

LSD and UML Treatment of Hospitalized
Disturbed Children

by Laurretta Bender, M.D., Gloria Faretra, M.D.,
and Leonard Cobrinik, Ph.D.

The use of LSD-25 has become well known in the production of experimental psychoses since its psychotomimetic properties were discovered by Hoffman in 1943. There have been a number of reports of its use as a psychotherapeutic agent, with varying degrees of success noted, since it was first described as facilitating the psychiatric interview in 1950 [1]. The heightened perceptual awareness, increase in rapport, and breaking through of repressive ego defenses suggested a possible use of the drug as an adjunct in psychotherapy, especially of neurotics [2], and has led to considerable experimentation in this area. In all of these studies, LSD was usually given in single doses of 30 to 400 μ g at weekly intervals, for varying periods of time, generally in conjunction with individual or group therapy.

There have been only occasional references in the literature to its use in therapy of children [3]. In March of 1962, Freedman et al. reported on the administration of LSD to 12 autistic schizophrenic children under the age of 12, who were attending a day school (League School) in New York [4]. Ten were given a single dose and the other two children received two treatments each, with most receiving 100 μ g per treatment. The observers described autonomic effects similar to those seen in adults, mood-swings, increased vocalization, and some changes in contact, but concluded that development of tolerance made its successful use in therapy a questionable value. There have been no reports, to our knowledge, of its extensive use in children on a daily basis, prior to 1961.

The first report of the use of daily LSD and UML in a group of autistic schizophrenic children at the Creedmoor State Hospital Children's Unit was given by Laurretta Bender at the annual meeting of the Society for Biological Psychiatry in June, 1961 [5]. In it she described our reasons for interest in the study of these drugs in our patients. Some of these points may be restated here.

In our search for understanding and for effective therapy of childhood schizophrenia, particularly the more severe, autistic type, we have utilized many kinds of treatment and methods of evaluation, both psychological and biological. In each case we hoped

that our therapy would not only help to relieve present symptoms, but would have significant relationship to the basic pathological process, and would have more long-term effects in accelerating development and organizing behavior.

Among other characteristics, schizophrenic children show disturbances in perception and awareness, and in autonomic nervous system patterning; they are unable to form identifications or meaningful interpersonal relationships or to break through autistic defenses. LSD-25 (d-lysergic acid diethylamide), with its known action in all of these areas, therefore seemed to have a possible significance in the treatment and study of our schizophrenic children, and to bear a relationship to the basic pathology in the patient.

In addition we have observed that children react differently from adults to physiological therapy; they develop tolerance more slowly, and have far fewer side effects.

The experiment with the first group of 14 autistic children is described in some detail in Dr. Bender's previous paper, and will be noted only briefly here. Because of the rather violent psychode reactions described when adults were given large doses of LSD, we were extremely cautious when first using the drug, even obtaining parents' consent. We soon observed, however, that the children showed no serious side effects, no evidence of severe disturbances, or of toxicity, so we felt no hesitation in increasing the frequency and dosage. The children were given small doses, 25 μ g at a time, intramuscularly and later orally. At first the drug was given once a week, then gradually increased to the dosage regime to be described.

Shortly after the original project was begun, a related compound became available, UML-491 (L-methyl-D-lysergic acid butanolamide bimalate), a methylated derivative of LSD. UML does not have the psychotomimetic effects of LSD, and is a more potent serotonin inhibitor, which is believed to be the basis for its effectiveness as a prophylactic agent in migraine headaches. Another group of eight autistic children was then started on this compound, and encouraging results with both LSD and UML led to the expansion of our investigations and to this report.

PROCEDURE

The selected children were not separated from the others, and continued with the usual school and activity program, home visits, and other routines of the Children's Unit. They were evaluated initially and during the study by the psychiatrists, psychologist, ward and activity personnel, and by interview and reports of parents. Biochemical studies were also carried out by Dr. Siva Sankar in the Children's Unit laboratories.

