

In an editorial in the same issue, the editors of the *New England Journal* suggested that the potential for the development or reappearance of adverse LSD reactions months to years after ingestion was particularly worrisome, and likened this possibility to the effect of the mysterious powders that irreversibly transformed Dr. Jekyll into his evil alter ego, Mr. Hyde. The editors stated that LSD was a "dangerous, toxic substance" and that existing inconclusive evidence of its therapeutic value was outweighed by its potential danger. They stated flatly that there was "no published evidence that further experimentation [was] likely to yield invaluable data" (Editor 1965: 1280).

The publication of Frosch, Robbins and Stern's article, and of the accompanying editorial, stimulated a spirited discussion. Frank Fremont-Smith (1966), medical director of the Josiah Macy Foundation and chair of the Second Conference on the Use of LSD in Psychotherapy, took exception to the editors' failure to distinguish the growing number of adverse reactions resulting from unsupervised use from the relative infrequency of such reactions in research and therapeutic users. He objected to the suggestion that further experimentation with LSD was unlikely to be of value as "hardly in keeping with the attitude that encourages sound scientific inquiry." Within a month, the *Journal's* editors replied that there was a "difference of opinion" about the potential value of continued LSD research, and that "at best a calculated risk [was] being taken" in such research (Editor 1966: 856). In April of 1966, the discussion of LSD research's standing in the scientific community was somewhat eclipsed by the manufacturer's withdrawal of its sponsorship from all studies of LSD and psilocybin because of the publicity related to these drugs.

IMPOSITION OF LEGAL CONTROLS

On July 15, 1965, the Drug Abuse Control Amendment (PL 89-74) was passed by Congress, and in February 1966 the manufacture and sale of psychedelic drugs became illegal in the United States. Possession for personal use was specifically exempted (McGlothlin 1966). Sandoz became

the only entity legally entitled to manufacture or distribute LSD. Although Sandoz did not design or supervise LSD research, the company, as the filer of the investigational new drug application for its product, remained the official sponsor for government-sanctioned research. Within weeks after the law went into effect, however, Sandoz directed the researchers obtaining their LSD from the company and working under its IND application to return their remaining supplies of LSD to the manufacturer. On April 7, 1966, the company notified the FDA that it was planning to withdraw sponsorship of investigators using LSD and psilocybin as soon as possible (Subcommittee on Executive Reorganization 1966). Sensational news of the "first known LSD murderer" on April 11 finally convinced Sandoz to stop distribution of its products, and all supplies of LSD and psilocybin provided by Sandoz were recalled (Anonymous 1966).

The Kessler Case

Stephen Kessler, a Harvard graduate and Downstate Medical Center medical student, was accused of stabbing the mother of his estranged wife on April 11, 1966. At the time of his arrest, Kessler was reported to have dazedly inquired about what he had done, and claimed amnesia after "flying for three days on LSD" (Anonymous 1966). His arrest prompted an emergency meeting of New York law enforcement officials, prosecutors, and representatives of the FDA, who recommended new legislation to make sale or distribution of LSD a felony in New York. It also provided a horrifying story (which was widely cited for years afterward) about the potential of LSD to cause harm.

At Kessler's trial in October 1967, it was revealed that he had taken doses of 10 to 50 μ g. of LSD on a total of five occasions between the Summer of 1964 and March of 1966, the month preceding the murder. On the days before the murder, Kessler had taken one and one half grains of pentobarbital, and drunk three quarts of laboratory alcohol, cut with water (Anderson 1967). Kessler made no mention of having taken LSD in the month before the murder, but a psychiatrist who examined Kessler after his arrest claimed that Kessler could have taken doses of LSD that he was unable to recall (Anonymous 1967). Because of his history of chronic paranoid schizophrenia, for which he had previously been hospitalized twice at Bellevue, the jury found that he was "not guilty by reason of insanity above and beyond his use of LSD" (Barter & Reite 1969).

Sandoz Withdraws Research Sponsorship

Following announcement of the murder, Sandoz ceased LSD production, and all LSD samples were recalled from investigators, except for 12 researchers conducting studies approved by the National Institutes of Health or the Veterans Administration. Sandoz's remaining stock of 21 grams of LSD was transferred by armored car to the Public Health Service (Subcommittee on Executive

Reorganization 1966). The company also relinquished investigational sponsorship of LSD research. Despite the fact that possession of LSD continued to be legal under federal law, researchers who had no investigational exemption were required to return their supplies and reapply for permission to conduct LSD research. When PL 89-74 went into effect, 13 grants (four for research on human subjects) were receiving NIMH funding (Anonymous 1965). However, Sandoz had been providing LSD (at no cost) to an additional 53 recognized studies; those studies were to be the most affected by the new legislation. Since Sandoz had acted as the sponsor of most of the ongoing research, most investigators conducting studies on human subjects had no IND approval apart from that drug company. In addition to the IND application needed to obtain LSD supplies from the NIMH, new regulations also mandated that investigators obtain approval of their IND from the FDA before the drugs could be used, not only on human subjects, but also for animal or biochemical studies. Differences between the goals and standards of the two agencies led to delays and policy problems (Cole 1968). Senator Abraham Ribicoff characterized this as "empire building" by the agencies involved (Subcommittee on Executive Reorganization 1966).

Sandoz's abdication was considered an act of cowardice by some scientists (Lowinger 1966), but Sandoz defended its action on the grounds that continued sponsorship of LSD studies had become too burdensome in the prevailing atmosphere of national hysteria (Henze 1966). Other researchers felt that the transfer of responsibility to NIMH would result in the authorization of more research projects than in the past (Dahlberg 1966), but in 1966 there were only 17 investigators studying LSD. By 1968 the number of active researchers had dropped to eight, and most of these were conducting studies of LSD abuse or seeking better methods of detecting LSD for forensic purposes (Louria 1968).

In Canada, even after the sale or transportation of LSD was prohibited, researchers who were listed with the Minister of Health could legally obtain LSD directly from Sandoz. Many had ordered more than was immediately needed for fear of supplies being cut off, and so were not severely impacted by Sandoz's termination of production (Abramson 1967). In England, therapists using LSD protested that Sandoz's interruption of their supplies was "petulant and ill-considered," and that the distress caused to patients being successfully treated with LSD would harm Sandoz's reputation more than misuse of LSD (of which there was little evidence in Great Britain) could ever do (Browne 1966: 1540). Sandoz's representative replied that the company would be happy to turn over a supply of the drug to the appropriate governmental authorities for distribution, but did not wish to risk its good name in association with "a preparation whose therapeutic usefulness is open to question" and which was, furthermore, "totally uneconomic to Sandoz" (Christen 1966).

The FDA and NIMH Assume Control of LSD Research

During Senate hearings on the psychedelics in May 1966, Senator Robert Kennedy questioned whether the requirement that investigators reapply for investigational new drug status indicated some unwillingness on the part of the FDA or NIMH for LSD research to continue. The FDA commissioner, James Goddard, acknowledged the need for further controlled experimentation with LSD, but categorically stated that "any new proposal by any investigator for the use of LSD [would] have to be fully documented to limit the use of the drug to specially qualified physicians in carefully controlled clinical environments. And the plans would have to be limited in scope to gain [the FDA's] serious attention" (Subcommittee on Executive Reorganization 1966: 63). Goddard assured Senator Kennedy that the FDA was "not trying to retard or thwart research" and that the highest priority would be given to processing the IND applications for these studies.

Nonetheless, complaints from researchers who had relinquished their LSD supplies were soon heard: they were being shuttled from one desk to another within the FDA and the NIMH, but no supplies of LSD for their formerly approved projects were forthcoming (Pollard 1966). One researcher reported that his correspondence with 30 colleagues in the field of LSD research revealed that "projects [had] been called off, doctors [had] been attacked by hospital associations as 'kooks,' and [he had] been diagnosed (the psychiatric method of character assassination)" (Dahlberg 1966). In June of 1967, the Joint Advisory Committee on Psychotomimetic Agents (the LSD Committee) was set up to review both requests to the FDA for permission to conduct LSD studies and requests to NIMH for supplies of LSD, but the two agencies continued to take different approaches to regulating LSD use. The FDA, which had responsibility for the control of all investigational drugs, promulgated rules directly from Washington. NIMH, which had the only legal supply of LSD, hoped to encourage self-regulation and peer review at the individual research institutions. The FDA was concerned primarily with safety issues and the protection of human subjects. NIMH required that studies be not only safe, but well designed (Curran 1967; Smith 1967).

The American Psychiatric Association Position on LSD

On June 12, 1966, the Council of the American Psychiatric Association approved a position statement on LSD:

The American Psychiatric Association notes and fully shares widespread public alarm about the irresponsible use of the hallucinogenic drug lysergic acid diethylamide, commonly called LSD.

The use of the drug should be confined to carefully controlled medical and research settings. The Association is opposed to regulatory measures which would make the drug unavailable for legitimate research. While neither laboratory nor clinical findings have yet adequately documented the

therapeutic usefulness of the drug, *they have elicited sufficient information to justify continuing research on its values* [italics added]. Further, the Association is confident that when conducted by qualified investigators, such research has been and will continue to be carried out with a degree of safety comparable to that of many other drugs.

The indiscriminate consumption of this hazardous drug can, and not infrequently does, lead to destructive physiological and personality changes. The Association most particularly deplores its use by some persons in this way as a "mind-expanding" or "consciousness-expanding" experience. There is now no substantive basis for this claim. The destructive consequences to some who use it in this expectation have not yet been adequately established in the professional and lay press.

In the Association's view, the proper way to ensure availability of the drug for research purposes is through the application of the same regulatory mechanisms and public education efforts that are customarily relied upon to protect the public from irresponsible use of experimental and dangerous drugs, and not through total prohibition of its manufacture and use for legitimate purposes. (American Psychiatric Association 1966).

Anti-LSD Legislation

Despite the numerous calls for continued research, the large body of scientific data on these drugs was obscured, at least for the lay public, by sensational newspaper and magazine articles; the governments of both the U.S. and Canada responded to the widespread unsupervised use of psychedelics with increasingly restrictive legislation. In the U.S., the California state legislature passed legislation in early 1966 making the possession of LSD illegal. Expert testimony at the U.S. Senate hearings had specifically discouraged the imposition of medical, criminal or civil commitment penalties for possession or personal use as tending to discourage persons in crisis from seeking needed help, and as criminalizing something that was less an anti-social act than a youthful adventure (Subcommittee on Executive Reorganization 1966). Thomas Lynch, the California Attorney General, strongly supported criminal penalties for possession, as well as for sale or manufacture of LSD (Lynch 1966), but such legislation was rejected twice before the Assembly Criminal Procedures Committee. Under pressure from the press, the gubernatorial candidates, and the Attorney General, the committee finally released the bill but deleted the clause making possession illegal. Criminal penalties for possession were restored by a bare two-thirds margin of the Assembly. The final bill, which was supposed to keep LSD "in the laboratory and the hospital where it belongs" passed almost unanimously (McGlothlin 1966: 3). Eventually every other state passed legislation prohibiting the possession of LSD, and state officials contended over who had passed the toughest laws first. A suit was filed in federal court by the New Jersey State Drug Study Commission to prohibit magazine coverage of the "consciousness-expanding" use of psychedelics after a photo essay in *Life* attracted widespread attention (Brecher 1972; Farrell 1966; Rosenfield 1966). The speaker

of the New York State Assembly allowed public hearings on anti-LSD legislation to be postponed until after the bill was passed, because of the perceived urgency of the LSD threat (McGlothlin 1966).

