The Experimental Use of Psychedelic (LSD) Psychotherapy

Walter N. Pahnke, MD, PhD; Albert A. Kurland, MD;
Sanford Unger, PhD; Charles Savage, MD; and Stanislav Grof, MD

The history of research with psychedelic drugs has produced a variety of methods for their use and conflicting claims about results. First came the wave of excitement among experimentalists in the 1950s when it was claimed that lysergic acid diethylamide (LSD) could produce a model psychosis which might be useful in understanding schizophrenia. While this promise was fading, enthusiastic reports about the possibility of LSD as an aid to psychotherapy in the treatment of alcoholism and other psychiatric disorders appeared. All these approaches were represented in 1959 at the first international conference devoted entirely to LSD.[1] Since then, there have been at least five more published proceedings of such conferences on various aspects of psychedelic drugs.[2-6] The most recent conference on various means of producing states of consciousness was sponsored by the Menninger Foundation and the American Association of Humanistic Psychology on April 7 to 11, 1969, in Council Grove, Kan, and was called "Voluntary Control Of Internal States."

In the 1960s we have seen research attempts to test scientifically the efficacy and safety of psychedelic drugs for the treatment of various forms of mental illness, chiefly alcoholism. At the same time, there has been a rapidly growing interest concerning these drugs by laymen for pleasure, excitement, mental exploration, and religious experience. The use of psychedelic drugs for all these purposes has produced conflicting claims both in the scientific and popular literature, intense public attention stimulated by the mass media, and legislative attempts at control of both research and the black market.

Effects in Man Facilitated by Psychedelic Drugs

Before we turn to the use of psychedelic drugs as a therapeutic tool, let us review briefly some basic facts. At the outset, it is important to remember that psychedelic drugs are a special class of psychopharmacological agents, not to be confused with sedatives like barbiturates or alcohol, stimulants like amphetamines or methylphenidate hydrochloride (Ritalin), tranquilizers like chlordiazepoxide hydrochloride (Librium) or meprobamate (Miltown), antipsychotic agents like the phenothiazines, or narcotic drugs like the opiates (whether synthetic or natural). Psychedelic drugs in contrast to true narcotics are not physically addicting and produce quite different psychological experiences from all these other groups of drugs.

What makes psychedelic drugs unique as a class are the psychological phenomena which they facilitate. Five major kinds of potential psychedelic drug experiences have been described in detail with examples elsewhere[7-8] and will only briefly be summarized here.

First is the *psychotic psychedelic experience* characterized by the intense, negative experience of fear to the point of panic, paranoid delusions of suspicion or grandeur, toxic confusion, impairment of abstract reasoning, remorse, depression, and isolation or somatic discomfort or both; all of these can be of very powerful magnitude.

Second is the *cognitive psychedelic experience*, characterized by astonishingly lucid thought. Problems can be seen from a novel perspective, and the inner relationships of many levels or dimensions can be seen all at once. The creative experience may have something in common with this kind of psychedelic experience, but such a possibility must await the results of future investigation.

Third is the *aesthetic psychedelic experience*, characterized by a change and intensification of all sensory modalities. Fascinating changes in sensations and perception can occur: synesthesia in which sounds can be "seen," apparent pulsations or lifelike movements in objects such as flowers or stones, the appearance of great beauty in ordinary things, release of powerful emotions through music, and eyes-closed visions of beautiful scenes, intricate geometric patterns, architectural forms, historical events, and almost anything imaginable.

From the Maryland State Psychiatric Research Center, the Johns Hopkins University School of Medicine (Drs. Pahnke, Unger, Savage, and Grof), and the Department of Mental Hygiene, State of Maryland (Dr. Kurland), Baltimore.

Read before the Symposium on Psychedelic Drugs at the 118th annual convention of the American Medical Association, New York, July 17, 1969. Based partially on a presentation by Albert Kurland, MD, at the American College of Neuropsychopharmacology, San Juan, Puerto Rico, Dec 20, 1968.

Reprint requests to Maryland Psychiatric Research Center, Box 3235, Baltimore 21228 (Dr. Pahnke).

Fourth is the *psychodynamic psychedelic experience*, characterized by a dramatic emergence into consciousness of material that was previously unconscious or preconscious. Abreaction and catharis are elements of what may subjectively be experienced as an actual reliving of incidents from the past or a symbolic portrayal of important conflicts.

The fifth and last type of psychedelic experience has been called by various names: *psychedelic peak, cosmic, transcendental,* or *mystical,* and can be summarized under the following six major psychological characteristics (described in more detail elsewhere[7]): (1) sense of unity or oneness (positive ego transcendence, loss of usual sense of self without loss of consciousness), (2) transcendence of time and space, (3) deeply felt positive mood (joy, peace, and love), (4) sense of awesomeness, reverence, and wonder, (5) meaningfulness of psychological or philosophical insight or both; and (6) ineffability (sense of difficulty in communicating the experience by verbal description).

