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LSD - A TOTAL STUDY

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Physiological Investigations

Besides the illusinogenic effects of LSD, the physiological effects stand out uniquely. From the early times (1) LSD has been known to produce dose-dependent effects on body temperature, mydriasis, piloerection, tachycardia and an increase in leucocyte count. It also produces hyperglycemia which was inhibited (1) by typical ganglion blockers such as hexamethonium. The early studies of Sankar and his colleagues (2, 55) on the metabolic effects of LSD, BOL and other psychotropic agents have shown that LSD decreased food intake and urinary inorganic phosphate besides engendering several other effects. While reporting raised blood sugar level, Matsuoko (3) could not find increased oxygen consumption subsequent to the administration of LSD (see 19). The work of Weltman *et al.* (4) on the effects of mescaline in mice showed that there were significant decreases in total leucocytes and at autopsy marked and/or significant decreases in the weight of the thymus accompanied with increased weight of the adrenals. These authors have studied the effects of pro-

longed administration of psychoactive drugs. Buckley (5) postulated that LSD affected glucoreceptor mechanism of the ventromedial nucleus in the central hypothalamus resulting in a release of the ergotropic system. Some of the effects of LSD are tabulated below:

EFFECTS OF LSD AND BOL

EFFECT	LSD	BOL
Heart Rate	Bradycardia	No effect
Heat Production	No increase, primarily, secondarily rise	Unknown
Body Temperature		
Rabbit, cat & dog	Rise	Decrease (high dose)
Rat	Decrease Toxic doses - rise	
Adrenolytic Effect in guinea pig	Ca. 50 times weaker than ergotamine	Ca. 5 times weaker than ergotamine
Pupil (Eye)	Mydriasis	No effect
Blood Pressure in the cat	Decrease	Non-specific weak action
Blood Sugar	Increase	No change
Effect *in vivo* (Rabbit uterus & vagina	Contraction	No contraction
EEG (Rabbit)	Activation	No activation
Effect on		
Normal mice	Excitation	Sedation
Waltzing mice	Wlatzing inhibited	Waltzing inhibited
Amphetamine excitation in mice	Potentiation	Inhibition
Psychic Effects in Man	Pronounced	Not usually found

The hyperthermic effect of LSD was first reported by Hoffman (6) in the pigeon. He suggested the use of this method to assess synergists and antagonists of LSD using the rabbit rectal temperature. Nakajima *et al.* (7) showed that methamphetamine and iproniazid were synergistic; imipramine and ANP-246 and ANP-293 potentiated the effects of, and chlorpromazine antagonized the effects of LSD. The technique of the hyperthermic effects as measured by rabbit rectal temperature and open field behavior of rats were used (8) in a study of interaction of several tryptamine derivatives with LSD-25. Another interesting method of producing hyperthermia is through the use of the lipo-polysaccharide pyrogen from *Escherichia coli.* Rabbits with liver damaged by carbon tetrachloride did not respond with hyperthermia to the *E. coli* pyrogen (9) but did respond to LSD. This may denote a differential mechanism of pyrogenic action between lipo-polysaccharide and LSD.

Involvement of serotonin in the pyrogenic effects again was suggested by Ornesi (10). Pretreatment of rabbits with reserpine produced lowered levels of serotonin in the brain and also inhibited the pyrogenic action of typhoid vaccine. If the reserpinized animals were pretreated with JB-516 or the serotonin precursor (5-HTP), the pyrogenic action was manifested again. Increased brain serotonin turnover and hyperthermia were shown to be related. However, the increased turnover of brain serotonin may be secondary to the peripheral hyperthermic effects of psychedelic drugs as shown by Reid (11) in an analysis of the hyperthermic action of amphetamines. MAO inhibitors potentiate, whereas antagonists of catecholamine (guanethidine and tranquillizers) antagonize the effects of LSD (12). Here again reserpine was found to have dual effects, displaying a potentiation if given much earlier. These findings were interpreted to indicate that the pyrogenic action of LSD may be mediated by the liberation of catecholamines in the central nervous system. Similar pyrexic effects of LSD have been reported (13, 14). Friedman and Hirsch (14) reported

extreme hyperthermia(106.4°F. axillary) in a subject who had a history of intermittent use of LSD, cannabis, amphetamines and barbiturates for six months. Friedhoff and Abrams (15) showed that pretreatment with glutamine and glutamic acid significantly inhibited the pyrogenic effect of LSD in rabbits. It was shown earlier (see 15) that the hyperthermic action of LSD occurred in decorticate, but not decerebrate preparations, suggesting that the site of action of LSD is centrally mediated in the diencephalon.

EFFECTS OF LSD ON RESPIRATION AND OXYGEN CONSUMPTION

LSD was found to not have a significant effect on the respiratory activity of brain homogenates while chlorpromazine exerted a marked inhibition (16). However, this may depend on the particular area of the brain that was being studied (55). LSD injected at a level of 200 micrograms per kilogram into conscious cats (17) produced the usual reactions of hyper-excitability, hyper-activity, hyper-ventilation and maximal dilation of the pupils. In cats anesthetized with chloralose-urethane, LSD depressed respiration and circulation. LSD also caused bradycardia and reduced blood pressure in the anesthetized cat as opposed to the effects of LSD in conscious animals. It was concluded (17) that the sympathomimetic effects of LSD required intact function of higher cortical centers. Chlorpromazine antagonized these effects of LSD. BOL-148 was found (18) to block the accelerated ciliary beating in the mussel, *Mytilus edulis*.