LSD dosage was gradually increased from 50 μ g to 150 μ g daily in two divided doses; UML was increased from 4 mg to 12 mg daily in two divided doses, using a long-acting tablet, "spacetab." Dura-

tion of treatment ranges from approximately two months with the newest group to 12 months with the original groups of patients. About half have been receiving LSD, and half UML, with the choice made merely on an arbitrary basis.

All the children had been previously treated with most of the known therapies—psychotherapy, drugs, electric shock, insulin, special schools—many even before coming to the hospital, with little or no lasting improvement. Most of them required medication for management of behavior, restlessness, and other problems in the Children's Unit before their inclusion in this study. This medication was discontinued at the time of the initial evaluation, and did not have to be resumed, except in a few cases which we will mention.

DESCRIPTION OF CHILDREN

Approximately 50 children have been involved in the program, though not all have continued.

The children, boys and girls, all were diagnosed in the hospital as having childhood schizophrenia, and many had been so diagnosed prior to admission. A few also showed evidence of minimal brain damage. Their ages ranged from 6 to 12 years. All were in the hospital for periods varying from two months to two to three years, and were therefore well known to the staff and ward personnel.

The children were in two major categories—about half were autistic, regressed, essentially nonverbal; the others, psychotic but verbal and alert.

AUTISTIC CHILDREN

The autistic children showed all degrees of severity of symptoms and anxiety. Many were completely unresponsive to their environment, sitting or standing alone, rocking, whirling, and staring at their fingers. Others made contact only by excessive clinging, pulling, and biting or scratching. Nearly all had no toilet training; all were erratic, unpatterned, and disorganized in their eating and sleeping habits. (One child, for example, had eaten nothing but bread, milk, and crackers throughout his childhood; another ate ravenously, not only his own food, but anyone else's he could reach.) A boy, one of twins, avoided contact with other persons by covering his eyes or ears with his hands, or turning his back when approached, occasionally darting anxious fleeting glances at the person addressing him. Another boy beat his cheeks and forehead violently with his fists, or banged his head against the wall, so that his face was continually bruised and a football helmet had to be worn for protection. Many of these children had not spoken any intelligible words; some made guttural sounds, screamed, or uttered other noises. Some had one or two words which were used rarely for communication; some seemed to understand directions and to be on the verge of speech; a few hummed or sang commer-

bits or bits of nursery rhymes. Rarely did one child play with another or with an adult, and even then the play was momentary, e.g., returning a ball thrown to them once and then losing interest. Some were pale, thin, and frequently ill with minor respiratory illnesses and fevers; others had cold, bluish fingers, flushed readily, or showed other evidence of homeostatic lability. They were untestable by most standard psychological tests, and for the most part had Vineland Social Maturity ages within the two to three year age range.

RESULTS IN THE AUTISTIC CHILDREN

In general, we have not yet distinguished important characteristic differences in the clinical response to either LSD or UML, though there seems to be moderately greater excitability with LSD, especially early in treatment.

No child showed evidence of serious side-effects, toxicity, or irreversible regression from either medication. All showed some type of response, which however varied in degree and characteristics. There were definite changes in response to the environment, which was most remarkable in these autistic children. They became gay, happy, laughing frequently, especially early in the treatment program. Nearly all of them were more alert, aware, and interested in watching other persons. Some showed changes in facial expression in appropriate reactions to situations for the first time; many were able to understand and follow directions more readily. This increase in awareness was noted by all observers, including families, and was one of the most encouraging signs in these very withdrawn, regressed children. Personnel and parents were enthusiastic about the changes in the children, describing them as "more affectionate," "more aware," and interested in them or in siblings for the first time. The twin no longer covered his eyes and ears with his hands, now seemed less afraid, more interested, alert and active, and came to the person who addressed him. (One anxious mother even complained to us about the medication, giving as her reason that her son, who was previously so quiet and easy to manage, now wanted to contact her, to sit in her lap, and to be noticed.)