New modifications of PL 89-74 made possession a federal misdemeanor and sale a felony in 1968. Under the Controlled Substances Act of 1970, the psychedelics became Schedule I Controlled Drugs, a designation that indicates lack of safety even in medically supervised use, high abuse potential, and no current accepted medical use. Some researchers continued to insist that "many types of neurophysiological and psychiatric investigation using LSD offer potential benefits" (Lowinger 1966); others felt that the essential questions had been addressed, and that interest in LSD waned because the basic research was not promising (Levine 1998). In any case, clinical studies of LSD using human subjects became fewer and fewer.

CONTROLLED STUDIES OF PSYCHEDELIC THERAPY FOR ALCOHOLISM

According to Sidney Cohen, there are good reasons why psychedelic therapy with LSD was administered to more alcoholics than to those in any other diagnostic category. There was a large number of potential candidates for treatment. Often these were persons who had failed one or more previous attempts at therapy for alcoholism. Few were expected to recover spontaneously. From a methodologic standpoint, evaluation was thought to be simple, involving only a straightforward assessment of the amount of drinking (Cohen 1964). LSD therapy as a method of alcoholism treatment characteristically employed a minimum number of experiences with large doses of 200 to 300µg. or more. Psychedelic therapy was inexpensive, easy to administer, and consistently reported to be more effective than previous treatments (Smart et al. 1967). The rapid acceptance of LSD in the treatment of alcoholics on the basis of extravagant claims of early success was followed by criticism of the methods, motives and conclusions of the early researchers. In the contentious atmosphere surrounding LSD research, arguments over the implications of the reported success of this enthusiastically received and seemingly successful treatment for alcoholism were among the most passionate.

The Addiction Research Foundation Study

By the time Smart and Storm's critique of the existing reports of LSD therapy for alcoholism was published in 1964, they had already begun work on their own study of the value of LSD treatment. The Addiction Research Foundation (ARF) of Toronto, Canada had undertaken to support a controlled trial of LSD therapy. Smart and Storm, as research psychologists, were responsible for the study design, the conduct of predrug evaluation and follow-up, and data analysis. Two psychiatrists, Earle F. W. Baker and

Lionel Solursh, administered the LSD and made psychiatric assessments. The patients were 30 randomly chosen volunteers from the ARF's Toronto Clinic.

Methodology of the ARF Study

The study was designed to avoid the methodologic problems of previous studies. The patients were randomized to one of three groups of 10: two drug groups, and a control group that received all the procedures and therapies given to the drug groups except the drug session. Of the drug groups, one received ephedrine sulfate 60 mg. IM as a control drug. The researchers believed that "the most consistent and immediate effect of LSD appear[ed] to be sympathetic activation" (Smart et al. 1967), and that the headache, nausea, vertigo, palpitations, and nervousness produced by ephedrine "could be confused with lysergide effects" (Smart et al. 1966). The other drug group received 800 μ g. of LSD intramuscularly. In 19 of the 20 patients who received a drug, the therapist who administered it guessed correctly which drug had been given. The post-treatment therapy and evaluations were completed by therapists who did not know which patients had received LSD.

The research team reported that "full blindness was achieved for the patient group," (Smart et al. 1967). Patients volunteered "for the study of a new drug" (Smart et al. 1966), and were not intended to be aware that LSD was being used. When media attention to LSD caused the patients to speculate that lysergide was being used, no clarification was provided by the clinical staff. The patients were told that responses to the study drug varied from slight to very dramatic, and were not aware that two different drugs were administered. The researchers claimed that "in nearly every case the patient continued to believe that he had received a magic 'new drug'" (Smart et al. 1966). Both patients and staff were aware of which patients were in the nondrug control group.

The groups were well matched for sex, age, educational level, marital status and pattern and extent of drinking. More of the patients in the LSD group were unemployed at the time of admission than in the other groups. All patients received the same series of group therapy sessions and informational sessions on alcohol problems, and all had individual opportunities for occupational and physical therapy, and for psychiatric interviews. The overall approach was described as similar to that of the Yale Plan Clinics (early residential treatment centers that provided multidisciplinary care for alcoholic patients), but with the decreased formalism and increased patient participation of a therapeutic community. The professional staff was oriented to the goal of total abstinence, and saw alcoholism as "an illness that can be cured or alleviated by medical and psychiatric treatment" (Smart et al. 1966).

Pretreatment evaluations included standard psychological tests and a questionnaire that sought quantifiable

answers on drinking behavior. A psychiatric diagnosis and prognosis was determined after a detailed examination by the therapist who would be administering the drug treatment. This interview was also intended to develop therapeutic rapport between patient and therapist. All the therapists administering the drug therapy had previous experience with LSD therapy, and had themselves taken LSD. Therapists conducting the pre- and posttreatment evaluations had no personal LSD experience. The investigators described themselves as skeptical about the value of LSD, and not committed to a belief in its efficacy (Smart et al. 1966).

The drug sessions were administered at a hospital near the ARF center, in single rooms, with the patients in Posey restraints (a belt of reinforced webbing used to strap patients to the bed). Before the experimental drug, 250 mg. of phenytoin (an anti-seizure medication which may cause sedation) was given intramuscularly to patients who were already receiving it; patients were otherwise drug-free and fasting. A co-therapist team of doctor and nurse conducted a three-hour interview at an unspecified time after drug administration; it is not clear who, if anyone, attended the patient during the remainder of the drug experience. Patients remained at the hospital overnight and "after the drug wore off . . . [were] sedated with chlorpromazine if necessary" (Smart et al. 1966). There was no specification of how this need was determined, nor of how many patients received posttreatment sedation. Although the patient was free to bring up the drug session in group or individual therapy, no effort was made to discuss the results of the drug treatment in the standard therapeutic milieu unless the patient initiated it. The drug group patients had a therapeutic interview with the therapist who had administered the drug approximately four days after treatment. Patients completed inpatient treatment an average of one week after their drug sessions. Follow up was planned for all patients at six months post-discharge, and all but two were evaluated within this time frame (Smart et al. 1966).

All groups showed a substantial gain in periods of abstinence compared to pretreatment, and a highly significant decrease in the number of drinking occasions. None of the groups differed significantly in the frequency of other alcoholic symptoms, such as drinking on workdays, black-outs, and drinking only to get drunk; nor was there any significant difference in the number of posttreatment contacts with the ARF clinic.

The researchers concluded that the lack of outcome differences among the treatment groups in any of the areas evaluated indicated "that lysergide, as used in the present study, failed as an effective adjunct to psychotherapy, in contrast to claims made in previous studies" (Smart et al. 1966: 481). The research group was aware that their method of LSD administration differed from that reported by other LSD therapists, and that this might affect treatment outcomes. They described this possibility as "debatable,"

however, since their treatment was just as effective as that of other therapists, and they did not expect much potential gain over 80% improvement. They acknowledged that "The results reported do not preclude the possibility of finding some effects of lysergide on drinking, given some very different procedures or personnel. They demonstrate, however, that such effects are not associated solely with its pharmacological properties or with the procedures used here. Nevertheless, no valid claim for any effects can be made until the treatment procedures have been in a controlled study similar to the one reported here" (Smart et al. 1966).

They also suggested that some other characteristic of alcoholic patients, such as social stability or personality variables, might be beneficially affected by LSD treatment, and stated that future analyses of their data would deal with these possibilities. The publication of a monograph on the study, which would provide a more detailed report of the data analysis and of the specifics of methods employed in the study, was in preparation.

The ARF research team had set out to design a study that would be more than "simply the chronicling of clinical routine" (Foulds 1958), which they had claimed described most of the existing LSD research (Smart & Storm 1964). Even with this goal clearly in view, their research was unable to fulfill some of the essentials of an adequate study as described by O'Brien and Jones (1994). The small sample size, with only 10 cases for each experimental condition, would have tended to make statistically significant results difficult to obtain. The criterion of a *specific diagnosis* was not fully met, as the patient group presented a variety of psychiatric diagnoses in addition to chronic alcoholism. A detailed questionnaire on many aspects of the patient's past year of drinking was administered pretreatment, and a detailed psychiatric examination also contributed to the establishment of *severity measures*. *Informed consent* was not obtained, and an attempt was made to prevent the patients from learning the nature of the drugs being studied. A nondrug control group as well as an *active placebo control* was part of the study design, as was *random assignment* of patients to all groups. The need for *standardized therapy* was addressed by assuring that all groups received the same clinic treatment, and by some standardization of the routine of the session day for both drug groups. Although parameters for the psychotherapeutic interview that accompanied all drug sessions were supplied, several aspects of the drug groups' treatment remained unspecified. How many patients received premedication with phenytoin, whether patients were left alone at any time during the drug sessions, and how the need for sedation and the endpoint of drug effects were assessed were particularly unclear. The study did employ a blinded *objective rater*, with all follow-up testing done by the same evaluator to decrease inter-rater bias. The study placed particular emphasis on the *importance of follow-up*; all but two of the patients were assessed

within the target interval, with the remaining two being followed up within a further two months.

Critique of the ARF Study

In March of 1967, the *Quarterly Journal of Studies on Alcohol* published the comments of several other LSD researchers on the design, attitude and conclusions of the ARF study (Fadiman 1967; MacLean & Wilby 1967). The ARF research group, whose members had previously criticized others' findings from uncontrolled and unblinded studies, were themselves criticized for their failure to maintain the double blind. While the ARF group had objected to what they perceived as a positive bias toward the usefulness of lysergide treatment in other researchers, they were admonished for their own display of skepticism. This was interpreted as negative bias, with a likelihood similar to a positive bias of evoking a placebo response. The procedures used in the administration of the LSD sessions were also criticized. There was insufficient opportunity for the development of therapeutic rapport. The interview technique used during the sessions was derided as one discarded years previously by other researchers in favor of more effective methods. Questions were raised about the use of pre-medication and the restraint of patients during the drug experience.

The most severe censure was reserved for the conclusion of the ARF study: "*that lysergide, as used in the present study failed as an effective adjunct to psychotherapy, in contrast to claims made in previous studies*" (Smart et al. 1966: 478). This judgment was criticized on two levels. The ARF study had placed, it was claimed, too much emphasis on the pharmacologic actions of LSD, even referring to it as a "magic new drug." This attitude was contrasted with that of other researchers who emphasized that the psychedelic experience produced by the drug was the therapeutic vehicle, rather than the drug's specific pharmacodynamic properties. Because the techniques used were unlikely, in the critics' opinions, to produce a psychedelic experience, the outcomes of the employment of these techniques were not comparable to those achieved by "true" psychedelic therapy (Fadiman 1967; MacLean & Wilby 1967).

The second and much stronger criticism was of the prepublication circulation of an earlier version of the report which had included a quite different conclusion. According to this 1964 ARF report: "The results of this study fail, completely, to show that LSD is useful as an adjunct to psychiatric treatment of alcoholism. The conclusion is, therefore, that LSD was not shown to be an effective adjunct to the existing clinical treatment of alcoholism. These findings represent a strong indictment of the previous unwarranted assertion that LSD is effective in the treatment of alcoholism" (MacLean & Wilby 1967). Critics of the ARF study found that this conclusion "exceeds the most liberal interpretation of the evidence

presented" and was "so fundamentally in error as to be offensive" (MacLean & Wilby 1967: 144). They accused the ARF research group of irresponsibility in allowing the article to be widely circulated before review by journal referees, and claimed that the prestige of impending publication in an important journal, combined with an exaggerated but uncritical confidence in the scientific authority of the double-blind controlled study design, had permitted their unwarranted conclusions to have far-reaching impact. Specifically, MacLean cited the influence of the prepublication report on the California governor and state legislature during their process of framing legislation to control the use of LSD (MacLean & Wilby 1967).