The Varieties of Psychedelic Drug Therapies

In the course of experimental therapeutic work with psychedelic drugs (especially LSD), three major approaches have evolved: (1) psycholytic therapy, (2) psychedelic-chemotherapy, and (3) psychedelic-peak therapy. Each of these methods has been described and discussed in detail at the international conference on LSD therapy held in 1965.[3] In any evaluation of therapeutic effects, it is essential to keep in mind the differences in procedure among the various methods, not only because different kinds of experiences are facilitated, but because conflicting results can be correlated with the method used. Reactions to LSD invariably involve a complex interaction between drug dosage, set, and setting.

In psycholytic therapy, which is practiced mainly in Europe, the aim is usually the uncovering of unconscious material which can be psychodynamically analyzed both at the time and in subsequent psychotherapy sessions. There is considerable time spent on psychotherapy before, during, and after the actual drug sessions. This type of therapy is relatively long-term with multiple sessions over time and usually with small doses of the drug (25μg to 150μg).

In psychedelic-chemotherapy, the major emphasis is on administration of the drug itself, during which limited psychotherapy may or may not be carried out. There is minimal preparation and follow-up therapy. A single session with a relatively high dose of the drug (200 μg or more) has been the usual practice, although there have been experiments which consisted of weekly sessions with little or no attempt at help with interpretation or integration. This method is called hypnodelic when hypnotic induction is employed during the preparation for the session or before the onset of drug effects or both with the aim of providing better control. The major differences between psychedelic-chemotherapy and psycholytic therapy are the number of drug sessions, amount of therapy outside the drug sessions, and drug dosage.

In psychedelic-peak therapy, one of the distinctive characteristics and immediate goals in the drug session itself is the achievement of a peak or transcendental experience, but just as important is the intensive psychotherapy which occurs in the weeks prior to the psychedelic drug session and the follow-up therapy in the weeks after to help with the work of integration. The LSD session can add meaningful emotional insight and dramatic validation of an individual's basic self-worth, but usually only after the achievement of psychodynamic resolution and self-understanding during the preparatory psychotherapy. This preparation, which averages about 20 hours per patient, enables the therapist to establish close rapport with the patient and to gain intimate knowledge of the patient's developmental history, dynamics, defenses, and difficulties. In specific preparation for the session itself the patient is encouraged to trust the therapist, himself, and the situation, to let go voluntarily of his usual ego controls and be carried by the experience, and to be completely open to whatever experiences he encounters.

The experimental drug sessions themselves are carried out in a special treatment suite furnished like a comfortable living room, with sofa, easy chairs, rugs, drapes, pictures, flowers, and high-fidelity music equipment. The patient's therapist and a psychiatric nurse are in constant attendance throughout the period of drug action (10 to 12 hours). For most of the session, the patient reclines on the sofa with eyeshades and stereophonic earphones, alternately listening to carefully selected classical music or interacting with his therapist. The function of the music is to help the patient let go more easily, to enter more fully into his unfolding inner world of experience, and to facilitate the release of intense emotionality.

Although the LSD session itself is only one part of psychedelic-peak therapy, it plays a unique and necessary role without which the total therapeutic impact would not be the same. In a dosage of 200 μg or more, LSD produces a 10- to 12-hour period of striking, varied, and anomalous mental functioning; the range of possible effects or episodes of reaction or both is multiform. Certain dimensions of possible reactivity are therapeutically irrelevant (eg, sensory changes) others have distinctly antitherapeutic consequences (eg, panic, terror, or

psychotic reactions). The major dimension of drug-altered reactivity with therapeutic relevance is the affective or emotional sphere; intense, labile, personally meaningful emotionality is uniformly produced, with periodic episodes of overwhelming feeling. In terms of sequence of events, the first several hours of a psychedelic session are nonspecific and pervasive; persistent preoccupations and emotional distress patterns are "broken" or fragmented, and subsequent recall for this period is nearly always poor. During the third to fifth hours, psychedelic reactivity usually appears at peak intensity. With skillful handling, the remainder of the session may be stabilized in an elevated mood state in which psychotic and other turbulent phenomena are no longer problems. Follow-up therapy begins during the reentry period of the session day and continues the next day as the patient and therapist review the events of the session and attempt to integrate them. The patient is encouraged to write a detailed description of his experience.

If a psychedelic-peak experience has been achieved and stabilized during the session, a clinical picture which we have termed the psychedelic afterglow can be observed in the days after the session. Mood is elevated and energetic; there is a relative freedom from concerns of the past and from guilt and anxiety, and the disposition and capacity to enter into close interpersonal relationships is enhanced. These psychedelic feelings generally persist for from two weeks to a month and then gradually fade into vivid memories that hopefully will still influence attitude and behavior. During this immediate postdrug period, there is a unique opportunity for effective psychotherapeutic work on strained family or other interpersonal relationships.