Some of the quieter autistic children became mildly aggressive, pushing, biting, or pinching other children, and defending themselves for the first time if interfered with. This behavior we considered an improvement, in that it represented a contact with the environment which was previously ignored. In a few cases, when such activity was excessive, the addition of reserpine calmed the child but did not eliminate the LSD or UML effect. Paradoxically, several of the children who had been showing such extreme aggressive behavior prior to LSD or UML medication became quieter, more manageable, and more "normal" in their contacts with other persons, leading us

to assume that these medications might tend to "normalize" behavior rather than subdue or stimulate it.

The boy who had beaten himself so severely required no other medication, and only rarely hit his face or forehead in response to some frustration or apparent anxiety. With some of the children there was a decrease in regressive behavior such as tearing clothes, smearing food and feces, and rocking and banging. A few children improved in eating habits and tried new foods for the first time. There was some attempt at simple play with adults and with one or two of the other children.

There were no sleeping problems, though several of the children previously had been unable to sleep without routine tranquilizing medication.

Changes in speech and verbal communication in autistic children are always difficult to evaluate. We did observe, however, that the vocabularies of several of the children increased after LSD or UML; several seemed to be attempting to form words or watched adults carefully as they spoke; many seemed to comprehend speech for the first time or were able to communicate their needs. Many times, words or even sentences were used at first only in the most familiar of circumstances, for example, with the child's mother or with his favorite ward attendant or teacher. Very few of these changes in communication had been noted previously in such a large number of children, and at such a relatively rapid rate.

VERBAL CHILDREN

The next group of children selected, though also schizophrenic, showed a different clinical picture. They were boys within the same age range, 6 to 12 years, and hospitalized for a somewhat shorter average period than the autistic children. All were testable by most of the standard psychological tests, all had attended public school with varying degrees of success, all were verbal and responded to the environment. This group was selected primarily because of this last characteristic, since we became interested in obtaining verbal descriptions of the effects of LSD and UML. We had also observed that this type of child often responded differently to physiological and drug therapies from the autistic child, and according to our biochemist, differed in some significant biochemical findings.

These boys, though often superficially alert and cooperative, showed impaired relationships with others. Some were overly clinging and dependent on adults while withdrawing from association with peers; some were excessively negativistic, hostile, aggressive, and could not identify normally with others. (One boy with a superior IQ spent every available moment sitting alone in a remote corner or empty room, totally absorbed in a comic book. He became annoyed when interrupted, and his only conversation with other boys was to inform them that the food was poisoned, or that they would probably never go home because the doctors were against them.)

They showed all degrees of depression and anxiety, from nail-biting to terrifying dreams and fantasies. Many showed irregular respiratory rates and rapid, irregular pulse rates. They often confused reality with fantasy or dreams, and on interview would describe elaborate flying fantasies, ghost stories, being pursued by monsters as if they were real. Some were overly concerned with physical illness, either their own or a significant person's, and one boy was especially fearful and preoccupied with his own death.

Perceptual distortions were often prominent. One boy stated: "I can see things no one else can see, small things that turn big. Once I stared at a kid, he was real small, then he got bigger and bigger every minute. I looked at him and he turned into a giant. I can see people growing." Another boy could feel his feet growing bigger. Several of the boys described voices telling them to do things, and one boy felt a person in his stomach controlling him.