When the monograph publication of the results of the ARF study was released, some of these criticisms had been addressed, or at least some of the positions taken in the initial report had been modified. In relation to the claim of negative bias, this more extensive report claimed that "all the investigators would have preferred to find that LSD was an effective therapy" but described the ARF researchers as more neutral about the potential usefulness of LSD therapy than previous researchers since "no one was committed to a belief in its value" (Smart et al. 1967:84).

In response to the possible antitherapeutic effects of their intensive therapeutic interview, and their failure to attend to the nuances of the set and setting in which the experimental drugs were administered, the ARF team pointed out that the existing literature contained "a great deal of variation in the procedural details of LSD treatment" (Smart et al. 1967: 27), which, if significant, ought to be expected to have resulted in a variation in reported outcomes. Unfortunately, according to the ARF researchers, the failure of previous studies of the therapeutic utility of LSD to meet the requirements for reliable research made it impossible for these reports to be used as a basis from which to predict outcomes based on variations in technique. They offered their own theory of the effect of LSD: that "many of the emotional and behavioral effects of LSD could be accounted for based on the activating [physiologic arousal] effect of the drug, interpreted and elaborated by the subject" (Smart et al. 1967). They described their belief that what happens under the influence of LSD is primarily an increase in susceptibility to social influence. They suggested that, absent specific and behavioral criteria for change, a therapist's belief in the drug's unique effects, particularly if reinforced by his own psychedelic experiences, could influence his assessments of the outcomes of drug treatment.

The aspect of the research that preceded their own study that the ARF group found most interesting was the reported effect of LSD on personality in alcoholics. Although they found claims of these effects suggestive, their dissatisfaction with the limitations of the early studies prevented any attempt to evaluate the nature of the changes reported. In their own data, "no clear benefits of LSD therapy were

detected," but tendencies "sufficient to provoke further interest in LSD research" were found (Smart et al. 1967). These included a decrease in neuroticism on the Maudsley Personality Inventory, more loosening of repression and less internal conflict on the Rorschach, and gains in the healthiness of self and in movement of self toward ideal on the Haigh-Butler Q Sort. They concluded that LSD promoted some therapeutic changes in self-concept, and suggested further experimentation with those aspects of the LSD experience concerned with personality variables would be valuable. In particular they suggested that studies of the types of alcoholic who would benefit most and least from the LSD experience, and of the specific effect of LSD on psychological mechanisms such as self-concept and ideal concept should be made (Smart et al. 1967).

Smart and his colleagues attempted to evaluate the effect of LSD on social variables such as family relationships, employment status, and residential mobility. They recognized that using drinking behavior alone as the criterion for treatment success might result in important effects of LSD therapy being missed. Few differences were noted among the three study groups in replies to questions on family, employment and social stability other than an increased number of the LSD subjects being employed post-treatment. The overall analysis of the data on social variables paralleled that of the data on drinking behavior and personality change: none of the changes were more striking in the LSD group than in the alternate and control groups (Smart et al. 1967).

Overall, although improvements in drinking behavior consistent with those reported by earlier studies of LSD therapy were found, they could not be attributed to the use of LSD since they were similar in all treatment groups. The ARF research group concluded that "earlier reports that LSD was an effective adjunct to therapy for alcoholism may have resulted from lack of adequate controls in the evaluation of its utility" (Smart et al. 1967).

Other Controlled Studies

By the time the ARF monograph was released, two other controlled studies of alcoholism treatment with LSD were nearly completed. Smart and his colleagues commented on the fact that the preliminary findings of these studies tended to support their contention that when control groups were available for comparison, the admittedly dramatic improvement in the drinking behavior of LSD-treated alcoholics was not different from that of alcoholics who had been exposed to other forms of treatment. One of these studies, conducted by Wilson VanDusen and his colleagues on all female patients, found that although those who had received lysergide described their experiences as among the most significant of their lives, they were "not noticeably more sober" (VanDusen et al. 1967) than the patients treated by the same alcohol program who received no LSD.

The other study mentioned by Smart and colleagues was conducted by Gordon Johnson of the London Clinic, the ARF facility in London, Ontario. Johnson's study compared four treatment groups. One received only routine clinic care, and no drugs were administered. A second received LSD but no therapist contact during the LSD experience. Another received LSD with four hours of therapist interaction. The fourth group received therapist interaction after administration of methamphetamine HCl and sodium amobarbital. Patients were in Posey restraints, and were sedated with chlorpromazine and secobarbital about six hours after drug administration. Only a single-blind of the patients was attempted, as it was assumed that the therapists would detect which drug had been administered. Six hours of intake interviews and personality testing preceded the random assignment of patients to experimental groups, and interviews and questionnaires were administered on the day following drug treatment. Follow-up was targeted for 12 months after admission and was conducted by independent observers who were not aware of the patients' treatment group. Although all four groups had a statistically significant improvement in drinking behavior, there were no significant inter-group differences. There were no significant changes in marital status, employment, social relations or housing for any group. Johnson concluded that LSD treatment "in this setting conferred no evident advantages over more conventional modes of therapy" (Johnson 1969). Smart and his colleagues found that both Johnson's and VanDusen and colleagues' studies supported their conclusion that controlled evaluations did not find LSD to be a useful adjunct to alcoholism treatment, and that the differences in procedures, dosages and control groups used in these studies tended to increase the generalizability of their findings (Smart et al. 1967).

A few controlled studies did produce positive findings but these mostly appeared to be short-term effects. A study done at the New Jersey Neuro-Psychiatric Institute at Princeton in 1966 referred to this phenomenon as the "LSD honeymoon," and pointed out that "dramatic shifts in attitudes and behavior which appear very promising are frequently reported" immediately after LSD treatment (Cheek et al. 1966: 56). This study compared 29 alcoholic controls who received the regular six-week program of the Institute's Earle Alcoholic Unit with 28 alcoholics who received this program plus two doses of LSD and a group therapy program. There was no *placebo control*, and the absence of a control group receiving the group therapy program without LSD limited the extent to which therapy was *standardized*. Limited *random assignment* was attempted by assigning patients alternately in groups of four to LSD or control groups. *Specific diagnosis* and *severity measures* were determined by pretreatment interviews and questionnaires. Pretesting established a scaled rating of each patient's alcoholism as "essential" (related to persistent inadequacies of personality) or "reactive" (precipitated by a markedly

stressful situation.) The LSD group as a whole scored higher in essential alcoholism than the control group, but this difference was not statistically significant. *Informed consent* was obtained. No attempt to assign *objective raters* was made, but the *importance of follow-up* was addressed by the use of several methods to assure that all patients were contacted. One member of the LSD group and six controls were lost to the 12-month follow-up. Patients were followed up at three, six, and 12 months post-treatment, and no statistically significant differences in sobriety outcomes, family relations or work patterns were noted. While not significant, the LSD group had "an initial marked advantage over the comparison group" in sobriety status at three months, which tended to diminish with time (Cheek et al. 1966: 68). The sobriety status of the LSD patients, but not of the control group, was significantly better at three and 12 months for reactive (versus essential) alcoholics. The researchers suggested that this might indicate that LSD therapy was of more benefit to patients with more social assets to help them in sustaining their recovery. They speculated that continued therapy, possibly including periodic redosage, might be a useful and economical intervention (Cheek et al. 1966).

Hollister, Shelton and Krieger (1969) also found slightly better short term results for patients treated with 600µg. of LSD than for a *control* group given dextroamphetamine 60 mg. In their study, no *specific diagnosis* other than acute alcoholism was provided. The Drinking Behavior Scale (DBS) used by Hollister and his colleagues was designed to provide a numerical value to indicate the *severity* of alcoholic impairment. *Informed consent* was not obtained, and patients were "given as little concrete information as possible about the drugs to be tested" (Hollister, Shelton & Krieger 1969) No attempt was made to provide psychotherapy, and the drug experience was intended to be primarily introspective. The only intervention other than the drug session was a discussion with the patient about problem drinking. There was no treatment manual detailing *standardized therapy*, but "every effort was made to see that patients were treated exactly alike" (Hollister, Shelton & Krieger 1969). *Objective raters* completed both the entry and follow-up administrations of the DBS, and the *importance of follow-up* was emphasized in the selection of only those patients whose stable job or residence history suggested that they would be available for follow-up. Despite this, by one year posttreatment, almost half of the patients in each group were not available for follow-up, with the remaining patients being mostly those who had responded well to treatment (Hollister, Shelton & Krieger 1969).

The mean change in DBS scores indicated that the drinking behavior of the LSD group had improved significantly more than that of the dextroamphetamine group at the two-month follow-up, but this difference had all but disappeared at six months, and any advantage remaining

for the LSD group at six months had diminished still further at one year. In discussing their results, the researchers mentioned that both groups showed remarkable improvement, highlighting the importance of a control group. This study was intended to consider LSD as the primary treatment, in the absence of any therapeutic preparation or intervention during the drug experience (Hollister, Shelton & Krieger 1969).

Criticism of Controlled Studies

The extent to which preparation or interventions might contribute to any beneficial impact of LSD treatment was not evaluated in most controlled studies, which were designed to test the experience elicited by the drug alone. This therapeutic method has been described as psychedelic chemotherapy (Kurland et al. 1971). Many LSD researchers took exception to research designs that assumed that the psychedelic experience, the central behavior-changing event in LSD therapy, was an automatic consequence of drug administration (Savage & McCabe 1973). Bowen, Soskin and Chotlos (1970) described this approach as "such a radical departure from accepted methods for producing a beneficial experience" that such studies "could not be regarded as a valid test of the psychedelic method." Bowen and his colleagues conducted a controlled study in which, despite adherence to the accepted psychedelic method described in studies with strongly positive findings, no significant difference in posttreatment adjustment status was found between LSD-treated patients and those receiving only a program of intense training in interpersonal problem solving. Although they found that long-term gains for LSD-treated patients were no greater than those of controls, "very real and often dramatic personality changes are frequently observed to occur over the *short term* [italics original]" (Bowen, Soskin & Chotlos 1970). In order to help patients integrate their insights and apply them to everyday problems, Bowen and colleagues recommended that a five-day follow-up program be provided at four months and one year post-discharge, including (if indicated) retreatment with LSD (Bowen, Soskin & Chotlos 1970).

The Spring Grove Studies

In a study designed to eliminate most of the methodologic flaws of previous research, a team of researchers (including Albert Kurland, Charles Savage, Walter Pahnke, Stan Grof and Sanford Unger) at the Spring Grove State Hospital in Maryland also found short-term improvement in drinking behavior in patients treated with a high dose of LSD; but differences from low-dose treated patients vanished by 18 months posttreatment (Kurland et al. 1971; Pahnke et al. 1971; Pahnke et al. 1970). The Spring Grove study was *placebo controlled*, using a treatment group of 90 patients who received 450µg. of LSD and a control group of 45 who received 50µg. of LSD as an active placebo. Although patients were *randomly assigned*,

randomization did not succeed in matching the groups for marital status, education or severity as indicated by number of previous admissions. *Informed consent* was obtained; patients received intensive preparation including 20 hours of psychotherapy. Although all patients were treated alike, there was no manual of *standardized therapy*. *Specific diagnoses* and some *measures of severity* were provided by a battery of psychological tests administered before treatment and at six, 12 and 18 months. Only about three-fourths of the patients were followed for the full 18-month period. Follow-up ratings of adjustment were made by *objective raters*, an independent team of social workers. Eighty-nine percent of the patients were available for six-month follow-up; 53% of the high dose group, as opposed to 33% of the low dose group, were "essentially rehabilitated" in their drinking behavior at six months. Forty-four percent versus 25% had "good attainment or adjustment" in their interpersonal relations and occupation, both statistically significant differences ($p < 0.05$) (Kurland et al. 1971). At 12 and 18 months, only 80% of the high dose and 78% of the low-dose patients were contacted for follow-up, and, although the high-dose patients tended to maintain their advantage over the low-dose patients, the differences were not statistically significant. The number of patients not available at follow up and the failure of randomization may have contributed to these results.