It should be emphasized, however, that even with optimal programming, such peak experiences are neither universally achieved nor stabilized, and certainly they do not automatically occur merely by administration of a psychedelic drug. In our research setting, profound or marked psychedelic-peak reactions were judged to have occurred in 63% (56) of 82 consecutive alcoholic patients who received a total of 450μg of LSD given in two equal doses 45 to 60 minutes apart.

Research Projects With Psychedelic-Peak Psychotherapy

Since 1963, at the Spring Grove State Hospital, Baltimore, and now continuing at the Maryland Psychiatric Research Center, research has been in progress to investigate the usefulness of psychedelic-peak psychotherapy with alcoholic, neurotic, and narcotic addict patients and patients who are dying of cancer.[9-18] The project which involved alcoholic and neurotic patients, both originally funded by research grants from the National Institute of Mental Health (NIMH) were designed as double-blind, controlled studies. In each project the experimental group received a relatively high dose of LSD (350μg to 450μg) in contrast to only 50μg for the control group; both groups received exactly the same therapeutic preparation. In the study of neurotic patients there was an additional control group of randomly assigned patients who received an equivalent number of hours of group psychotherapy without any LSD. Evaluation of each patient's status was performed by an independent rating team before treatment and at 6, 12, and 18 months following the treatment phase. Full and final analysis and evaluation of these data are still in progress.

Results are now completed at the six-month checkpoint for the study of a total of 135 alcoholic patients who were treated with psychedelic psychotherapy. While the study design made it possible for the patients to have up to three sessions, the vast majority in both experimental and control group (total of 117 patients) received only one treatment with LSD. The 18 patients who had more than one LSD session were not found to be different from the other 117 in psychological and social measures based on pretreatment testing, but as a group they received more average hours of treatment. Therefore, in the interests of uniformity concerning amount of treatment, results were analyzed separately for the 117 patients who had only one LSD session (either a high or low dose). Out of these 117 pateints, 104 were personally located for follow-up interview after six months. It should be noted that the 13 patients not reached for follow-up were properly proportioned according to the original random assignment in which two thirds of the patients were allotted to the high-dose procedure.

Comparison of means before treatment and six months after treatment for global adjustment and drinking behavior are shown in Table 1. Global adjustment included occupational, interpersonal, and residential factors as well as the patient's reaction to alcohol. Ratings were made on each patient on a predetermined 0 to 10 behavior rating scale. The end points of the scale measuring drinking behavior were 0, indicating daily alcohol consumption, and 10 indicating total abstinence. Patients were also categorized according to whether a profound, marked, or minimal psychedelic-peak experience was achieved during the LSD session as rated by the patient's therapist immediately after the session. In Table 1, comparison of means before and after treatment between groups receiving high and low doses and among the psychedelic reactivity groups may be seen to show statistically signifi-

cant differences using an analysis of covariance statistical procedure (one-tailed test).

The percentage of patients functioning in an "essentially rehabilitated" fashion is shown for the various groups in Table 2. A score of 8 or more on the 0 to 10 scale was considered a rigorous criterion, indicating for global adjustment that a patient was making "good attainment or adjustment" with regard to drinking, occupation, interpersonal relations, etc. A score of 8 on the drinking scale indicated some, but only minimal, departure from total abstinence. Statistical analysis revealed that there were significant differences between the high and low-dose groups in percentage of patients reaching this criterion, both in global adjustment and on the scale measuring drinking. The group of patients with the most profound psychedelic-peak experiences had the highest percentage of patients who showed evidence of rehabilitation. This trend was statistically significant among the three psychedelic reactivity groups for global adjustment, but not for drinking, and thus must be interpreted with caution.

In evaluating these findings in practical terms, we can say that a given alcoholic patient receiving a single high dose of LSD in the context of psychedelic-peak psychotherapy and experiencing a profound psychedelic-peak reaction has the best likelihood for improvement six months later. Within the context of our method, dosage appears to be a more certain outcome predictor than type of experience, although peak experiences do occur more frequently with high doses of LSD. Also the estimation of psychedelic reactivity (from the individual judgments of different therapists) is probably not as reliable as the measurement of therapeutic outcome made by evaluators independent from the treatment team.

Table 1.—Comparison of Means of Alcoholic Patients Receiving One LSD Session

	Global Adjustment		Drinking Behavior	
Patient Group	**Before Treatment**	**6 mo After Treatment**	**Before Treatment**	**6 mo After Treatment**
Dosage				
High (N = 64)	4.16	6.52	2.83	7.02
Low (N = 40)	3.28	5.13	2.93	5.75
Psychedelic reactivity				
Profound (N = 31)	4.43	7.13	2.65	7.52
Marked (N = 31)	3.87	6.16	2.94	6.94
Minimal (N = 50)	3.50	5.34	2.92	5.82
Results of Covariance Analyses For Above Data	*F*	*P**	*F*	*P**
High dose vs low dose	3.76	0.05	4.43	0.025
Psychedelic reactivity groups	2.42	0.05	3.09	0.025

*P values are for one-tailed tests of significance.