Extensive work was done by Sankar and his associates (19) on the effects of LSD-25 on the oxygen uptake in the conscious rat. These studies determined the dependence of the action of LSD on endocrine function. In intact rats, LSD produced increased oxygen uptake. However, the surgical removal of the pituitary or of the thyroid (but not of the adrenals) produced a decrease in oxygen uptake on treatment of the animals with LSD. Hypothalamic lesions also produce decreased oxygen consumption. It was concluded

that the effects of LSD were mediated more through the thyrotropic action of the pituitary rather than through the thyroid itself. This hypothesis would also explain the several confusing observations on the potentiation of catecholamines by the thyroid.

The effects of LSD analogues on the blood-clotting process has been studied (20). UML and BOL decreased the maximum clot elasticity in both humans and rabbits. Anti-serotonin compounds produced a significant increase in clot accretion time in bleeding subjects with impaired blood clotting. The effects of LSD on the rat leucocyte and eosinophil count (21) suggest stimulation of adrenal function by LSD. Decreased oxygen consumption, metabolic rate, and leucocyte and eosinophil counts along with increased urinary output of 17-ketosteroids in the rat were reported by Weltman and Sackleer (22). As mentioned earlier, some of the results of this group may be due to the prolonged treatment technique employed. In the baboon, administration of LSD resulted (23) in the appearance of morphologically abnormal blast cells and increased leucocyte alkaline phosphatase activity; transient hypodiploidia was also observed (24), but no alterations in peroxidase activity.

THE EFFECTS OF HALLUCINOGENIC DRUGS ON BLOOD PRESSURE AND VASCULAR SYSTEM

The effects of LSD on blood pressure are probably complicated by its *in situ* action on the blood vessels, cardiac and other muscular systems, lungs, respiration and its effects on the central nervous system and on the carotid sinus. This is further complicated by the experimental techniques adopted, the route of administration of LSD and the species used.

Milani and Segre (25) reported in 1954 that dihydroergotamine produced an inhibition of the carotid sinus reflex and there was neither an immediate nor delayed hypotensive action. Iontophoresis of LSD, applied to the skin of humans, suggested the relation of LSD to serotonin (26).

Serotonin (5-hydroxytryptamine) has been shown earlier to cause contraction of rat uterus and LSD antagonized the effects of serotonin. Apparently, serotonin may be involved in preserving the integrity of microcirculation. Ginzel (27) reported that LSD administered by injection into the lateral ventricles of the brain of anesthetized cats did not significantly reduce blood pressure. However, LSD did reduce spontaneous respiration. LSD administered through the cerebral spinal fluid may inhibit the reflexes from the chemoreceptors of the carotid sinus.

The antagonistic effects of LSD and BOL on the pressor and depressor responses to serotonin was reported by Salmoiraghi *et al.* (28). LSD poorly antagonized the vasoconstrictor response to serotonin in a perfused extremity. Further, LSD, like ergotamine, did not prevent the chemoreceptor stimulating action of serotonin in dogs. In anesthetized rats LSD, administered by quick injection, caused a short reduction in arterial pressure. The species differences have been shown in this study. Further, inactivation of the sympathetic nervous system enhanced the pressor response to LSD and diminished the depressor activity of LSD in rats and in cats. Chronic oral administration had no effect on the arterial pressures of hypertensive dogs.

The work of Sokoloff *et al.* (29,30) on the effects of LSD on metabolism and cerebral circulation is of interest. In spite of the manifestation of the mental and psychological effects of LSD in humans, there were no concomitant changes in cerebral blood flow, vascular resistance, oxygen or glucose utilization, or respiratory quotient. There was a small increase in mean arterial blood pressure and a moderate increase in arterial hemoglobin concentrations. These authors concluded that LSD did not produce significant changes in the several physiological functions or in the chemical constituents of blood. Mescaline, like epinephrine, accelerated cerebral circulation and metabolism. LSD did not have this effect. Chlorpromazine, promazine, methylphenidate or reserpine also did not affect cerebral hemodynamics. Hassler (31) could not find any changes in

erythrocyte count in rabbits or mice administered LSD by the intravenous route. The spleen and the liver, however, showed an increased weight.

LSD and other hallucinogens like bufotenine, psilocybin, and mescaline produced contractions of isolated strips of human umbilical veins and especially umbilical arteries (32). Cinanserin, in small doses, antagonized these effects, while atropine sulphate and tripelennamine did not. Inasmuch as atropine and tripelennamine did antagonize the effects of epinephrine, histamine and acetylcholine, but not of serotonin, it was inferred that the hallucinogens produced the vascular contractions acting more directly through serotonergic receptors.

Blood pressure in human subjects was increased slightly when LSD was administered subcutaneously at a level of 100 micrograms (33). There was also increased esterification of xylene by sera and decreased esterification by plasma of subjects receiving LSD (33). This difference is hard to explain inasmuch as the major difference between serum and plasma is the lack of the clot factors in serum preparation.