The patients in this study were intensively prepared for their LSD experience by a three- to four-week period during which they received approximately 12 hours of therapist contact. The LSD sessions themselves were conducted using the psychedelic method, in comfortable surroundings and with constant therapist attendance. Opportunities for integration of the drug experience were provided by several post-session interviews. This intensive nondrug therapy was one of the possible factors suggested by the researchers to account for the good results seen even in the low-dose patients. They also speculated that, since even 50µg. produced considerable abreaction and catharsis in some patients, this may have been something other than pure placebo effect (Kurland et al. 1971; Pahnke et al. 1971; Pahnke et al. 1970).

The Mendota Hospital Study

The most methodologically elaborate and rigorously constructed study of LSD therapy for treatment of alcoholism was conducted at Mendota State Hospital in Madison, Wisconsin by Ludwig and colleagues (Ludwig, Levine & Stark 1970; Ludwig et al. 1969). A total of 195 patients were *randomly assigned* to one of four treatment groups. Three experimental LSD treatment conditions were compared to a "no treatment" *control* group that received the standard thirty-day milieu therapy provided by the hospital's Alcoholic Treatment Center. The *specific diagnosis* for all patients was alcoholism with no overt psychosis, and an extensive battery of pretreatment tests provided *severity*

measures. A comprehensive, manual-guided introduction to the various treatment conditions was part of all patient intake processing, and *informed consent* for LSD therapy was obtained. The patients were not informed that their assignment to one of the treatment conditions would be random, however, but were told that the therapy they would receive was chosen for them based on their pretreatment testing.

The LSD-treated patients were assigned to one of three treatment conditions: hypnodelic therapy (hypnosis, LSD and psychotherapy); psychedelic therapy (LSD and psychotherapy); or drug therapy (LSD alone) (Ludwig, Levine & Stark 1970; Ludwig et al. 1969). Therapy for each treatment condition was *standardized* to the extent that all 13 participating therapists were trained in each treatment method by the principal investigators. Comparative analyses of the biases, levels of training and patient clinical assessments of each therapist were also analyzed. These studies, which were completed before the treatment condition to which each patient was assigned was known to the therapists, revealed no significant differences in treatment outcome for any variance in therapists' characteristics. In addition, patients were randomly assigned to therapists, with each therapist being assigned an equal number of patients from each treatment condition. The treatment team was entirely separate from the *objective raters* of the follow-up team. Follow-up evaluations were conducted at three, six, nine and 12 months posttreatment; and included contact with relatives at six and 12 months for corroboration of patient reports. All *follow-up* was by face-to-face interview, and less than 10% of patients were lost to follow-up over the 12-month period.

Pretreatment assessments were made in several areas of patient functioning. The Psychiatric Evaluation Profile (PEP) was used to assess patients' attitudes and symptoms. Personality characteristics related to social interaction were evaluated using the California Psychological Inventory (CPI). Information on observable or reportable drinking behavior was obtained by administration of a questionnaire, and by Breathalyzer testing at the time of each follow-up encounter. Patients and their relatives completed the Behavior Rating Scale (BRS) in order to evaluate general areas of behavior (including social, employment and legal functioning) as well as to give further information on drinking patterns.

The Mendota State Hospital researchers also administered the Linton-Langs Questionnaire (an instrument designed to evaluate the effect of LSD on affect, self-image, perception and cognition) during the pretreatment assessment and again during the experimental treatment session. The resulting measure of the degree of consciousness alteration produced by each treatment was then compared to the scores for therapeutic or personality change and behavioral adjustment obtained from the CPI, PEP, and

BRS. There was no relationship between the depth of alteration in consciousness achieved in any of the treatment conditions and subsequent personality or behavioral change (Ludwig et al. 1969).

At follow-up, all treatment groups had a statistically significant change "in the direction of health" over baseline PEP and CPI scores but "no differential outcome results based on the different treatment techniques" (Ludwig et al. 1969). Change in attitude measured at discharge did not significantly predict behavior during or after the first three-month follow-up period. Although the percentages of LSD-treated patients returning to drinking tended to be lower in the first two months post-discharge, these differences were not statistically significant. By the third month, differences in drinking behavior between treatment groups were minimal, and about 65% of all patients were drinking to some extent by the fourth post-treatment month.

There were no significant inter-group differences in social adjustment as measured by the BRS. Although some substantial gains occurred, they were similar for all patients, regardless of the therapy they received. The researchers attempted to determine whether certain kinds of patients responded best to certain kinds of treatment using a multifactorial analysis. They described themselves as disappointed "to find that neither patient, treatment nor therapist variables bore any consistent relationship to treatment outcome" (Ludwig, Levine & Stark 1970).

The researchers speculated that the "relatively sustained therapeutic gains" seen in all treatment groups were not surprising considering the extreme physical and emotional deterioration of the patients at the time of admission (Ludwig, Levine & Stark 1970). Simply being involuntarily committed, and thereby forced to stop drinking for 30 days, was expected to leave the patients in a better state than they had been in previous to treatment.

Based on their rigorous design, their thorough follow-up, their extensive analysis of findings, and their consideration of such previously unstudied factors as the influence of therapist characteristics, and the relationship between altered states of consciousness and treatment outcome, the research group felt that they had arrived at a definitive analysis. They were forced, they said, "to conclude on the basis of overwhelming, consistent, empirical findings emanating from this investigation and by the findings of other studies that the various LSD procedures do not offer any more for the treatment of alcoholism than an intensive milieu therapy program, and the latter, at best, is quite ineffective at deterring drinking" (Ludwig, Levine & Stark 1970: 243). In addition, they determined that their report "[gave] rise to such inescapable conclusions about the purported efficacy of LSD for the treatment of alcoholism as to preclude any further investigation, at least as far as evaluating the usefulness of the particular techniques used in this study" (Ludwig, Levine & Stark 1970: 9).

Questions Raised by Mendota Hospital Study

This categorical statement stands as Ludwig and Levine's answer to the *three essential questions* which some of their own earliest work posed as the standard for evaluation of any new drug or therapy (Ludwig & Levine 1964). The question, *Does the new agent offer an appreciable advantage over existing forms of therapy?* would seem to have been answered by their study. As used in their research, LSD therapy, alone or in combination with other treatments, did not demonstrate any significant advantages over intensive milieu treatment for alcoholism.

The answer to the second of their essential questions seems less clear: *To what extent and in what disorders does the agent bring about relief or effect change?* Working from the assumption that treatment implies an intention to change for the better, Ludwig and Levine considered the factors that might be expected to change: knowledge, attitudes, beliefs, symptoms, behavior or social functioning. Additionally they questioned the standards by which change would be evaluated as positive: those of the patient, the family, the therapist, or of society. Ludwig and Levine noted that the gains made by alcoholic patients in some areas of performance are not necessarily lost if patients return to drinking after treatment. They pointed out that experiences of insight or changes of attitude such as those described after psychedelic drug therapy may or may not be related to behavior, may have no observable consequences for the patient, or may have consequences that adversely affect the patient's social functioning, well-being and welfare. Furthermore, any change in attitude or behavior that does occur may be strengthened or undermined by the reaction of important persons in the patient's social environment (Ludwig, Levine & Stark 1970)

Ludwig and Levine's findings might be variously interpreted as indicating that either patients do not benefit from LSD therapy, that benefit occurs in an important area that is not well or clearly measured by the criteria examined, or that benefits in one domain are counterbalanced by detriments in others or diluted by lack of change in others (Kraemer & Telch 1992). In any case, it was perhaps somewhat premature to assume that there was no need to inquire further as to how LSD might bring about relief or effect change in alcoholism or in other conditions.

It is the third of Ludwig and Levine's essential questions, however, which seemed the most crucial at the time their study was published: *What are the dangers or risks involved when this agent is employed?* From 1964 to 1968, the four years during which their study was conducted, the risks and dangers reported to be associated with the use of LSD changed significantly. Although panic reactions, successful and unsuccessful suicide attempts, episodes of paranoia, and psychotic decompensation had been reported in association with LSD use, the incidence of such effects was quite low for those under therapist supervision, even

for patients being treated for psychiatric illnesses. LSD as used in a therapeutic setting compared favorably to other forms of psychological treatment in terms of possible adverse effects. As unsupervised use of LSD increased, however, so did the reported frequency of adverse reactions. With the publication in 1967 of reports of chromosomal abnormalities produced by LSD and the possibility of genetic damage or carcinogenesis, serious questions were raised about the safety of LSD treatment, or even of further experimentation. While the risk of adverse psychological reactions seemed to be low enough to justify continued exploration of the therapeutic potential of LSD, the possibility of unseen physical damage with potentially disastrous consequences could only be counterbalanced by the probability of significant benefit. In the absence of other methodologically acceptable controlled studies, and in an environment of growing concern over the potential societal and physiological implications of unsupervised psychedelic experimentation, the implications of Ludwig and Levine's research findings were clear and discouraging. To these once-optimistic researchers, the effectiveness of LSD therapy for alcoholism appeared to have been a mirage (Ludwig 1970).

In 1970, the Lester N. Hofheimer Award for research excellence was presented to Louis Stark, Jerome Levine and Arnold Ludwig by the American Psychiatric Association. The citation for the Hofheimer Award states that: "In a four-year study, these investigators developed a technique for administering a complex but precisely defined schedule for LSD treatment of chronic alcoholic patients, a method for studying it under controlled conditions and for evaluating the clinical outcome in both qualitative and quantitative terms. Their research design can serve as a paradigm for the study of other psychiatric treatments" (American Psychiatric Association 1970).

Criticism of the Mendota Hospital Study

Despite its meticulous design, however, Ludwig, Levine and Stark's study was severely criticized by other LSD researchers. Charles Savage, speaking in 1971 to the staff of the Maryland Psychiatric Research Center, complained that the preparation of both the patients and the staff for the experimental sessions was inadequate, there was no commitment to psychedelic therapy on the part of the staff, and the continuous verbal exchange specified during the minimal amount of therapist contact provided tended to interfere with deep regression and to increase resistance. According to Savage, there was insufficient opportunity provided for post-session integration of the experience, and only a small fraction of the patients reported that they had mystical or transcendent experiences, which were of utmost importance in the success of psychedelic therapy. Savage found the set and setting of the Mendota State Hospital study to be more typical of a

chemotherapeutic than a psychedelic treatment process (Grof 1980).

Previous to the publication of their complete findings in 1970, Savage had expressed similar misgivings about the differences between Ludwig, Levine and Stark's "hypnodelic" techniques and those of researchers employing psychedelic therapy. At the 1969 Hahnemann Symposium on psychedelic drugs, in addition to critiquing their therapeutic practices, he noted that Ludwig and Levine had reported good results from their early attempts to treat drug addiction with LSD and hypnosis. Savage claimed that Ludwig's embarrassment at being associated with positive findings on LSD treatment at a time when researchers working with LSD were coming to be regarded with suspicion had "changed his thinking" about LSD, and that this change in attitude had been reflected in the negative findings of subsequent studies (Fink et al. 1969: 51).