RESULTS IN THE VERBAL CHILDREN

None of them was a problem in management on the ward or in activities, even though some had previously required medication to control their acting-out behavior. There was some change in their superficial interpersonal relationships. One boy who had been sullen and negativistic for several weeks prior to treatment soon became friendly and cooperative, greeting the personnel with a smile and a pleasant remark. On individual interviews it was more apparent that changes had occurred. The childish flights into fantasy, distortions, and poor reality orientation gave way to more mature, controlled, reality-bound reactions. Many of the boys were depressed by the realistic situation of their hospitalization, family problems, and by new insights into their psychological deviations. They tended to deny or repress previously described hallucinations or fantasies, or explained them by saying "That's when I was sick," or "I was acting crazy then like a cartoon." Although many still showed schizophrenic symptomatology, the picture had become one of an adolescent or adult type of schizophrenia, with attempts at formation of defenses by projection, denial, repression. Several described aggressive wishes or dreams no longer involving monsters and ghosts, but directed toward people who were frustrating them in some way, for example the doctor who would not send them home or the attendant who deprives them of some desired activity or privilege. One boy, only ten, and of dull normal IQ, said in a surprisingly adult manner: "I don't believe in God anymore. I can't pray. God put me here, I know."

In connection with our evaluation, psychological tests were administered to ten verbally responsive children in our sample, and seemed to support our clinical findings. The tests used included the Rorschach, Bender-Gestalt, and Human Figure Drawings. Four of the children were examined twice, at the beginning of treatment and after a three-month interval; the rest were

examined a third time, from six to eight months after initiation of the study.

Preliminary findings show that the children vary considerably among themselves in their test-retest pattern, with four of them demonstrating noticeable shift on the Rorschach. There was a certain consistency in the types of changes observed, although not all children showed any given one.

There were two major changes observed: (1) There was a decrease in personalized ideation and a corresponding gain in accuracy of response. There was noticeably less body preoccupation expressed. Whereas initial Rorschach records contained perseverated "body insides" and "stomach" responses, later records do not show this. Or, the anatomical concepts have been diminished in a peculiar way; "Inside of the body" may become a "nose," perceived in a smaller area and with some rationalization. Other perseverated fantasy themes ("monsters," "devils," etc.) are also found less frequently on later examinations.

In a more positive vein, we note a developing capacity to perceive the human figure in an appropriate way, as well as improvements in the ability to respond to more usual configurations. This improvement in form perception is especially noted on Card 9, where the color provides a severely distracting element.

(2) An inhibition of strongly emotional or "feeling" reactions to the cards. Pure color reactions ("fire," "blood") and descriptive color reactions show a decline, as do the dark shading actions ("shadow," "spider").

It is interesting to note that the children who demonstrated most change during treatment showed certain common features in their pre-treatment testing. They were generally over-responsive, both in an emotional sense and in the extent to which fantasies and fears color their responses. These children also were characterized by a somewhat higher level of perceptual maturity to begin with. All of them were capable of human figure perceptions on the Rorschach, although usually these responses were not forthcoming on the expected cards. These children were also noted to be among the youngest in the sample of verbal children and showed higher functioning levels on the intelligence tests.

Another interesting finding concerns the great variability in level of functioning over the course of this study which is observed in a few of the children. We note marked shifts, for example, in the representation of the human figure. At one time we may observe a high-level profile elaboration of the human figure at the same time as the head is much too large for the body; the next time the drawing is full-face and generally less mature although the head is now in better proportion with the body. One boy shifted over the course of three examinations from vague, feeling type reactions on the Rorschach to an immature confabulatory pattern, and, finally, to a more accurately perceived but highly individualized pattern of

response. This direction of change is observed to be in contradiction to the general pattern of change. It sometimes appeared as if developmental changes were telescoped during the course of this study, although the changes were not always in a given direction and could be observed to go forward and then regress.

It has been stated that chronic, "burnt-out" schizophrenic adults did not respond to LSD or required much higher doses to produce the psychotomimetic effect (6, 7).

We are also aware that our adolescent patients respond differently to physiological treatment than the younger patients. Therefore, a group of eight children was recently included in the program. These are chronically ill, autistic, regressed children, ages 12 to 15, who are considered more severely ill than the younger, similar group, in that they have been ill their entire lives, have been in the Children's Unit from three to six years, and have not responded to any treatment methods. We hoped that they might benefit from treatment with LSD and UML, as the younger patients were apparently doing.

These patients, early in the treatment, showed the same types of responses obtained in the younger autistic group: excitability, frequent laughing, attempts to bite and pinch, flushing, and over-activity.