The importance between the tissue preparations was shown by Borgstedt *et al.* (34). Using dog ureteral segments, serotonin failed to depress activity of segments stimulated by histamine or by LSD. The effects of LSD were not blocked by serotonin, atropine or diphenhydramine. This observation is of interest as LSD is presumed to be both anti-serotonin and anti-histamine in several of its actions. In an interesting experimental technique, Balint (35) monitored the blood pressure of cats injected with several psychoactive drugs. The effects of these drugs on the changes elicited by exposing these cats to a dog or a mouse or the application of capsaicin, were studied. In the untreated cat, there was an increased blood pressure. Amphetamine and LSD inhibited such increases in blood pressure and decreased the blepharospasmic responses to capsaicin. Amphetamine-treated cats did not react to mice and showed no fear of dogs.

Serotonin infused into the brachial artery in man produced vasodilation in muscle (36) and vasoconstriction in skin. UML administered similarly antagonized the vasoconstrictive effects of serotonin. Pentobarbital-anesthetized dogs were bilaterally vagotomized and artificially ventilated in a study on the relation of the effects of LSD and morphine (37). The drugs were administered through an intraventricular cannula in the left lateral cerebral ventricle. Under these conditions, LSD produced a drop in blood pressure, while pretreatment with morphine blocked the effect of LSD-25. The effects of morphine disappeared within twenty minutes, and morphine itself did not affect blood pressure. These studies may indicate short acting competition for binding sites among the several psychotropic and other drugs. Competition in such cases may not be directly related to the mechanism of action of the drug.

EFFECTS OF LSD ON MUSCULAR ACTIVITY AND TREMOR

Uyeno (38) found that small doses (16 micrograms per kilogram) of LSD did not affect the mean running time of rats. However, on introduction of a novel stimulus, the running time of the treated rats was significantly longer. This may not be an effect on the muscular system as much as on ability to work around a new hurdle. Similarly, the nest-building behavior (39) of mice may not be related directly to the impaired motor activities produced by hallucinogenic agents.

One of the complications in drug abuse has been shown to be (40) *myositis ossificans*, even though no direct causative action was shown. The injection of the abused drugs might have produced defects in motions of the arm at the right elbow and in the related hand-wrist movements. The effects of LSD on insects have been considered in another part of this book. BOL when injected into late instar wax moth larvae (41) produced a reversible body-wall paralysis, but did not affect the electrical activity of nerve and muscle.

The swimming response of rats was studied by Uyeno (42) to evaluate the effects of hallucinogenic drugs. The

effect of LSD was maximum twenty minutes after administration while the peak time for BOL was forty minutes. The hallucinogenic amphetamines and LSD were significantly more effective in increasing the starting latency and swimming time. While low doses of LSD increased the swimming time, Wilbur and Burke (43) found that high doses depressed it. The stimulating effect of LSD was obscured by temperature and by crowding.

Ahmed and Taylor (44) studied drug-induced tremor in mice using an oscillograph, a phonograph and a camera for permanent records. LSD was found to reduce drug-induced tremor in mice (45). The effect of LSD was most pronounced when the tremors were produced by treatment of the mice with iproniazid and serotonin.

Garrett (46) found that both epinephrine and norepinephrine stimulated human uterus to contract *in vitro*. However, *in vivo*, epinephrine inhibited while norepinephrine stimulated the uterine contractions. Dihydroergotamine did not modify *in vivo* the effects of epinephrine or norepinephrine, when given to healthy humans in late pregnancy or labor. It was concluded that the effect of the ergot alkaloid may be due to its interaction with oxytocin rather than mediated through the sympathetic system. Garrett also reported (47) that dihydroergotamine blocked the stimulating action of epinephrine or norepinephrine on the spontaneous contractions of the human myometrium obtained at the various stages of the menstrual cycle, after menopause, during pregnancy or at parturition. Holzbauer and Vogt (48) showed that LSD and dihydroergotamine antagonized the inhibitory action of epinephrine on rat uterine contraction induced by carbachol. Serotonin caused contractions of the annular muscle of the human ileum whereas it relaxed the colon muscle (49). LSD blocked the contractile effects of serotonin.

The effects of several drugs including LSD on perfused human placenta was studied by Ward and Gautieri (50). The compounds which displayed an ability to antagonize the vasoconstrictor action of serotonin were (in decreasing order) as follows: cyproheptadine, LSD, diphenhydramine,

chlorpromazine, promethazine etc. Cyproheptadine displayed the shortest duration of action while chlorpromazine and diphenhydramine showed the longest duration of action, It may be pointed out that the occurrence of LSD in this series of compounds may indicate not only its anti-serotonin action, but also its anti-histaminic action. LSD was also shown (51) to contract isolated human uterine arteries. UML antagonized the responses to serotonin in this study while tripelennamine antagonized the effects of histamine.

THE EFFECT OF LSD ON GASTROINTESTINAL ACTIVITIES

Thompson (56) has reviewed extensively the involvement of serotonin in the gastrointestinal tract. Serotonin (52) increased the longitudinal muscle contractions of the guinea pig intestine in response to acetylcholine while it first facilitated and then blocked the ganglionic action of nicotine. The reflex arc was blocked by several drugs including LSD and BOL. The latter drug, though non-hallucinogenic, shares the properties of LSD on uterine muscular contraction. LSD has been shown to possess anti-emetic activity (53) in dogs and pigeons. Ergotine (54) increased peptic secretion in man.