In a 1998 interview, Jerome Levine stated unequivocally that neither the social stigmatization of LSD and psychedelic researchers, nor the influence of governmental regulation had negatively influenced the progress or the outcome of the Mendota Hospital study. He described the study as neither primarily chemotherapeutic nor pharmacologic in design, but rather as an attempt to use hypnosis to direct the LSD experience to a particular goal. He pointed out that the Mendota Hospital study was not intended to replicate or to evaluate the techniques used by other investigators (Levine 1998).

Nevertheless, the objections raised by Savage and others to the overall therapeutic design of Ludwig, Levine and Stark's study tend to emphasize its failure to adhere to some of what were considered the most basic and well-recognized principles that had guided previous psychedelic therapy. As early as 1959, a World Health Organization study group on ataractic and hallucinogenic drugs had observed that: "... the same drug, in the same dose in the same subject may produce very different effects according to the precise interpersonal and motivational situation in which it is given" (World Health Organization 1958).

Early work with psychedelics at Boston Psychopathic Hospital disclosed surprising differences in the reactions of subjects to LSD depending on the characteristics of the experimental environment, and showed that "impersonal, hostile, and investigative attitudes" aroused hostile responses and increased anxiety and discomfort (Hyde 1960). Many researchers had described the responsiveness of the psychedelic experience to the expectations of the person receiving the drug and those of the person administering it as among its distinctive features (Smith 1968; Alnaes 1964; Cole 1961; Elkes 1959). Psychedelic therapists held that it was "the experience, and not the medication that was therapeutic" (p. 43), making the treatment situation and the therapeutic relationship overwhelmingly important (MacLean et al. 1961).

Ludwig and Levine accepted that both "the actual psychological content and consequences of the psychedelic drug experience are capable of considerable modification" (Ludwig & Levine 1966: 21). While acknowledging that it had been "shown that the environment or setting (context) in which LSD is given can influence the type of experience produced," they specifically selected a clinical setting in preference to "mystic and 'esthetic'" settings preferred by other LSD therapists (Ludwig & Levine 1965: 432).

THE DECLINE OF LSD RESEARCH

Savage's concern that adverse publicity and fear of disapproval might have affected the environment of LSD research was shared by other investigators. In the U. S. Senate hearings on research and regulation of LSD held in 1966 (the year in which the Mendota State Hospital study began) Daniel X. Freedman, Charles Clay Dahlberg, and Assistant Secretary of Health, Education and Welfare Phillip R. Lee all testified on the impact of public pressure on LSD research. Lee claimed that adverse publicity made scientists less willing or less eager to study LSD; Dahlberg asserted that research projects, particularly in state hospitals, had been restricted in response to the labeling of LSD researchers as deviant; and Freedman pointed out that the atmosphere of sensationalism about LSD abuse obscured the importance of LSD research and made fair and dispassionate consideration of its potential usefulness difficult. Senator Robert Kennedy declared that excessive negative publicity about LSD had caused everyone associated with it to be inaccurately labeled as "a criminal or a kook of some kind" (Subcommittee on Executive Reorganization 1966: 96).

Daniel Freedman's pivotal 1968 paper "On the Use and Abuse of LSD" concluded that "we have been more awed than aided by our experience with these drugs" (Freedman 1968: 345). According to Abraham, Aldridge & Gogia's (1996) review of scientific publications on LSD in *Index Medicus* from 1960-1994, a dramatic reversal from a preponderance of positive to negative reports occurred in 1968, which reflects a strong cohort-period effect on scientific activity in this area. This effect describes a biphasic change in the tone taken by socioscientific publications toward a new pharmaceutical discovery in which early enthusiasm is replaced by later "sober reconsideration" of adverse findings (Abraham, Aldridge & Gogia 1996: 287). At a time of major social and political upheaval, the controversy around psychedelic drugs epitomized many of the conflicts between traditional values and new social and moral arrangements (Bunce 1979; Carstairs 1969; Keeler 1963). The emphasis and funding of LSD research shifted toward efforts to prove its potential for harm and to discourage its use (Research Task Force 1975).

Based upon the work of Ludwig, Levine and Stark and other contemporary research, the National Institute of Mental Health declared in 1975 that: "Attempts by investigators over the years to use LSD as an adjunct to psychotherapy or as a special type of psychotherapeutic intervention have not clearly demonstrated therapeutic value" (Research Task Force 1975).

If social policy considerations influenced the direction and findings of LSD research, it was not a unique episode in the history of science. According to Heath (1988), "the results of scientific research are often ignored or distorted in the interest of furthering specific national or international policies." In alcoholism research, for example, Fillmore (1984) found that problem definitions, prevalence estimates and cost appraisals were all subject to influence by policy considerations as sentiments related to temperance and prohibition shifted over time.

SOCIAL SIDE EFFECTS OF LSD AND THEIR IMPLICATIONS

When the first report of adverse reactions to self-administration of psychedelics was published by Frosch, Robbins and Stern in 1965, the researchers pointed out that the usual order of medical investigations, which generally begin with a clinical observation, progress to clinical investigation of observed phenomena, and culminate in laboratory experimentation, had been reversed in the case of LSD (Frosch, Robbins & Stern 1965). LSD was first synthesized and studied in a laboratory environment. Overwhelming anxiety and panic reactions, suicide attempts, and occasional prolonged psychotic episodes were known to occur in patients and research subjects, but the incidence of such effects was quite low in supervised settings (Cohen & Ditman 1963, 1962; Chandler & Hartman 1960; Cohen 1960; Eisner & Cohen 1958; Whitelaw 1957; Elkes, Elkes & Mayer-Gross 1954; Sandison & Spencer 1954). By the second decade after the discovery of LSD, intense public interest and increasing availability had led to its use outside a research or treatment setting, where neither the professional skill nor the pharmacologic interventions that had been used to terminate adverse reactions in patients and research subjects were readily available. No prescreening of highly vulnerable individuals, no control of drug purity, and no accurate determination of dosage were possible. In 1965, a sudden surge in psychiatric admissions after the ingestion of LSD was noted by psychiatrists, and adverse psychedelic reactions were described by Frosch and his colleagues as a clinical syndrome that included three overlapping types of reaction (Frosch, Robbins & Stern 1965). This taxonomy was later confirmed by the observations of others (Ungerleider, Fisher & Fuller 1966), and refined to include two subtypes for each major category of reactions: acute panic and acute confusional

states, early and late recurrence of drug effects without further ingestion, and prolonged psychosis or prolonged anxiety (Robbins et al. 1967).

The major deleterious effects of unsupervised LSD use, as described in the work of Frosch, Robbins, Ungerleider and others, were explained for the May 1966 Senate hearings on research and regulation of the psychedelics by Stanley Yolles, head of NIMH. In addition to the major adverse psychiatric effects identified by front-line psychiatrists, Yolles described a fourth effect, which he characterized as "a gradual deterioration of efficient and effective reality-oriented behavior—loss of interest in work or study, in social relationships or obligations" (Subcommittee on Executive Reorganization 1966).

At the time that the Senate hearings took place, although several researchers had observed and remarked on similar phenomena, only Sidney Cohen had identified them as one of LSD's principal dangerous effects. In a paper read at the Ninth Annual Conference of the Veteran's Administration Cooperative Studies in Psychiatry in March of 1966, Cohen had described "dyssocial" behavior as one of the acknowledged nonpsychotic disorders that might complicate the extralegal use of LSD. In LSD-associated dyssocial behavior "a complete loss of previously held values and aspirations might result. Motivation to study or work disappears, family ties dissolve and personal cleanliness is neglected. Speech consists of pseudophilosophical jargon. There is a tendency to form cults or to affiliate with 'beat' elements" (Cohen 1966).

Richard Blum, writing in 1964 about a sample of LSD users drawn from psychedelic party-goers, former LSD therapy clients, public psychiatric clinic patients, police-identified drug users, and medical and mental health professionals, included reduced work interests and goal striving, greater preoccupation with internal events and self, and changes from prior chronic states, including reduced competitiveness, in a list of major mental effects of LSD use. He denied that this represented a retreat from the world, and suggested instead that a meaning and order which could not be found in empiricism and worldliness were made available by the LSD experience and became part of a personal life endowed with significance and order (Blum 1964).

In another study comparing LSD users with persons who had been given an opportunity to take LSD and had refused it, Blum and his associates found that LSD acceptors were more inner-focused, or contemplative, and less likely to strive for power or be caught up in work than rejecters. LSD rejecters cared more about work and events in the external world, and also reported more tension, overeating, and alcohol use (Blum, Blum & Funkhouser 1964).

Sherwood, Stolaroff and Harmon (1962) had reported a "shifting of basic beliefs" after the psychedelic experience, but this was related primarily to the subjects' sense

of self-worth and self-acceptance. Farnsworth (1963), in his JAMA editorial, had noted "some distressing indications that habitual use of the [psychedelic] drugs will lead, in some individuals at least, to looseness in thinking and difficulty in communicating coherently." Some of these "distressing indications" may have been Farnsworth's observations, as head of the Harvard Student Health Service, of the behavior of Timothy Leary and Richard Alpert. According to David McClelland, their chief at the Harvard Center for Research in Personality, the more psychedelics Leary and Alpert and their associates took, "the less they were interested in science" (Anonymous 1963a).

McClelland was well placed to emphasize the potential impact of psychedelic drugs on achievement, as he had published two books on the subject: *The Achieving Society* (1961) and *The Achievement Motive* (1963). While McClelland was later credited by some observers as having had a prophetic insight into the possible amotivational consequences of widespread use of the psychedelics because of his observation that they "seemed to encourage withdrawal from social reality and satisfaction in interior reflective existence" (Caldwell 1968), others disagreed.

Gerald Klerman, assistant director of the Massachusetts Health Center, criticized Leary and Alpert for failure to observe the rules of scientific investigation, but also used McClelland's concern for the potential impact of psychedelics on achievement as an example of "pharmacological Calvinism," an attitude motivated by fear of social change, and disavowal of emotion and bodily satisfaction (Klerman 1970: 316). In Klerman's assessment, the environment of psychedelic research had been poisoned by a combination of disregard for the scientific proprieties and overreaction that amounted to an academic witch hunt (Caldwell 1968: 28).

In his 1963 overview of the uses and misuses of LSD-type drugs, Jonathan Cole pointed out that evaluation of personality and behavior changes that might occur after drug use involved value judgments, such as whether a decreased interest in success or competition, replaced by an increased interest in music or poetry, was a positive transformation (Cole & Katz 1964). None of these observations had led, at the time of the Senate hearings, to a clinical investigation or to a laboratory experiment including operationalization and measurement of "efficient and effective reality-oriented behavior."

In 1967, one year after Cohen's identification of dyssocial behavior as an effect of LSD use, Smart and Bateman called for basic psychological investigations of the presumed, but undocumented, ability of LSD to cause "personality changes, [and] damage to employability, family relationships, and moral and ethical controls" (Smart & Bateman 1967: 1220). Hollister, in a comprehensive monograph on the psychological, neurophysiological, and biochemical effects of LSD and related drugs, noted that a personality deterioration consisting of unproductivity in

previously promising individuals had been seen to follow the repeated use of psychedelics. He did not attribute this unequivocally to the use of drugs, however, suggesting instead that repeated drug use might be a symptom of an already disturbed personality, or a type of modern anti-intellectualism which made coherent thinking impossible (Hollister 1968).

In 1969 the National Institute of Mental Health summarized the previous two years' congressional testimony of its chief in a report to the medical community. Dr. Yolles again described his concern, not only with drug misuse, but also about the "alienation" of the student population, and students' "rejection of many goals of society, unwillingness to model themselves on any stable adult leaders, and . . . inability to acquire the necessary attitudes and skills for responsible adult behavior" (National Institute of Mental Health 1969). Yolles feared that this widespread rebellion, rejection and refusal would make it difficult to educate young adults about the dangers of drug use, and raised the possibility that many of them might reach adulthood "embittered toward the larger society, unequipped to take on parental, vocational and other citizen roles, and involved in some form of socially deviant behavior" (National Institute of Mental Health 1969).