There has been an increase in their usual behavior patterns, such as climbing, compulsive bouncing of a ball, repetitive rocking and pacing motility. One boy who had been occasionally verbal showed a definite increase in verbalization and appropriate speech, which has continued to improve. Fleeting attempts to contact and approach adults have been noted in some of these patients for the first time. In general they have all shown reactions which we have come to recognize as typical responses of autistic children to these medications, but to a lesser extent than the younger group. Three have required reserpine because of excessive biting or pinching.

BIOCHEMICAL STUDIES

Investigations show that the uptake of serotonin- C^{14} by blood platelets from autistic children is reduced and inorganic phosphate in RBC is high. It was found that LSD and UML increase the RBC inorganic phosphate while imipramine and reserpine do not affect inorganic phosphate levels. Uptake of serotonin by blood platelets was increased (in autistic children) for the first two weeks of medication, while it decreased afterward. In most of the children treated with reserpine and imipramine the serotonin uptake decreased to a certain extent only.

Recently half of the children were taken off medication for four weeks. Within a short time, many showed evidence of regression and loss of some of their previous gains, but no child regressed completely to previous behavior. They were then given either reserpine or imipramine for four weeks, with little remarkable

change. Some of the verbal children became depressed with reserpine or overstimulated with imipramine. Resumption of the LSD and UML again produced the previously noted responses, though they were not so intense as when the medication had been given originally.

There has been much discussion in the literature and among the staff participating in this project regarding the development of tolerance with continued use of LSD and UML. Repeated administration of LSD at daily intervals has been said to cause development of tolerance in animals and in man, i.e., the psychotomimetic effects in man no longer occur or are decreased after several doses [8,9]. We have not noticed this occurring in our patients, though there does tend to be a leveling off of response after several weeks or months of medication. Whether this is due to a tolerance effect is yet to be determined, and is one area which will continue to be investigated.

Other studies in these areas of crossover and drug combinations are in progress or contemplated. We also hope to combine EST or insulin therapy, to take maximum advantage of the intensified awareness and responsiveness shown when our children are treated with these two medications.

REFERENCES

1. Busch, A. K., and Johnson, W. C.: LSD-25 as an aid in psychotherapy, *Disease Nervous System* 11:241, 1950.
2. Dille, J. M., Moderator, Panel: The Hallucinogens, in Featherstone, R. M., and Simon, A. (eds.): *A Pharmacologic Approach to the Study of the Mind*, Charles C. Thomas, Springfield, Illinois, 1959, p. 229.
3. Abramson, H. A. (ed.): *The use of LSD in psychotherapy*, Transactions of a Conference on LSD-25, Josiah Macy, Jr. Foundation, New York, 1960.
4. Freedman, A. M., Ebin, E., and Wilson, E. A.: Autistic schizophrenic children, *Arch. of Gen. Psych.* 6(3):35, 1962.
5. Bender, L., Goldschmidt, L., and Siva Sankar, D. V.: Treatment of autistic schizophrenic children with LSD-25 and UML-491, in Wortis, J. (ed.): *Recent Advances in Biological Psychiatry*, Plenum Press, Inc., New York, 1962, p. 170.
6. Bierer, J., and Browne, I. W.: An experiment with a psychiatric night hospital, *Proc. Royal Soc. Med.* 53:930, 1960.
7. Hoch, P.: Experimental psychiatry, *Am. J. Psychiat.* 111(10):767, 1955.
8. Abramson, H. A., Jarvik, M. E., Corin, M. H., and Hirsch, M. W.: Lysergic acid diethylamide (LSD-25): XVII. Tolerance development and its relationship to a theory of psychosis, *J. Psychol.* 41:81, 1956.
9. Freedman, D. X., Aghajanian, G. K., Ornitz, A. M., and Rosner, B. S.: Patterns of tolerance to lysergic acid diethylamide and mescaline in rats, *Science* 127:1173, 1958.