REFERENCES

1. Rothlin, E., Cerletti, A., Konzett, H., Schalch, W.R. and Taeschler, M., *Experientia [Basel] 12,* 154 (1956).
2. Sankar, D.V.Siva, Gold, E. and Sankar D.B. *Recent Adv. Biol. Psychiat.* Vol. IV, Wortis, J., (Ed.) 247 (1962).
3. Matsuoko, M., *Folia Pharmacologica Japonica [Kyoto] 60,* 88 (1964).
4. Weltman, A.S., Sackler, A.M., Gennis, J., Steinglass, P. and Schwarts, R., *Fed. Proc. 27,* 220 (1968).
5. Buckley, R.E., *Schizophrenia 1,* 172 (1969).
6. Hoffman, R.A., *Amer. J. Physiol. 195,* 751 (1958).
7. Nakajima, H., Grandjean, J.L. and Kurihara, M., *Proc. Meet. Coll. Intern. Meuro-Psycholpharmacol., 3rd, Munich, 1962,* 494 (1964).

8. Brimblecombe, R.W., *Int. J. Neuropharmacol. 6,* 423 (1967).
9. Venulet, J. and Desperak-Naciazek, A., *J. Pharm. Pharmacol. 18,* 38 (1966).
10. Ornesi, A., *Atti. Acad. Med. Lombarda 17,* 156 (1962).
11. Reid, W.D., *Fed. Proc. 29,* 747 (1970).
12. Bapat, S.K., Chandra, V., Jauhari, A.C., Ansari, K.U., and Dhawan, B.N., *Ind. J. Med. Res. 58,* 622 (1970).
13. Nakaura, S., Tanaka, S., Kawashima, K., Nagio, S., Kawamua, T, Omori, Y. and Nakao, K., *Folia Pharmacologica. Japonica 67,* 235 (1971).
14. Friedman, S.A., and Hirsch, S.E., *J. Amer. Med. Assoc. 127,* 1549 (1971).
15. Friedhoff, A.J. and Abrams, B., *J. Clin. Exper. Psychopathol. XXI* 7 (1960).
16. Starbuck, W.C., and Heim, H.C., *J. Amer. Pharmaceut. Assn. 48,* 251 (1959).
17. Tauberger, G., and Klimmer, O.R., *Arzneim-Forsch. 18,* 1489 (1968).
18. Paparo,A.A., and Aiello, E., *Comp. Gen. Pharmacol. 1,* 241, (1970).
19. Sankar, D.V.Siva, *Res. Commun. Chem. Pathol. Pharmacol. 3,* 321 (1972).
20. Badya, C., Bielski, J., Chodera, A. and Owczarek, L., *Acta Physiol. Polon. 14,* 599 (1963).
21. Kulbertus, H., *Nature 199,* 1194 (1963).
22. Weltman, A.S. and Sackleer, A.M., *J. Endocrinol. 34,* 81 (1966).
23. Ruffie, J., Colombies, P. and Ducos, J., *Compt. Rend. Acad. Sci., 270,* 644 (1970).
24. Ruffie, J., Colombies, P. and Grozdea, J., *Bull. Acad. Nat. Med.* [*Paris*] *155,* 180 (1971).
25. Milani, M. and Segre, G., *Boll. Soc. Ital. Biol. Sper. 30,* 949 (1954).
26. Blair, E.L., Wakefield, M., Ingram, G.I.C. and Armitage, P., *Nature 176,* 563 (1955).