Arguments about the relation of drug use among the young to social alienation and rejection of traditional values often concerned which was the cause and which the effect. Writing for "Current Concepts" a section of the *New England Journal of Medicine* in which an authority is invited to express his views on a topical issue, Donald Louria raised the possibility that the widespread use of psychedelic drugs "could lead to a whole generation of psychedelic dropouts, incapable of and uninterested in addressing themselves to the important sociologic problems of our times" (Louria 1968). Letters to the editors subsequently challenged his article, describing it as a panicky morality lecture, using polemical language, and suffering from the injection of personal prejudice. In particular dispute was his conclusion that the socialization problems of young adults were the result, not the cause, of LSD use—a premise for which no support had been offered (Miller 1968). This issue was still unresolved in 1984, when Rick Strassman, in an extensive review of the literature on adverse psychedelic reactions, suggested that the use of LSD may follow, rather than precede, certain social attitudes. Overall, Strassman's appraisal was that the evidence seemed to indicate that particular personality characteristics, including eccentricity and noncompetitiveness, may predate the use of LSD (Strassman 1984).

In a 10-year follow-up study of 247 persons who had received medically supervised LSD sessions, McGlothlin and Arnold found little evidence that LSD produced any lasting change in beliefs, values, attitudes, or behavior. Persons who preferred a less structured life tended to be more attracted to LSD than those whose preference was for the

systematic, structured and orderly. A few respondents said that they had experienced decreased competitiveness as an adverse effect of LSD use (McGlothlin & Arnold 1971). In a study of 20 paid volunteer subjects who had taken LSD eight or more times outside a medical setting, Barron, Lowinger and Ebner (1970) found no evidence of increasing personality or social disorganization.

Ludwig and Levine included the "drop-out" effects of LSD use as one of the purported risks or dangers of unsupervised or prolonged LSD use in their 1970 monograph. They reported that the consensus of experienced clinicians was that long-term LSD users "become progressively more passive, lose ambition and initiative, become more preoccupied with subjective reality, and develop an increasing antagonism toward social expectations and 'establishment' values" (Ludwig, Levine & Stark 1970). Ungerleider and Fisher (1970) noted that LSD users frequently described a dramatic shift in their value system, in which work, conformity, organization, and materialism had become less interesting to them. They suggested that these users had taken Leary's slogan, "Turn on, tune in, drop out," quite literally.

Others pointed out that "dropping out" could be used to describe any kind of negativism, failure, or avoidance of responsibility, but that the intention of Leary's injunction had been something quite different. Brian Wells (1974) insisted that dropping out meant "giving up ambitions and the symbolic rewards of society to pursue the aim of developing inner wisdom and philosophical satisfaction." It was not intended to be a permanent state, but was supposed to enrich the individual, who then was expected to return to organized society. Significantly, Wells observed that a major obstacle to reintegration following a period of philosophical exploration and growth was the possibility that society might seek to maintain the alienation as punishment for questioning its core values. Wells also speculated that psychedelic drug use might also have no causal role in shaping philosophies, but might simply be a behavior of people who question customs and viewpoints, or even the result of pervasive shifts in cultural values.

REPORTS OF GENETIC DAMAGE AND BIRTH DEFECTS

Fears that LSD might induce psychosis or unpredictable sociological consequences were eclipsed in March of 1967 by reports of damage to human chromosomes caused by LSD. Maimon Cohen, a geneticist from the State University of New York at Buffalo, is reported to have become interested in the possible deleterious effects of LSD during a short visit to the Haight Ashbury district of San Francisco while attending a medical meeting in 1966 (Fort 1970). In March of 1967, Cohen and his associates published their first report of the effect on frequencies of chromosome breaks in cultures of human peripheral

leukocytes of exposure to various concentrations of LSD for four, 24, and 48 hours. At least a twofold increase in chromosomal abnormalities was detected with all but the lowest concentration at the shortest exposure. In addition, the researchers noted a more than threefold excess in the number of damaged chromosomes over normal in a schizophrenic patient who had received 15 treatments with LSD (Cohen, Marinello & Back 1967).

Cohen's findings of *in vitro* chromosome damage were quickly extrapolated to a potential for teratogenic effects *in vivo*. The teratogenic potential of drugs used during pregnancy had been fully appreciated for the first time with the occurrence in the early 1960s of 12,000 cases of phocomelia, a rare congenital defect involving reduction of the proximal portion of the extremities, after pregnant women had ingested the sedative thalidomide. The possibility that LSD could have teratogenic effects was quickly and widely reported in the popular press. *McCall's* advertised an article on chromosome damage with a picture of a dismembered baby. The report, "LSD: Danger to Unborn Babies" actually cast doubt on the validity of Cohen's findings, but advised against the casual use of any medications during pregnancy (Brecher 1967). A *Saturday Evening Post* feature story, "The Hidden Evils of LSD," claimed that new research had found that LSD was "causing genetic damage that poses a threat of havoc now and appalling abnormalities for generations yet unborn," and that "if you take LSD even once your children may be born malformed or retarded" (Davidson 1967). It is possible that the social utility of Cohen's chromosome studies contributed to their rapid dissemination. At an NIMH conference on adverse reactions to psychedelics in September of 1967, Daniel Freedman suggested that "a dire somatic consequence" was just what was necessary to put an end to the controversy over LSD (Freedman 1969). Jonathan Cole told the *Saturday Evening Post* that NIMH was so concerned about these findings that it was encouraging new research on chromosome damage. More than 60 studies in this area were completed in the next five years.

The lead article in the November 17 issue of the *New England Journal of Medicine* was a collaboration by Maimon Cohen, Kurt Hirschorn, and William Frosch (1967), author of the account of adverse LSD effects seen as psychiatric emergencies at Bellevue. This paper presented the results of a comparison of the number of chromosome breaks found in a sample of 18 LSD users who had been admitted to the Bellevue psychiatric emergency service with those of 16 control subjects. Two controls with a very high percentage of breaks were dropped from the study before data analysis because of the onset of the symptoms of a viral infection soon after blood samples were obtained. With the exception of these two, the LSD patients had chromosome breakage rates two to four times higher than the controls. There was no mention of the occurrence of viral illness in the LSD patients. In addition,

four children who had been exposed to LSD *in utero* were evaluated and found to have morphologic rearrangements of their chromosomes.

The researchers recommended that a large epidemiological study be undertaken to evaluate the potential dangers that they identified: a possible increase in leukemia and other neoplasms in LSD users; a potential for teratogenic effects on the fetus exposed *in utero*; and the risk of genetic translocations producing damage in future generations (Cohen, Hirschorn & Frosch 1967). An accompanying editorial described LSD as "radiomimetic"—causing somatic mutations and cell depletion similar to those caused by chronic whole-body radiation. The editorial emphasized that these findings would require users to reconsider their attitudes toward drug use. For the sake of the biological fitness of the next generation, it said, "the time [had] come to stress the negative attributes of psychotomimetic drugs (Editor 1967).

Others were not as quick to accept Cohen's conclusions. Daniel Freedman was one of the first to point out that "reports of chromosomal changes in preparations of lymphocytes raised in tissue culture are not identical with 'genetic damage'" (Freedman 1968). Maryland Psychiatric Research Center, one of the few sites of ongoing LSD research on human subjects, took the opportunity to set up a double-blind, controlled study of the before and after rates of chromosomal aberrations in patients exposed to pure LSD, but found no definitive evidence of damage after LSD exposure (Tjio, Pahnke & Kurland 1969). A Danish study administered massive doses of LSD to mice (1mg/kg) and found definite evidence of bone marrow damage (Skakkebaek, Philip & Rafaelson 1968), but these results were not reproducible in subsequent studies (Waranky & Takacs 1968). Other studies questioned the teratogenicity of LSD (Jarvik & Kato 1968) or pointed out the multitude of chemicals known to produce chromosome breakage in cultured cells, including salicylates, caffeine, theophylline, theobromine, hydrogen peroxide, calcium deficiency, penicillin, sulfas, tetracycline, and water that was not twice distilled in glass (Judd, Brandycamp & McGlothlin 1969).

Two extensive reviews of the literature published in the early 1970s attempted to synthesize the numerous conflicting findings of various studies. Dishotsky and colleagues (1971) reviewed 68 studies and case reports published from 1967 to 1970, and concluded that "pure LSD ingested in moderate doses does not damage chromosomes *in vivo*, does not cause detectable genetic damage, and is not a teratogen or a carcinogen in man." They found no contraindication to the continued controlled experimental use of LSD other than pregnancy. A review by Sally Long (1972) in *Teratology* examined the possibility of direct or indirect genetic or teratogenic effects on children, and concluded that the risk of such effects from research or treatment using LSD was small enough that it might be outweighed by potential therapeutic benefits—a decision that should be left to the researcher. Because of the curtailment of

research on LSD with human subjects, few subsequent studies provide data on possible chromosome damage effects in humans. Research in animal models has continued to support the consensus that LSD is neither teratogenic nor oncogenic, and that it is at most a weak mutagen (Abraham & Aldridge 1993).

The issue of chromosome damage presented the first physiologic reason not to engage in controlled scientific study of psychedelic drugs. Potential subjects of LSD research raised questions about genetic risks, and scientists raised ethical questions about the safety of research subjects (Dahlberg, Mechaneck & Feldstein 1968). Officials of the government agencies charged with programming and funding research experienced conflicts between a scientific approach and their personal opinions and morals (Freedman 1969). The kinds of studies considered to be useful and important by funding agencies were linked to social policy by their dependence on congressional appropriations (Fort 1970). The use of LSD was seen by some as symbolic of a social movement of rebellious opposition to government policies, predominant values and conventional behaviors (Neill 1987; Levine 1968). Dramatic and exciting publicity, even when negative, acted as a lure for those disposed to use psychedelic drugs, and created hostility and anger in those who opposed their use. Drug policies depending primarily on prohibition and law enforcement for control increased profits for those illegal entrepreneurs willing to take the increased risks, and added the danger of adverse legal consequences to the list of possible harms resulting from psychedelic drug use. What did not deter the drug entrepreneur, however, demoralized many clinical investigators (Curran 1967).

BARRIERS TO THE CONTINUATION OF RESEARCH

Writing in 1965, Abram Hoffer expressed his dismay with what he suggested were excessively cautionary statements about the harmful potential of psychedelic drugs made by "reputable scientists who are forced to issue pseudo-scientific statements in order to hide their desire to work with these compounds" (Hoffer 1967). By November of 1968, when Hahnemann Medical College Department of Psychiatry sponsored what was described as a comprehensive, multidisciplinary symposium on psychedelic drugs, the sponsors suggested that the initial furor over psychedelic drugs had begun to subside. While it was true that the number of popular articles and news stories about psychedelics peaked in 1967, the effects of the past few years of controversy were only beginning to be felt in the research environment. This was reflected in the content of the Hahnemann Symposium itself, in which the majority of the papers presented dealt either with the known or suspected hazards of psychedelic drugs, legal issues related to their use, or attempts by researchers studying

therapeutic use to address various sources of difficulty and embarrassment in their work (Hicks & Fink 1969).