An NIMH-sponsored project to investigate the effect of psychedelic-peak psychotherapy with narcotic addicts is well underway, but it is too early for any indication of therapeutic outcome. These patients in general seem to have a greater degree of psychopathology than the alcoholics with whom we have worked, but the skilled implementation of psychedelic psychotherapy seems to be proceeding smoothly. An observation of interest is that the character of the drug experience with LSD has been reported by the addicts to be distinctly and qualitatively different from what they experienced under heroin (ie, a confrontation with their problems rather than an escape from them).

During the past several years, we have also been exploring the potential of psychedelic-peak psychotherapy with patients with cancer.[16-18] The purpose has been to treat the depression, anxiety, psychological isolation, and intractable pain which so many of these patients face. The families, too, must cope with psychological problems which relate to their own fears and impending sense of loss. How to relate to the patient and what to tell him about his diagnosis further complicates what is already a grim situation. This use of LSD is similar to that already outlined, except that not quite as much time is spent in preparation, and the treatment takes place in a private room of a general medical facility (Sinai Hospital, Baltimore). Also, family therapy plays a larger role.

Thus far, we have treated 35 patients in a pilot project. Our findings must remain only suggestive at this point, but they do give some promising indications of the potential of this form of treatment. Measurements before and after LSD on depression, anxiety, emotional tension, psychological isolation, fear of death, and amount of medication required for pain have shown change in a positive direction in about two-thirds of the patients. In half of these the improvement was dramatic, and those patients who had the most profound peak experience tended to show the most benefit. Also, patients treated earlier in the course of their disease were able to use the experience more rewardingly.

While not all patients were helped dramatically, none, even the most ill, appeared to have been harmed. This finding in regard to the safety of the procedure has been consistent with our results in alcoholic and neurotic patients.

The following case summary will serve to illustrate both the method and possible outcome.

Table 2.—Alcoholic Patients Improved Six Months After One LSD Session

Patient Group	No. of Patients With Global Adjustment Scores of 8, 9, or 10 (%)	No. of Patients With Drinking Behavior Scores of 8, 9, or 10 (%)
Dosage		
High (N = 64)	44 (28/64)	53 (34/64)
Low (N = 40)	25 (10/40)	33 (13/40)
Psychedelic reactivity		
Profound (N = 23)	61 (14/23)	61 (15/23)
Marked (N = 31)	39 (12/31)	48 (48/31)
Minimal (N = 50)	24 (12/50)	36 (18/50)

χ^2 Results For Above Data

	Global Adjustment χ^2	Global Adjustment P*	Drinking Behavior χ^2	Drinking Behavior P*
High vs low dose	2.97	0.05	3.44	0.05
Psychedelic reactivity groups	7.74	0.025	3.07	Not significant

*P values are for one-tailed tests of significance.

Report of a Case

The patient, a 58-year-old Jewish married woman, had suffered from cancer of the breast for 12 years. In spite of numerous surgical and medical procedures which included hysterectomy, oophorectomy, and adrenalectomy, the disease had spread widely in her spine. At the time she was referred for LSD treatment, pressure on nerves in her spine had caused numbness and a paralysis of the lower half of her body. When first interviewed, the patient was anxious and depressed.

After six hours of preparatory psychotherapy with the patient and her family over the period of a week, during which the nature and purpose of the treatment was explained, the patient was given 300 μg of LSD. The first few hours of her psychedelic session went well and were pleasant, but a complete psychedelic-peak experience was not obtained. There were a few moments of intense positive psychedelic reactivity; for example, at one point the patient exclaimed, "This is one of the happiest days of my life. I will always remember it." There were also transient episodes of apprehension, confusion, and paranoia which were easily handled by reassurance and support.

During the latter part of the session, the patient raised the question of whether or not she would walk again. This issue was handled by a realistic review of the patient's condition, and the therapist finally stated in a direct answer to her question that it was very unlikely that she would be able to walk again. The patient then expressed her reluctant acceptance of the idea that her life could still go on even if she were confined to bed, a condition which she had previously greatly feared. However, the patient spontaneously expressed her determination to try her best in physiotherapy, in spite of the odds against her. She was supported in her resolve to try, but also discussed was acceptance of her condition, if it could not be improved. During the evening after the patient had emerged from the effects of the drug, the patient's family visited. This was a time of intense closeness and interpersonal sharing. The family remarked on the change in her mental condition from that of anxiety and depression to one of peace and joy.

In the days after the session the patient's mood was cheerful and hopeful. Upon discharge from the hospital six days after her LSD treatment, the patient returned home and began intensive work with a physiotherapist. She made remarkable, quite unexpected progress and within four months was able to use a walker. Six months after treatment the patient was doing some limited walking with a cane.