27. Ginzel,K.H., *Naunyn-Schmiedeberg's Arch. Exptl. Pharmakol. 228,* 149 (1956).

28. Salmoiraghi, G.C., McCubbin, J.W. and Page, I.H., *J. Pharmacol. Exp. Therap. 119,* 240 (1957).

29. Sokoloff, L., Perlin, S., Kornetsky, C., and Kety, S.S., *Ann. N.Y. Acad. Sci. 66,* 468 (1957).

30. Sokoloff, L., *Pharmacol. Rev. 11,* (1959).

31. Hassler, O., *Psychopharmacologia,6,* 311 (1964).

32. Dyer, D.C., and Grant, D.W., *J. Pharmacol. Exp. Therap. 184,* 366 (1973).

33. Kuhn, E., and Vitek, V., Vojtechnovsky, M., *Activitas Nervosa Superior* [*Prague*] *3,* 212 (1961).

34. Borgstedt, H.H., Emmel, V.M., and Benjamin, J.A., *Arch. Internat. Pharmacodyn. Therapie 162,* 345 (1966).

35. Balint, G.A., *Isr. J. Med. Sci. 8,* 556 (1972).

36. Walsh, J.A., *Brit. J. Pharmacol. Chemother. 30,* 518 (1967).

37. Gupta, G.P., Dhawan, K.N., and Dhawan, B.N., *Japanese J. Pharmacol.* [*Kyoto*] *18,* 255 (1968).

38. Uyeno, E.T., *Psychonomic Sci. 18,* 52 (1970).

39. Schneider, C.W., and Chenoweth, M.B., *Nature 225,* 1262 (1970).

40. Deutsch, I., *J. Amer. Med. Assocn. 216,* 1035 (1971).

41. Asher, W.C., *J. Insect. Physiol. 17,* 1801 (1971).

42. Uyeno, E.T., *J. Pharmacol. Exp. Therap. 159,* 216 (1968)

43. Wilbur, C.G. and Burke, J.A., *Life Sci. 2,* 134 (1963).

44. Ahmed, A. and Taylor, N.R.W., *Brit. J. Pharmacol. Chemotherap. 14,* 350 (1959).

45. Yen, H.C.Y. and Day, C.A., *Arch. Internat. Pharmacodyn. Therap. 155,* 69 (1965).

46. Garrett, W.J., *Lancet 266,* 1060 (1954).

47. Garrett, W.J., *Brit. J. Pharmacol. 10,* 39 (1955).

48. Holzbauer, M. and Vogt, M., *Brit. J. Pharmacol. Chemotherap. 10,* 186 (1955).

49. Fishlock, D.J., *J. Physiol. 170,* 11p (1964).

50. Ward, C.O. and Gautieri, R.F., *J. Pharm. Sci. 55,* 474 (1966).

51. Dyer, D.C. and Gough, E.D., *Amer. J. Obstet. Gynecol. 111,* 820 (1971).

52. Bulbring, E. and Crema, A., *Brit. J. Pharmacol. Chemotherap. 13,* 444 (1958).

53. Bhaven, B.N. and Gupta, G.P., *Indian J. Physiol. Pharmacol. 6,* 25 (1962).

54. Wava, G. and DeBac, C., *Arch. "E Maragliano" Patol. e Clin. 7,* 691 (1952); *Excerpta Med., Sect. II, 7,* 86 (1954).

55. Sankar, D.V.Siva and Bender, L., *Recent Adv. Biol. Psychiat* (Ed.) J. Wortis, vol. 2, Plenum Press, N.Y. (1960).

56. Thompson, J.H. *Res. Commun. Chem. Pathol. Pharmacol. 2,* 687 (1971).

GENETIC ASPECTS

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BIOCHEMICAL EFFECTS OF LSD

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EFFECTS ON ENDOCRINE SYSTEM HORMONES, AND AMINES

MEDICAL AND OTHER POSSIBLE USES FOR LSD

Hallucinogenic drugs have been tested widely for their usefulness in psychotherapy, in rehabilitation of alcoholics, pharmacotherapy in schizophrenia and in autism, and in enhancing self-realization in cancer patients, in hormonal therapy, etc. It has been even suggested as an agent in chemical warfare. One only has to thank God for no threats on society that LSD would be put in drinking water of a town unless some demands were met!

Busch and Johnson (1) were among the earliest to suggest the use of LSD in aiding psychotherapy. Even though some of these claims have been seriously challenged, Lewis and Sloane (2) have concluded that LSD provided a useful aid to psychotherapeutic technique. Katzenelbogen and Fang (3) used LSD up to 50 micrograms to facilitate interviews with schizophrenic subjects and to help ventilate emotion. Abramson and his associates (4, 5, 6, 7, 8) have been among the earliest to study the use of several

lysergates in psychotherapy. In small doses LSD was found to be pharmacologically safe, maintaining the patient in a conscious and cooperative state. LSD facilitated ego enhancement leading to reconstruction of the ego and reinforcement of its integrative functions. The ego enhancement was accompanied with a mobilization of the psychodynamic vectors and helped group therapy also. Analysis was expedited by LSD. Abramson has often used 20-40 micrograms of LSD and rarely high doses.

Grof (9) has more recently reviewed the uses of LSD in various forms of psychotherapy, psycholytic therapy, psychedelic therapy, symbolysis, hebesynthesis, lysergic analysis, oneiroanalysis, hypnodelic therapy, transintegrative therapy, etc. In psycholytic therapy 100-500 micrograms of LSD are used in the framework of dynamic psychotherapy. In psychedelic therapy emphasis is placed on the mystic and transcendental aspects using a massive dose of 400-2,000 micrograms. The British have used LSD to aid analysis. In hypnodelic therapy, both hypnotherapy and psychedelic therapy are used. Pahnke, *et al.* (10) have made use of psychedelic psychotherapy, especially psychedelic-peak psychotherapy with cancer patients. They list the five major kinds of potential psychedelic drug experiences to be: 1) psychotic, 2) cognitive, 3) esthetic, 4) psychodynamic, and 5)psychedelic peak, or mystical, etc. Under the fifth psychedelic-mystical experience, there are several positive attributes which may contribute to ego transcendence working for the benefit of the "un-normal" subject.

Unger (11) collected a bibliography on LSD and psychotherapy in 1974. He pointed out the conclusions of Sandison on the "utmost value" (of LSD) in psychotherapy. Abramson (12, 13) has cited several clinical cases that were benefited by psychotherapeutic support with LSD. These cases included a woman who was afraid of becoming a homosexual, a father in conflict during the oedipal phase of his son, and patients with intractable eczema and asthma.

Eisner and Cohen (14) used LSD on patients with problems ranging from depressive states to borderline

schizophrenia. Successful results in behavioral adaptation were noted in 16 out of the 22 cases. Frederking (15) found that LSD and mescaline produced a psychocathartic effect and shortened the course of therapy, reactivated a stalled treatment of neurosis, and helped break down affect or memory blocks. The monoethylamide analog of LSD was less hallucinogenic than LSD (16). Subjective symptomatology due to LSD was much richer and more localized in the hysterical patients. LSD allowed (17) psychiatric observations of great diversity, serving as an analyzer of personality. It not only revealed unsuspected conditions, but made possible contact where every other method failed. Chandler and Hartman (18) found that LSD therapy showed greater depth and acceleration of drugless psychotherapy. However, one of their suicidal patients committed suicide following one LSD treatment.