Few studies designed to address legitimate criticisms of previous research were subsequently performed. The series of NIMH-funded studies of LSD therapy that had begun in 1963 at Spring State Grove Hospital in Baltimore, and later continued at Maryland Psychiatric Research Center and the Johns Hopkins University School of Medicine was mostly completed by 1968. Although research with related substances such as dipropyltryptamine (DPT) continued there until the mid-1970s, the Spring Grove studies were the last U.S. clinical trials using LSD and human subjects for more than two decades. Hybrid models of therapy using aspects of both the psycholytic and psychedelic approaches, which emerged as psychedelic research was coming to an end, received limited exploration, and primarily used drugs other than LSD (DiLeo 1981, 1975; Grof 1970).

The national attitude toward psychedelic drugs had become profoundly negative. Although this change was rationalized by citing reports of harmful effects (Myers 1968), some researchers claimed that mass media sensationalism had led publicity-sensitive agencies to become overcautious and fearful (Yensen 1985; Dahlberg, Mechaneck & Feldstein 1968). Others noted that the scientific respectability of LSD research had been so compromised that: "Qualified, recognized researchers, who would be authorized to do the work, apparently, just do not seem to want to risk the possible notoriety, or taint of, or embroilment in, the controversy and mass media confrontations that surround investigations of the psychedelic use of LSD" (Unger 1969: 209).

LIMITATIONS OF THE EXISTING STUDIES

At a 1967 conference reviewing the previous 10 years' progress in psychopharmacology, Arnold Ludwig wryly declared that the necessity for more controlled, methodologically rigorous studies of the therapeutic uses of psychedelic drugs was "the obvious and now hackneyed conclusion of almost all the review articles in this area" (Ludwig 1968). Hollister (1968), in his comprehensive monograph on the history, pharmacological activity, and possible therapeutic applications of the multitude of natural and synthetic psychedelic drugs, asserted that "by modern standards of clinical pharmacology" there had not been even one adequate evaluation of the therapeutic use of psychedelics. Although Ludwig and Levine in their own study concluded that LSD therapy did not offer any advantage over other forms of alcoholism treatment, they also noted that there was no way to determine for what disorder or to what extent LSD therapy might be of benefit given the confused and incomplete state of previous research (Ludwig, Levine & Stark 1970). The publication of their study essentially ended the program of LSD research.

In their review of studies on LSD treatment of alcoholism published through June 1970, Abuzzahab and Anderson (1971) offered no conclusions about the overall effectiveness of LSD treatment for alcoholics because disparities in improvement criteria and in study designs did not allow them to generalize from the accumulated data. Major variations existed between studies in a number of areas: the theoretical framework of the therapist; the personal experiences of the therapy team with psychedelics; whether other therapies were provided concomitantly; and in what attempts were made to influence the "set" (the expectations, issues and personal characteristics of the patient) or the "setting" (the place and atmosphere of the session). Even within studies, these factors—which were acknowledged to modify the experience obtained—were nevertheless poorly described and controlled. Although several thousand psychiatric patients, and an equal or greater number of volunteers, were given LSD in treatment or experimental settings, no researcher attempted to determine if LSD therapy was most effective with a particular type of patient, or a specific treatment setting (Smart et al. 1967).

Definitions of drinking behavior as an outcome measure were imprecise, and no common outcome criteria allowed for comparison of study results. *A priori* determination of criteria for improvement was uncommon. Efficacy of treatment was conflated with treatment outcome, and there was little discussion of how factors other than the experience of treatment might influence the patients' condition. In addition, important effects of treatment may have been missed, as little consideration was given to social, medical, legal, familial and occupational changes.

In his review of the status of LSD psychotherapy, Yensen (1985) declared the literature on the subject to be "rich in the variability of its results, and premature in most of its conclusions." Yensen attributed this dubious distinction to the collective naïveté of the investigators of psychedelic drugs, which was shared with their professional contemporaries to an extent that prevented the deficiencies of this body of research from being outstanding for their time. Uncontrolled studies and post hoc definitions of success were commonplace in psychiatric research in the middle decades of this century. In a 1958 critique of psychiatric research, Foulds randomly sampled 72 papers from British and American journals and found that only 44% of the British and 11% of the American studies were controlled. Twice as many uncontrolled studies reported successful treatments versus the controlled studies ($p < .001$). Colin Smith complained in 1960 that psychiatry was "in danger of becoming a foetid quagmire of anecdotalism" (Smith 1961). He claimed that psychiatric research was rich in ideas, but bereft of testable hypotheses, and that training of psychiatrists in research methodology was notably deficient.

Since the 1970s, psychotherapy research techniques have changed, as have the expectations and processes of

evaluation of modern pharmacology. What has remained fairly constant, however, is the therapeutic vacuum that exists in the treatment of alcoholism. The most visible change in this area has been the emergence of other problems with comparably deficient therapeutic solutions: the widespread occurrence of polydrug abuse in the alcoholic and the growth of other substance-related disorders as significant public health problems.

A negative social and political environment served to discourage the pursuit of LSD research at a time when changes in research techniques were just beginning to influence its conduct; the psychedelic program was discontinued at a crucial point in its development. The few methodologically adequate studies of LSD treatment of alcoholism that had been completed had predominantly negative outcomes, but were criticized for failure to adhere to the psychedelic model of therapy that had been used in the numerous positive exploratory studies. Studies that might have answered these objections were not subsequently performed; governmental support disappeared, the pharmaceutical industry lost interest, and investigators became reluctant to conduct research in a sensitive and controversial area.

Grinspoon and Bakalar (1979) have suggested that it was "time to take up the work that was laid down unfinished in the sixties." In fact, lack of money, lack of trained personnel, lack of a sponsoring pharmaceutical house interested in testing the safety and efficacy of LSD, and public disapproval and mistrust of psychedelic drugs have prevented the resumption of research with these substances until very recently. Scientists at the University of New Mexico, Harbor-UCLA Medical Center, the University of Miami, and elsewhere have attempted cautiously to resume human studies of the psychedelics (Kurtzweil 1995). The University of Maryland and North Charles General Hospital had a small LSD program until the mid-1980s. A new amendment to this protocol for substance abuse treatment was approved in 1995, and supplies of LSD have been obtained from the FDA, but no research has yet been undertaken (Yensen & Dryer 1997; Strassman 1995). Research with DMT and psilocybin at the University of New Mexico has been suspended by the investigator, and ibogaine research at University of Miami has failed to obtain NIDA funding. Outside the United States, a comprehensive medical-psychiatric study of ayahuasca use in an officially sanctioned syncretic church has been completed in Brazil (Grob et al. 1996a); MDMA research in human subjects is in progress in Zurich, and in the planning stages in Barcelona. Three protocols for MDMA research in the United States are in various stages of the state and federal approval process, and an approved Phase 1 study on the effects of MDMA as a function of dosage in healthy volunteers has been completed by the Harbor-UCLA research group (Grob et al. 1996b). A study by John Halpern of Harvard University on the neuropsychological effects of peyote use by Native American Church members is in the

planning stages (Grob 1998). What Sanford Unger 30 years ago hoped for LSD and other psychedelics—that they might enjoy a "rebirth of sober consideration and exploration of use" (Unger 1969)—may or may not now be possible.

QUESTIONS GENERATED BY LSD ALCOHOLISM TREATMENT RESEARCH

Despite the confusion about the efficacy of LSD treatment occasioned by the limitations of previous studies, the possibility that LSD could be useful in the treatment of alcoholism remains engaging. Many possible constructions of the findings of historic LSD research have been left unexplored, and many aspects of the data remain unevaluated.

An initial difficulty in evaluating the results of LSD therapy is the lack of consistent comparison data on other contemporary alcoholism treatments. In Abuzzahab and Anderson's final tabulation of the 31 alcohol treatment studies they reviewed, 75% of patients receiving a single dose of LSD in controlled studies were "improved" after approximately 10 months of follow-up, versus 44.1% of the controls. At approximately 20 months, 57.5% of the multiple-dose patients were improved, versus 53.8% of controls. The authors' interpretation of these data did not offer any comparison of LSD therapy results to those of other treatments then being offered for alcoholism (Abuzzahab & Anderson 1971).

Bacon (as cited in Smart et al. 1967) claimed that improvement rates under all existing therapies for alcoholism were about 40% in 1963. In a 1967 panel discussion with Jerome Levine and others, Ross MacLean asserted that LSD-treated alcoholics experienced twice as much improvement as those treated with other methods, including Antabuse® and conditioning techniques (MacLean et al. 1967). In his review of the literature on drug treatment for alcoholism, J. M. Mottin (1974) found no consistent support for *any* of the then-current drug therapies, including "antidipsotropics, aversives, ataractics, and hallucinogens." A meta-analysis of controlled studies published between January 1974 and March 1993 found that patients who received widely differing forms of alcoholism treatment all consumed substantially less alcohol at the time of follow-up than controls (effect size = 1.17), regardless of the treatment received (Agoosti 1995).

An essential inconsistency exists in the way improvement is defined. Many researchers have used the achievement of complete abstinence from alcohol as the only criterion for improvement, whereas others include better social functioning, decreased legal or medical problems, moderation in continued drinking, or increased insight and self-acceptance as demonstrations of improvement. Contemporary studies of treatment effectiveness are expected to be far more precise in evaluating improvement than were the studies of LSD treatment, and to consider not only reduction of substance abuse, but also improvement

in the personal health and social function of the patient, and reduction of public health and safety risks as treatment outcomes (McLellan et al. 1996).

"Alcoholics" have commonly been treated as a homogeneous population in studies of alcoholism treatment, although current thinking suggests that there are subtypes who may respond differently to different forms of therapy (Babor et al. 1992). Measures of the severity of alcohol-related impairment have evolved considerably in the last decade. Since the studies of LSD therapy for alcoholism were completed, measures (such as "number of years of drinking," or "previous treatment failure") used in those LSD studies in which any assessment of severity was attempted have been superseded by more precise and comprehensive evaluation tools like the Addiction Severity Index (McLellan et al. 1992a).

Although the dose of LSD used and some description of the session environment are usually included in the existing LSD therapy studies, details of the conduct of the sessions are frequently sketchy. Historic controversies related to therapist experience with the psychedelic drugs, differences in the physical circumstances of sessions, and techniques employed during LSD administration have never been resolved. Descriptions of the precise nature and "dose" of other treatment services provided to the patient are generally lacking, and differences in efficacy associated with the non-drug aspects of the treatment programs have never been evaluated.

The concept of alcoholism as a chronic health problem has evolved since the LSD studies were performed, and the expectation that relapse is likely without ongoing therapy beyond immediate detoxification and stabilization has gained acceptance. To be considered effective, contemporary treatment programs need not necessarily set total abstinence as their goal. They must, however, produce "significant, pervasive and sustained positive change in the lives of [alcoholic] patients" (McLellan et al. 1982).

RECOMMENDATIONS FOR FURTHER STUDY

The question of whether LSD treatment is effective for alcoholism has not been convincingly answered by the existing research. Because of the differences in treatment procedures, theoretical backgrounds, biases and beliefs, and definitions of terms that existed among the various teams which conducted LSD research, the question has scarcely been properly asked. The prevalence of alcohol use disorders, the hope that improved treatments will not only reduce problem drinking but also will decrease its costs to society, and the contemporary emphasis on the control of health care costs make questions about the effectiveness of LSD treatment timely and interesting. Recent advances in outcome research on substance abuse treatment and psychotherapy make the achievement of more definitive answers feasible (O'Brien & Woody 1989).