In spite of her impressive accomplishments, the patient again became depressed and difficult to manage at home because of her feelings that she would always be an invalid. She was especially distressed because the backbrace which she had to wear out of bed (four to six hours a day) was cumbersome and she needed assistance by another person in order to put it on. Because of her increasing depression, both the patient and her family requested another LSD treatment. She was seen regularly for preparation. Interpersonal relations, her self-concept, and some realistic expectations for the future were the major issues explored.

Ten months after her first session the patient was readmitted to the hospital for her second LSD treatment. Her initial reaction to the session was one of anxiety, and then the issue of her disease was encountered. She faced the fact that throughout her illness she had tended to deny that she was really sick. She remembered patients she had known with cancer, and her fear of decaying flesh was symbolized by visions of vultures feeding on rotten meat. After confronting rather than retreating from these unpleasant feelings and experiences, the patient had the experience of passing through a series of blue curtains or veils. On the other side she felt as if she were a bird in the sky soaring through the air. Then she was on a high mountain top in a small cabin alone with the snow falling. She experienced wonderful feelings of peace and harmony and visions of beautiful colors like the rainbow. After this, she stabilized the experiences and had enjoyable reliving of happy memories from her past, the best of which was her wedding day, which she relived in great detail including a reexperience of the way her mother sighed as she came down the aisle. These happy memories were in contrast to the early part of her experience when she had relived some unpleasant events such as the prejudice she felt against her as a child because she was Jewish and her failure to take advantage of the cultural opportunities her father had provided. In the latter part of the experience the patient thought deeply about her family while looking at their pictures. She was able to resolve some of the ambivalence she had about her younger daughter who was to be married in three months. She felt sorry for some of the strife they had had and came out of the experience with a resolve to make a more constructive attempt to relate to this girl in the future. When the patient's family arrived after supper, she had a serene smile on her face, but was reluctant to talk about her experience too much. She said, "You wouldn't believe me if I did tell you."

Subsequently, the patient left the hospital in good spirits and was able to participate actively in her daughter's wedding. She fulfilled her desire to walk down the aisle without the aid of even a cane, and during the wedding reception she amazed all the guests by dancing with her husband. Her sister said she had been the life of the party.

Table 3.—Means of Chromosomal Aberration Rates* Before and After LSD Among Various Experimental Groups

Group	Before LSD	After LSD	Difference	P
32 patients	4.28	5.91	+1.63	Not significant†
5 users	2.81	3.57	+0.76	Not significant‡
8 experimental subjects	...	2.79	...	...
2 normal subjects	2.65	...	...	...

*Aberration rate = percentage of aberrant cells/total metaphases analyzed (at least 200 per culture).
†Wilcoxon matched-pairs, signed-ranks, two-tailed test.
‡Fisher exact probability test.

Within six months the patient requested a third LSD treatment. At this time she had increasing pain and was discouraged because she had not worked in over two years although she had kept the hope alive that she would eventually return to her old job. The session began smoothly but the patient became frightened when she saw a huge wall of flames. After support and encouragement by the therapist, the patient was able to go through the middle of the flames, and at this point experienced positive ego transcendence. She felt that she had left her body, was in another world, and was in the presence of God which seemed symbolized by a huge diamond-shaped iridescent Presence. She did not see Him as a Person but knew He was there. The feeling was one of awe and reverence, and she was filled with a sense of peace and freedom. Because she was free from her body, she felt no pain at all. She was quiet during most of the day and emerged from the session with a deep feeling of peace and joy. When her family had arrived, she radiated a psychedelic afterglow of peace and beauty which all remarked upon. During the course of the evening the patient had a serious talk with her daughters about her condition and what might lie ahead. Shortly thereafter the patient was discharged from the hospital in good spirits. One effect of the treatment was that when the patient was troubled with pain, she could push the pain out of her mind by remembering her out-of-the-body LSD experience.

The patient did very well for about one month, until she slipped on the stairs one day and injured her back, which began causing her considerable pain again. She also became sick with influenza and was confined to bed. Prior to this she had been considering going back to work at her old job, part-time, but with the worsening of her physical condition these plans had to be postponed. With these physical setbacks and especially the recurrence of her pain, the patient again became somewhat depressed. Both the patient and her family requested another LSD treatment. The patient was seen weekly for about a month as an outpatient, and then readmitted for a treatment with LSD, almost six months after her third treatment.

The evening before her session, during the final preparation, the patient suddenly asked a direct question about her diagnosis for the first time in the almost two years she had been in the LSD-treatment program. Although she knew that her breast had been removed for a tumor, she had believed there was no further growth, but the increasing pain in her back had made her wonder. Her questions were answered gently, but without evasion, and the meaning and emotional impact were discussed with her. The family members were informed of this conversation immediately thereafter, and they reacted by becoming quite upset and angry. That very evening, in a general family discussion with the patient and therapist, however, most of them were able to resolve their feelings. Some felt embarrassed because of their previous pretense; most felt relieved when they saw how well the patient had dealt with the situation. The patient stated that she was glad to know the truth and was obviously not psychologically shattered or further depressed as some of the family members had feared.