There have been several reports where psychotherapy was expedited by LSD. Proper selection of cases should be based (19) on the patient's motivation, ego strength, intelligence and possible contraindications of risk of suicide, homicide; and acute psychic reactions with flashbacks should be seriously considered. Successful treatment is possible (20) in cases of severe character neuroses and even in chronic neuroses, psychopathic disorders, etc. Special care must be paid to the setting, the training of the personnel and indications of possible accidental, unwanted reactions and prognostic indicators.

Butterworth (21) has treated many patients with LSD on an office basis. Ditman, *et al.* (22) studied the nature and frequency of claims of therapeutic value following LSD. They found that approximately two-thirds of the patients reported some degree of benefit, suggesting that LSD could be psychotherapeutic in itself. Analysis of long-term studies (23) showed that LSD was of definite psychotherapeutic use and was a very powerful tool (24) in speeding up movement and overcoming resistances in psychotherapy. Terrill (24) concluded that LSD did not show promise as a diagnostic tool. In a Canadian study, Baker (25) found that 100-150 patients with non-psychotic functional psychiatric disorders

were benefited by LSD psychotherapy. Four patients became psychotic and required electroconvulsive therapy. However, none were permanently harmed. Regression to early infancy (26) may also be involved in the psychotherapeutic effects of LSD.

Terrill, *et al.* (27) reported recovery rates as high as 70% with LSD psychotherapy of alcoholics. LSD may provide a genuine transcendental or mystic experience instead of the spurious one which the alcoholic has been seeking. The regression to early infancy is apparently incompatible with the transcendental reaction and may depend in part on the subject, the guiding hand of the therapist and the setting. Greater awareness of ultimate reality accompanied with improvement in the MMPI profile ratings was reported by Savage, *et al.* (28, 29). Psychedelic experience is neither a replacement for, nor an adjuvant to traditional modes of therapy. It adds a new and perhaps neglected dimension to therapy. Psychological tests like MMPI, ICL, Value-Belief Q-Sort, Behavior Change Interviews, and psychotherapeutic evaluations seem to indicate (30) that psychedelic therapy produced a shift towards more ego-syntonic behavior.

Multi-therapist interviews were preferable in some cases (31) to the single-therapist situation. In the former setting, one therapist may be selected as a parent figure or protector; another as the enemy, etc., under the influence of LSD. This would give rise to a better acting out and better ventilation of the psychopathologic material.

The claims of damage from LSD have not always been sustained, especially under psychotherapeutic conditions. Spencer (33) called the abrupt withdrawal of LSD by the Sandoz Company without prior notification and without regard to the patients, as unethical. Similarly, the use of LSD in ambulant, analytical psychotherapy was not found to produce any toxic damage if applied appropriately (32). The interrelation between hypnotherapy and psychotherapy has been pointed out by Solursh and Rae (34). *Medical World News* (35) reported in 1967 that while the therapeutic use of LSD in USA has fallen into disfavor, the drug was gaining acceptance in the treatment of alcoholics and depressives in Europe, especially in Eastern Europe.

A controlled study (35) at the V.A. Hospital in Lexington indicated that chronic alcoholics given LSD therapy had more days of total abstinence from alcohol, more days of gainful employment, fewer arrests, and fewer instances of delirium tremens. Patients with a history of sexual exhibitionism seemed to have profited (36) from psychotherapy aided by LSD. Cutner (37) suggested that LSD could be used in supervised psychotherapy as a possible "mediator" between the emotional needs of the drug addict and the societal need for control. More study in the areas on the use of LSD in psychotherapy was suggested (38) in order to delineate systematically and quantitatively such effects. Kurland, *et al.* (39) who have used LSD in psychedelic therapy of alcoholics, neurotics, terminal cancer patients, and others under supervised settings, concluded that the hazards of psychedelic therapy did not appear either special or unusual.

Kast (40) found that LSD had an analgesic action in a series of 128 patients. He found the drug relatively safe in spite of some occasional undesirable pharmacological effects. His subjects were preterminal cancer patients suffering with metastases. Thirty per cent of his patients said they would be unwilling to repeat the administration of LSD. The administration of LSD effected less disturbed sleep in Kast's patients. A detailed account of psychedelic therapy was presented by Unger (41).

Hypnodelic therapy was found appropriate by Lyle (42) for the treatment of sociopathic offenders. Ditman (43) reviewed the value of LSD both in psycholytic and psychedelic therapies. Psycholytic therapy involves a continuing series of LSD sessions over a period of months, whereas psychedelic therapy consists of the administration of a single, massive dose, 200-1500 micrograms, of LSD in one protracted session. Unsupervised, non-medical settings could lead to adverse experiences. Psychedelic therapy emphasizes more on the transcendental state of consciousness (44). Kurland (45), while pointing out the useful nature of LSD in the alcoholics, neurotics, drug addicts, and terminal cancer patients, emphasized the need for future research to

produce new drugs of valuable psycholytic, psychedelic, psychotropic potencies of better therapeutic use.