One development in outcome research has been the use of techniques for synthesizing the existing knowledge about psychotherapy. Past attempts to compare psychotherapy outcomes discarded a large portion of the existing data on methodological grounds, in an effort to make sense of the chaos of a large set of studies with different treatment techniques, therapist philosophies, patient samples and outcome measures (Luborsky, Singer & Luborsky 1975). The resulting analyses do not assign more weight to larger or better-designed studies, and valuable data may be lost (Andrews 1981). This effect was evident in the attempt of Holder, Longabaugh, Miller and Rubonis (1991) to use a weighted evidence index to compare the cost-effectiveness of LSD therapy for alcoholism with other treatments for which more methodologically adequate studies are available, and in Abuzzahab and Anderson's assessment of 31 studies of LSD treatment.

An improvement on this technique is direct comparison of studies with different outcome scales by their effect size. Effect size is a statistic that indicates the ratio of the average difference in outcome score for the treated and control groups, and the standard deviation of the outcome score of the control group. The effect size will be a number from -3 to +3 that represents the distance between the score distributions of the treated and control groups (O'Brien & Woody 1989). A reexamination of the studies reviewed by Abuzzahab and Anderson might be possible using effect size, but only eight of those studies would be eligible for consideration.

Even with improved analytic methods, the present body of psychedelic research on alcoholism treatment is difficult to assess, as it consists mostly of hypothesis-generating studies, or hypothesis-testing studies with serious methodologic flaws. Professional interest in the psychedelics waned just as these flaws were being acknowledged and better-designed studies demanded.

Renewed human research with the psychedelics is now becoming possible (Kurtzweil 1995; Strassman 1995; Nichols 1987). Rather than abandon any attempt to profit from two decades of historic LSD research, new studies should build on the strengths and remedy the deficiencies of this large body of work. If further hypothesis-generating/pilot/exploratory studies are performed, they should be used to formulate research questions and document the quality of measures as a basis for designing new hypothesis-testing studies (Kraemer & Telch 1992).

QUESTIONS FOR FUTURE RESEARCH IN LSD TREATMENT FOR ALCOHOLISM

What is Expected from LSD Treatment for Alcoholism?

Expectations of what treatments for alcoholism should do are not confined to elimination of excessive drinking. The "effectiveness" of any alcoholism treatment is measured not only by its ability to change drinking behavior,

but also by its impact on social, medical, family, legal and employment problems that are related to alcoholism. Whether these problems contribute to or result from problem drinking, the patient, and his or her family, insurance carrier, employer, probation officer and community may expect that effective treatment will help to bring about their resolution (McLellan et al. 1992b). Successful treatment ideally would lead to better health and social functioning for the alcoholic patient, and decreased impact on the public health and safety, as well as a reduction in drinking (O'Brien & McLellan 1996).

Treatment of alcoholism, whether with LSD or otherwise, is not merely the detoxification and stabilization of an individual whose drinking has reached a crisis point. Alcoholism is a chronic disease and, although patients should be expected to improve with treatment, relapses after acute treatment is completed are the rule rather than the exception. It is realistic to expect that long-term care will be needed to maintain symptom remission (O'Brien & McLellan 1996).

At the time that research came to an end, the program of LSD therapy was evolving from emphasis on a single conversion-like experience to a type of extended psychedelic therapy in which periodically repeated high-dose sessions were employed. This hybrid treatment was intended to allow periodic access to the transcendental experience that has been postulated to permit rapid personality change, and to encourage self-exploration and therapeutic interaction, with a gradual resolution of underlying psychodynamic conflicts (McCabe & Hanlon 1977; Pahnke et al. 1970). Periodic redosage with LSD has also been suggested as a possible method for sustaining the short-term improvement observed after LSD treatment (Bowen, Soskin & Chotlos 1970; Cheek et al. 1966). With the resolution of some of the questions about the somatic consequences of repeated LSD treatment and the evolving understanding that addictive disorders require life-long treatment, this avenue of inquiry should be reopened and explored.

Is There a Particular Type of Patient Who Will Be More Likely to Benefit from LSD Treatment?

Patient populations in the present body of LSD research were generally neither adequately described nor precisely diagnosed. Many patients were known to have coexisting psychiatric diagnoses or other substance use problems, but researchers did not attempt to control for these factors. There was a wide variation in the timing and rate of follow-up, and criteria for improvement were not uniform or clearly defined. Contemporary research on substance abuse treatment generally recognizes that, in addition to the amount, duration and frequency of substance use, the patient's social assets and liabilities at entry to treatment may predict treatment outcomes. Medical conditions, family supports, work and educational skills, legal complications

and the patient's living environment may present treatment problems. (McLellan et al. 1980).

An adequate study of LSD treatment for alcoholism should begin with the application of accepted diagnostic criteria to obtain a homogeneous patient population with a specific diagnosis (O'Brien & Jones 1994). Reliable and valid instruments for the assessment of substance abuse problems, such as the Addiction Severity Index, allow the evaluation of patient status before and after treatment (McLellan et al. 1994). Pre- and posttreatment comparisons of both alcohol use and psychosocial problems should be performed at predetermined intervals and should incorporate techniques for quality control, such as collateral reports from friends and family, or objective biological measurements used to validate patient reports of drinking behavior. To minimize demand effects, independent evaluators should perform these assessments. At least an 85% rate of success in contacting patients at follow-up at six months posttreatment is considered an appropriate rate of contact (McLellan et al. 1992b).

If the problems that patients bring to treatment cannot realistically be affected by the intervention provided, an inaccurately negative assessment of the effectiveness of the treatment will result (McLellan 1993). If areas of functioning and well-being in which the patient may experience change are not assessed by evaluative measures, the effect of treatment may not be accurately reflected (Kraemer & Telch 1992).

Past LSD treatment research has suggested that patients may come to accept the severity of their problems and develop motivation for change after LSD therapy (Jensen 1963; Unger 1963; O'Reilly & Reich 1962; Terrill 1962). LSD treatments for alcoholism were primarily directed to the achievement of abstinence, and few interventions specifically emphasized the reduction of psychosocial problems. The effects of these problems on the post-treatment environment of the patient and on the likelihood of sustained improvement are now better appreciated (McLellan et al. 1994). Improved techniques for the assessment of psychosocial adjustment before and after treatment now permit the evaluation of the possible impact of LSD therapy in areas other than the amount, duration and frequency of alcohol use. Further research with LSD should use these improved evaluative methodologies to determine the impact of LSD therapy in these areas.

Exactly What Procedures Are Used?

Since the early 1960s, the influence of nondrug variables (including the purpose of the study, the expectations of the subject, and the setting in which the drug was administered) have been acknowledged as crucial factors in determining the nature of the research subject's psychedelic experience (Cohen 1985). Despite this,

psychotherapeutic research on LSD has generally failed to assess, control, or systematically modify any variables beyond the drug and dose used (Mogar 1965). Future psychedelic research should explore the ways in which the content, intensity and effects of psychedelic sessions could be intentionally arranged to facilitate a particular type of experience. In addition to the use of common techniques for quantifying the dose of psychotherapy provided (such as the use of manual-guided procedures for standardization, and training and periodic supervision of therapists) specific processes that are claimed to be significant in LSD therapy (such as changes in defensive structures of the patient and increased expressiveness) might be operationally defined, attempts to facilitate these processes described, and the effect of LSD treatment in these areas objectively measured (Mechaneck et al. 1967). Unless the characteristics of the patient and of the therapist, the conditions under which the treatment is delivered, and the methods and goals of therapy are specified, any claims about therapeutic effectiveness remain vague and nonspecific.

While neither excessive enthusiasm for a promising treatment nor skeptical negativism is appropriate in the researcher, the impossibility of conducting value-free research should be acknowledged. Contemporary psychedelic researchers should locate themselves in the studied environment by examining and revealing their biases and ideology (Janesick 1994). While this practice is common in the conduct of qualitative research, in the design of quantitative research it would be an innovative or even radical departure. Nevertheless, in the history of LSD research, the preconceived ideas of research scientists and public officials have contributed greatly to the creation of an atmosphere of confusion and mistrust. The renewal of research in this area is an opportunity to avoid perpetuating this problem.

Does LSD Treatment Produce Specific Measurable Improvement?

Although LSD researchers have noticed and discussed such LSD effects as increased self confidence, decreased tension and frustration, greater emotional stability, and less defensiveness, how these effects might be reflected in long-term changes in behavior has had very little systematic study (Bowen, Soskin & Chotlos 1970; Ludwig, Levine & Stark 1970). An effort using modern research techniques to determine in what specific way LSD effects might be of benefit is both possible and warranted.

Improvements in baseline measures of severity, quantification of treatment services, and instruments measuring the intensity of psychedelic drug effects should make it possible to assess changes produced in both clinical and functional outcomes by the addition of psychedelic experiences to existing alcohol or other drug abuse treatments. A new instrument, the Hallucinogen Rating Scale,

correlates drug effects with specific dosage levels (Strassman 1995). Improved assessment tools have been developed for evaluation of substance abuse treatment programs, including the kind and amount of program services provided, the effectiveness of specific elements of those services in decreasing drinking and reducing psychosocial problems, and the relationship of patient and treatment factors to treatment outcome. New studies of LSD treatment for alcoholism should systematically assess the effect of LSD on processes that are claimed to be of significance in therapy (Mechaneck et al. 1967).

How Does LSD Treatment Interact with Other Interventions?

LSD therapy may potentiate the effects of both specific substance abuse services and psychosocial interventions. In a recent study of 649 opiate-, alcohol- and cocaine-dependent adults in 22 treatment programs, similar factors predicted treatment outcome, independent of the patient's drug problem, or whether treatment was public or private, inpatient or outpatient. The severity of patients' pretreatment problems significantly predicted the outcome of treatment at six months. Provision of specific substance abuse services—such as group therapy for denial, 12-Step meetings and drug and alcohol education—fostered patient acceptance of a substance abuse problem, increased motivation, and influenced changes in substance use behavior. Psychosocial services helped to improve the patient's functioning in family, legal, social and employment situations (McLellan et al. 1994). LSD therapy should be evaluated in combination with other patient and treatment factors that have been shown to predict treatment outcomes.

New pharmacologic treatments such as naltrexone may help prevent relapse in alcoholic patients by reducing alcohol craving (Hartmann 1997). The possibility that insights achieved during LSD sessions might increase motivation to use these medications should be explored.

CONCLUSIONS

The possible value of LSD in a psychiatric or therapeutic context has been almost completely obscured by media sensationalism, unsupervised self-experimentation, poorly designed research, and misinformation. It is difficult to obtain legal permission to work with LSD, and there is no federal, institutional, or pharmaceutical industry support for LSD research. Nevertheless, interest in its potential usefulness persists, and preliminary work to reopen research is under way after more than a quarter century of quiescence.

A major part of the existing research on LSD therapy has investigated its potential utility as a treatment for alcoholism. Since this program of research came to an end, progress in research design and treatment evaluation has

made available tools and techniques that could help to resolve historic controversies and clarify confusion about its usefulness.

The enormous economic impact of alcohol abuse, and its associated morbidities and mortality, is well documented (Robert Wood Johnson Foundation 1994). Between 25% and 30% of U. S. hospital admissions are due to direct or indirect medical complications from alcohol. Approximately 52% of the American population drinks some beverage alcohol, and for about 10% to 12%, or about 11 to 13 million Americans, the use of alcohol has become an addiction (Inaba, Cohen & Holstein 1997). Only a fraction of those

who are dependent on alcohol ever receive formal treatment (Emrick & Hansen 1983), and even for those who are treated, expectations are limited to improvement rather than cure (O'Brien & McLellan 1996). Treatment for alcoholism, arguably even more than most medical or psychological interventions, has room for improvement.

Despite the methodologic problems of the existing studies, the possibility that LSD might be useful in the treatment of alcohol problems remains tantalizing. What is now known about LSD therapy for alcoholism neither provides evidence of its efficacy, nor assurance that its maximum therapeutic potential has been achieved.

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