The fourth session the next day went smoothly, except for some nausea which was experienced shortly before admission when she had eaten some spoiled food. Much psychodynamic material emerged concerning her feelings about various members of her family, especially her two daughters. In the evening the patient felt very close to her family and spent some time in talking to each of them alone in a very personal way. She was reluctant to have them leave at the end of the evening, even though she was very tired. In the days after the session the patient felt relaxed and in good spirits. She was not pessimistic about the fu ture, in spite of the new knowledg about the diagnosis of metastatic can cer of the spine. She was able to tol erate the pain in the back with the ai of narcotic drugs, but did not hav complete relief from pain.

While still in the hospital, an hy pophysectomy was attempted as a pos sible means to stop further spread c her metastatic process. Because c hemorrhage the operation could not b completed, and the patient died a fe days later.

This patient experienced consic erable relief from pain, depressior and anxiety over the period of a most two years during which sh received four LSD treatments. He first session was not judged to hav had much psychedelic content, bu the second, third, and fourth ses sions did. The third session was th most complete psychedelic-peak ex perience and seemed to provide th most benefit. This patient's gratify ing physical improvement can b attributed only indirectly to th LSD treatment in that her own un derlying resolution to pursue phys iotherapy emerged when her depres sion and anxiety were relieved. B a fortunate coincidence, her cond tion responded well to these effort on her part, contrary to the mos informed medical prognosis. All ou patients are told that LSD is fo treatment of psychological distres and not a cure for their physica disease. In this case, as happens nc infrequently, sometime during th course of LSD treatment the issu of diagnosis was brought up by th patient and had to be worked ou with the patient and the family.

The Question of Safety

When psychedelic drugs are ad ministered under controlled medica conditions (as has been the case i several large-scale research project in recent years), permanent advers effects have been rare. Since 196 at the Spring Grove State Hospita and now at the Maryland Psych atric Research Center, Baltimor

over 300 patients have been treated with LSD without a single case of long-term psychological or physical harm directly attributable to the treatment, although there have been two cases in which disturbances persisted in the days following the actual LSD session. Both patients subsequently responded to conventional psychiatric treatment.

Throughout the years of research with LSD many possible harmful physical effects have been suggested, but careful subsequent investigation has failed to furnish much conclusive scientific evidence. Most recently, the question of chromosomal damage has been raised following the positive in vitro findings in white blood cells by Cohen.[19] Retrospective studies on persons having taken LSD (most from the black market and only a few under medical supervision) have produced conflicting reports. Some researchers[20-22] found increased chromosomal breakage over normal rates, and others no increase.[23-25]

Because we were in a position to study the effect of pure LSD of known amount on patients who were to be treated with psychedelic psychotherapy, we entered into collaboration with the cytogenetics laboratory of Joe-Hin Tjio, PhD, at the National Institute of Arthritis and Metabolic Diseases to carry out a rigorously controlled study. Blood samples from 32 patients being treated at the Spring Grove State Hospital were drawn and cultured both before and after LSD administration. The white blood cell (WBC) chromosomes were then studied without prior identification of the slides, and at least 200 metaphases were analyzed per culture. In addition, the WBC chromosomes of five chronic LSD users were studied before, during, and after the administration of known doses of LSD in research on sensory, cognitive, and perceptual functions at the National Institutes of Health.

No difference was found in the rate of chromosomal aberrations before and after administration of LSD when the data from these 37 separate individuals were statistically analyzed. Also, chromosomal analysis after LSD administration was done on eight normal subjects who had received LSD in research experiments in the past, and no increase over normal chromosomal breakage rate was found. A summary of these results is presented in Table 3. The mean rates before LSD in the 32 patients (4.28%) and the five LSD users (2.81%) are comparable to each other and to the values obtained from samples from two normal control subjects for eight to ten consecutive days (2.65%). The differences between the rates before and after receiving LSD for both the 32 patients (+1.63%) and the five LSD users (+0.76%) are not statistically significant. The mean chromosomal aberration rates for the 32 patients and five LSD users (including those both before and after administration of LSD), eight experimental LSD subjects (after LSD administration), and two normal controls (no LSD) only vary from 2.65% to 5.91%. Detailed reports of this research have been presented and published.[26,27]

Comment

Part of the conflicting evidence about the efficacy of psychedelic drugs as a therapeutic tool for the treatment of mental illness comes from the differences in the methods employed by various groups of researchers. Unfortunately, rather than replicating each other's methods, each research team seems to have developed its own procedure.