Savage (46) found LSD of definite therapeutic value even though work with LSD was more difficult than without the drug. LSD sets in motion (47) certain processes within the patients which are out of the therapist's and the patient's control. It may produce solicitude, anxiety, and helplessness in the therapist, emphasizing a need for a well-trained therapist and a well-supervised setting. Fisher (48) suggested a dose of 300-500 micrograms of LSD with premedication of 10-20 milligrams Librium, 5 milligram of methedrine and 6-16 milligrams of psilocybin for an initial psychotherapeutic experience. The administration of 25-100 milligrams of chlorpromazine may be used to terminate an LSD session. In the case of afraid, anxious or frightened subjects, low doses of LSD (25-75 micrograms) should be used. Psilocybin was not recommended for an initial psychedelic experience while mescaline or mescaline and LSD together could be used. The dose of mescaline when used alone could be 500-800 milligrams whereas in combination 200-400 mg mescaline with 100-300 micrograms of LSD were recommended. The present author feels that these doses are very high and should certainly be used only by therapists highly experienced in the use of psychedelic drugs. The dose should also be variable depending on the state of the patient. On the other hand, the use of subthreshhold doses could only provide little therapeutic opportunity and more tolerance. The useful nature of LSD in psychotherapy has been repeatedly asserted (49 and 50).

Mogar (50) quoted the research of Mackinnon and his associates, indicating that a truly creative person is distinguished from the non-creative individual by his capacity for "transliminal experiences". The "transliminal experience" is characterized by an illuminating flash of insight occurring at a critical threshold of the conscious-unconscious continuum. This "transliminal experience" could resemble the peak experience in psychedelic therapy. Bieberman (51) pointed out "session games people play". She pointed out some of the preferred group settings, etc. for the sessions. The patterns of conduct to be avoided (51) are:

entering the experience for any trivial purpose without adequate planning, assuming an attitude of arrogance toward non-users, panic, confusion, and pleas or demands to end the experience immediately, evasion of responsibility during the session, leaving the group before the effects wore off, attempts to import the experiences of the session before it is over, etc.

Caldwell (52) has discussed in detail LSD psychotherapy. She considered the nature of the LSD session, the effects that are relevant to the therapy, the risks and advantages of psychedelics in therapy. Speaking in terms of psychological orientation, she pointed out that within our own consciousness, there is a memory, waiting to be recalled, of every movement, feeling and desire in our lives. This implies that everything survives in a way more complete than just intellectually. The psychedelic experience heightens this recall, and if handled properly, could pass through beneficial channels leading to psychotherapy and rehabilitation. The further a patient regresses, the more insubstantial does his memory become. As therapy progresses, the patient's personality and his grasp of the facts of his childhood, his identity, etc. become sharper, more specific, better controlled and even more mundane. The knowledge of the self, as revealed by the LSD experience, if properly channeled, buttressed, and built, could lead to a helpful alteration or even reconstruction of the psychobiology of the patient.

Cohen (53) considered the pros and cons of psychotherapy with LSD. He listed seventeen desirable aims in terms of personality structure. He put in a better perspective the emotional claims both denying any usefulness for LSD and miraculous, evangelical cures by the drug. McGlothlin and Arnold (54) made a ten-year, follow-up study of the medical use of LSD. They considered both experimental and psychotherapeutic settings for the use of the drug in the period 1955-61. Surveying 247 persons, they found the usual experimental dose to range from 50-1,000 micrograms with a median of 125 micrograms. In the psychotherapeutic administration, the range was 25-700 micrograms with a

median of 125 micrograms. They could not find any measureable lasting changes in personality,belief,value,attitude, or behavior in this relatively unselected, adult population. Further, the nature of the effect of LSD use was such that the drug became less attractive with continued use, and in the long term was almost always self-limiting.

It may be pointed out that after 1964 LSD has certainly fallen into the category of a gruesome, awful drug. This is perhaps correctly so, but the present author bemoans the lack of better funded governmental research on psychotropic drugs. Commercial firms in this area would conduct research, invest in economic areas, leaving the basic research out. Further, the accepted use, marketability and sales of a drug depend not only on its basic usefulness, but to a larger extent, on the merchandising and marketing practices of the drug industry. This leads to the conclusion that the better drug may not always have better sales!

The long list of factors cited above on the useful nature of LSD could be partly counterbalanced with a list of publications that point out the relative ineffectiveness and the considerable danger involved in the psychotherapeutic use of LSD. Hoch (55) was among the early research workers on the use of LSD and concluded that psychedelic drugs aggravate schizophrenic symptoms and questioned the claims made for LSD early in 1957.

Faillace (56) reviewed the clinical use of psychotomimetic drugs. Hollister, *et al.* (57) could not conclude definitely that the psychedelic drugs facilitated psychotherapy. *Medical World News* (58) reported the possibility or irreversible risk of delirium and depersonalization in the use of LSD.

Leuner (59) reported in 1968 that wisdom counselled against the use of LSD in view of the multitude of increasing reports on general abuse, etc. The shorter-acting hallucinogen, psilocybin, or its derivatives, CEY-19 and CZ-74, could be safer substitutes in psycholytic therapy. Caldwell (60) stated a 65% recovery or improvement in 110 patients by the use of LSD in 1963.

UML-491 or Methysergide (Sansert) is used in the treatment of migraine headache. However, vascular insuffi-

ciency and retro-peritoneal and pleuropulmonary fibrosis are some of the adverse somatic reactions resulting from the use of UML. The psychiatric adverse reactions to a single exposure of just one 2 milligram tablet of UML consisted of (61) extreme agitation, compulsive urges for abnormal, bizarre behavior, loss of self-control, depression etc.