In spite of such diversity of approach, several points seem to be clear by now. Use of LSD is not a substitute for skilled psychotherapy. Experiments where LSD was used primarily as a chemotherapeutic agent or with a minimum of psychotherapy have not shown any greater efficacy regarding therapeutic outcome, especially with alcoholics, than control groups.[28-31] The evidence from the psycholytic use of LSD by European researchers and psychedelic-peak therapy as practiced at the Maryland Psychiatric Research Center indicates that LSD can be an enhancer of skilled psychotherapy when integrated with an intensive psychotherapeutic program of sufficient duration (30 to 50 hours).

The scientific evidence concerning possible genetic hazards of LSD is conflicting and inconclusive. The difference in results between our carefully controlled study before and after administration of LSD in patients and the research on LSD abusers may be explained by the many uncontrolled variables such as viral infections and the effects of other drugs. Certainly much more research needs to be done in this complex area before valid conclusions can be drawn.

Research with psychedelic drugs needs to be continued to learn more about their effective use. Questions need to be answered, such as what kinds of patients will benefit most and under what circumstances. As our research progresses and we gain more experience we expect to modify our implementation of psychedelic-peak psychotherapy. Newer psychedelic drugs may have certain advantages over more well-known ones. For example, we have been testing dipropyltryptamine (DPT) developed by Szara[32] at the NIH, which has a duration of action of from two to four hours depending on dosage. If this drug proves to be as effective and safely manageable as the much longer-acting LSD, it could result in a psychedelic procedure that could be more flexibly and easily implemented than that with LSD.

In spite of the potential uses

for psychedelic drugs suggested by our work, the future of such research, unfortunately, seems uncertain. Contributing factors for this dim prognosis are sensationalism of the effects of LSD along with a continuing spread of illicit use, public fear stimulated especially by reports of irreversible genetic and psychological damage, the decreasing amount of research being initiated, the dearth of investigators who have had first-hand clinical or research experience with LSD, and the difficulty of obtaining such training.

Our hope is that the current public concern over abuse can give way to a resurgence of careful and informed research including specialized training and experience for those interested in this area. Our past and present research continues to intrigue us with the promise of psychedelic drugs, but they are obviously powerful tools that need to be used and handled wisely. Hopefully, it is not too late for them to be harnessed for medical and research use in a variety of ways in the future.

These investigations were supported in part by Public Health Service research support grants MH-13747 (Psychedelic Therapy Research Program), MH-15555 (Program for Treatment of the Narcotic Addict), MH-08474 (Controlled Study of LSD Therapy with Alcoholics), MH-11001 (A Controlled Study of LSD Therapy with Neurotics), and FR-05546 (General Research Support Program). These grants were administered by Friends of Psychiatric Research, Inc, Baltimore.

The lysergic acid diethylamide used in this research was manufactured by the Sandoz Pharmaceutical Co., Basel, Switzerland, and distributed by the FDA-NIMH Committee for psychomimetic drug research.

Lee McCabe, PhD, Sidney Wolf, MA, William Richards, STM, and Thomas Cimonetti, MD, collaborated in these studies. James Olsson, PhD, performed the statistical analyses. Harry Shock, LLB, headed the independent evaluation follow-up team. Louis Goodman, MD, Sinai Hospital, Baltimore, Md, arranged the clinical facilities for the study of patients with cancer.

References

1. Abramson HA (ed): *The Use of LSD in Psychotherapy*. New York, Josiah Macy, Jr, Foundation Publications, 1960.

2. Crockett R, Sandison RA, Welk A (eds): *Hallucinogenic Drugs and Their Psychotherapeutic Use*. London, HK Lewis & Co Ltd, 1963.

3. Abramson HA (ed): *The Use of LSD in Psychotherapy and Alcoholism*. New York, Bobbs-Merrill & Co, 1967.

4. Leaf R, Debold R (eds): *LSD, Man and Society*. Middletown, Conn, Wesleyan University Press, 1967.

5. Cavanna R, Ulmann M (eds): *Proceedings of an International Conference on Hypnosis, Drugs, Dreams, and Psi, 1967*. New York, Garrett Press, 1968.

6. Hicks RE, Fink PJ (eds): *Psychedelic Drugs*. New York, Grune & Stratton, 1969.

7. Pahnke W, Richards W: Implications of LSD and experimental mysticism. *J Religion Health* **5**:175-208, 1966.

8. Pahnke WN: LSD and religious experience, in Leaf R, Debold R (eds): *LSD, Man and Society*. Middletown, Conn, Wesleyan University Press, 1967.

9. Kurland AA, Unger S, Shaffer JW, et al: Psychedelic therapy utilizing LSD in the treatment of the alcoholic patient: A preliminary report. *Amer J Psychiat* **123**: 1202-1209, 1967.

10. Kurland AA, Unger S, Shaffer JW, et al: Psychedelic psychotherapy (LSD) in the treatment of alcoholism: An approach to a controlled study, in Abramson HA (ed): *The Use of LSD in Psychotherapy and Alcoholism*. New York, Bobbs-Merrill & Co, 1967, pp 496-503.

11. Kurland AA, Savage C, Shaffer JW, et al: Therapeutic potential of LSD in medicine, in Leaf R, Debold R (eds): *LSD, Man and Society*. Middletown, Conn, Wesleyan University Press, 1967, pp 20-35.

12. Unger S, Kurland AA, Shaffer JW, et al: LSD-type drugs and psychedelic therapy, in Shlien J, Hunt H, Mataruzzo J, et al (eds): *Research in Psychotherapy*. Washington, DC, American Psychological Assoc Inc, 1968, vol 3, pp 521-535.

13. Unger S: The psychedelic use of LSD: Reflections and observations, in Hicks RE, Fink PJ (eds): *Psychedelic Drugs*. New York, Grune & Stratton Inc, 1969, pp 199-209.

14. Savage C: Psychedelic therapy, in Shlien J, Hunt H, Mataruzzo J, et al (eds): *Research in Psychotherapy*. Washington, DC, American Psychological Assoc Inc, 1968 vol 3, pp 512-520.

15. Savage C, McCabe OL, Olsson JE, et al: Research with psychedelic drugs, in Hicks RE, Fink PJ (eds): *Psychedelic drugs*. New York, Grune & Stratton Inc, 1969, pp 15-22.

16. Kurland AA, Pahnke WN, Unger S, et al: Psychedelic psychotherapy (LSD) in the treatment of a patient with a malignancy, in Cerletti A, Dove FL (eds): *The Present Status of Psychotropic Drugs: Proceedings of the Sixth International Congress of the Collegium International Neuropsychopharmacologicum*, publication 180. International Congress series, Amsterdam, Excerpta Medica Foundation, 1969, pp 432-434.

17. Pahnke WN, The psychedelic mystical experience in the human encounter with death. *Harvard Theological Review* **62**:1-32, 1969.

18. Pahnke W, Kurland AA, Goodman LE, et al: LSD-assisted psychotherapy with terminal cancer patients, in Hicks RE, Fink PF (eds): *Psychedelic Drugs*. New York, Grune & Stratton Inc, 1969 pp 33-42.

19. Cohen M, Marinello M, Bach N: Chromosomal damage in human leucocytes induced by lysergic acid diethylamide. *Science* **155**:1417-1419, 1967.

20. Cohen, M, Hirschhorn K, Frosch W: In vivo and in vitro chromosomal damage induced by LSD-25. *New Eng J Med* **227**: 1043-1049, 1967.

21. Egozcue J, Irwin S, Maruffo CA: Chromosomal damage in LSD users. *JAMA* **204**:214-218, 1968.

22. Nielsen J, Friedrich U, Tsuboi T: Chromosome abnormalities and psychotropic drugs. *Nature* **218**:488-489, 1968.

23. Loughman WD, Sargent TW, Israelstam DM: Leukocytes of humans exposed to lysergic acid diethylamide: Lack of chromosomal damage. *Science* **158**:508-510, 1967.

24. Bender L, Sankar DVS: Chromosomal damage not found in leucocytes of children treated with LSD-25. *Science* **159**: 749, 1968.

25. Sparkes RS, Melnyk J, Bozzetti LP: Chromosomal effect in vivo of exposure to lysergic acid diethylamide. *Science* **160**: 1343-1344, 1968.

26. Tjio JH, Pahnke WN, Kurland AA: Pre- and post-chromosomal aberrations: A comparative study, in Costa E, Greengard P (eds): *Advances in Biochemical Psychopharmacology*. New York, Raven Press, 1969, vol 1, pp 191-204.

27. Tjio JH, Pahnke WN, Kurland AA: LSD and chromosomes: A controlled study. *JAMA* **210**:849-856, 1969.

28. Smart RG, Storn T, Baker EF, et al: *Lysergic Acid Diethylamide (LSD) in the Treatment of Alcoholism*, publication 6. Bookside monograph of the Addiction Research Foundation, Toronto, University of Toronto Press, 1967.

29. Johnson FG: LSD in the treatment of alcoholism. *Amer J Psychiat* **126**:481-487, 1969.

30. Ludwig A, Levine J, Spark L, et al: The clinical study of LSD treatment in alcoholism. *Amer J Psychiat* **126**:59-69, 1969.

31. Hollister LE, Shelton J, Krieger G: A controlled comparison of lysergic acid diethylamide (LSD) and dextroamphetamine in alcoholics. *Amer J Psychiat* **125**: 58-63, 1969.

32. Szara S, Faillace LA, Speck LB: Metabolic and physiological correlates of the psychological reaction to three short-acting tryptamine derivatives, in Brill H, Cole J, Deniker P, et al (eds): *Proceedings of the Fifth International Congress of the Collegium Internationale Neuropsychopharmacologicum*, publication 129. International Congress series, Amsterdam, Excerpta Medica Foundation, 1967, p 115.