Vangaard (62) summarized his findings on treatment of 22 patients. He concluded that LSD treatment was contraindicated in patients in whom the habitual personality and the psychopathic state revealed signs of ego-weakness and possibilities of psychopathic, schizophrenic-form psychoses. But these are exactly the areas where other workers have found LSD useful.

Considerable work has been done on the use of LSD in the treatment of schizophrenia. Sandison, *et al.* (63) found that LSD disturbed the unconscious so that repressed memories are relived;e.g., clarity with a change to an infantile body image. Schizophrenics and control subjects could react differently to LSD(64). Using a low dose, Sloane and Lovett-Doust(64) found limited changes due to LSD in a total of thirty subjects. Cholden, *et al.* (65) also could not detect consistent beneficial effects or overt reactions to LSD in chronic schizophrenics.

Distinction should be made of the schizophrenic as opposed to the psychoneurotic subject in these cases. For example, Martin (66) found that 45 out of 50 chronic psychoneurotics were benefited by LSD treatment. Least benefit was obtained in cases of chronic tension. Abramson, *et al.* (67) explored the stablemate concept of therapy. The ratio of the patient interaction:stablemate interaction was higher for the LSD group. The schizophrenic patient showed more change in behavior than did the normal stablemate.

Shagass and Bittle (68, 69) found that the patients who respond to LSD (LSD responders) showed considerably more improvement. The responder group consisted mostly of patients with diagnoses of psychopathic personality. This

work was done on a small number of cases and pointed out that patients treated with LSD showed greater improvement than those in whom LSD was not used. LSD has been shown to be beneficial (70) in the treatment of exhibitionism and termination of hallucination in schizophrenics (71). Kato (71) found dynamic correlation between monologue, auditory hallucination and automovement. LSD replaced in these patients, delusions of persecution by feelings of protection. De Ropp (72) reviewed therapeutic use of LSD and other drugs.

Pfeiffer *et al.* (73) studied the effects of LSD on ten chronic male schizophrenic patients. Instead of a decrease in variability of the EEG observed in normal subjects, a significant increase occurred reaching its peak in ninety minutes. Kornetsky and Mirsky (74) did not find an attenuated response with centrally acting drugs in schizophrenics as opposed to previous studies which showed greater resistance to drugs in schizophrenics. The schizophrenic syndrome includes a state of chronic hyperarousal and perhaps compensatory mechanisms. Smythies (75) reported that schizophrenics were less reactive to histamine than normals. The recall of LSD used for therapeutic purposes was criticized by Brown (76).

Considering the above literature, psychedelic therapy with a peak experience should be further investigated in chronic schizophrenics, especially the "burnt-out, backward" cases which are difficult to be returned to the community.

LSD has been used as an adjunct to psychotherapy in children (77). The doses used here were 1-2 micrograms per kilogram, larger doses being as high as 300 micrograms. This is certainly a high dose approaching pharmacotherapeutic levels. Good results were obtained with LSD as shown by improvement of the language, greater naturalness in playing, improved affect, disappearance of autoaggression, hallucinations, sleep and behavior disorders, accompanied with an improvement of learning abilities. Many of these workers have found that LSD is well tolerated by children.

Pharmacotherapy with LSD in children, either alone or

in combination with other drugs and UML, has also been reported to yield therapeutic results (78). Bender and her group (79) were among the earliest to test the efficacy of psychedelic pharmacotherapy in schizophrenic children, especially autistic children. These children tolerated LSD well for a period of a few years even at daily doses of 100-150 micrograms of pure LSD. Improvements in terms of a happy mood, less hostility and positive affect, less stereotyped whirling and rhythmic behavior, etc. were found. Alterations in neurological signs in the perceptual motor function, body image function, etc. were also noted.

Abramson (81) and his associates tested LSD on children. They could not produce positive results in one case (80), but concluded that (81) comparatively large doses of LSD and UML may be safely administered to autistic children without apparent brain damage, but with improvement. LSD therapy was reported (82) to be useful in the treatment of severely disturbed children who cannot speak, cannot relate to other children and make continuous rhythmic movements. Simmons (83, 84) reported that LSD could be profitably used as a therapeutic adjunct, especially in autistic children, altering the "autistic barrier".

Under the effect of LSD, the formerly lifeless drawings of an autistic schizophrenic patient (85) assumed violent color, realism and a sense of motion. Alcoholism caused a blurring of the picture while psilocybin administration produced indications of an intellectual approach in the picture drawing. Psilocybin apparently helped the patient verbalize. Fisher (86) administered LSD to autistic and schizophrenic children and found that LSD helped the individual patient to reexperience himself in a far less distorted way and to reevaluate the worthiness of his essential self. While there are more positive reports on the beneficial nature of LSD, there have always been several occasions where negative results were obtained. However, psychedelics seem to be not without some value in the treatment of autism. More research should be carried out on psychedelic therapy in cases of infantile autism and mental retardation. Training and rehabilitation of the patient should be planned

in advance to take advantage of the three or six months of psychedelic therapy before the patient begins to tolerate the drugs.

The induction of a psychotic state by LSD in the patient to be treated is equivalent to induction of natural schizophrenia. The LSD-psychosis is more an acute toxic chemical reaction characterized with higher temperature, hallucinations, and may or may not be attendent with the psychopathology, etc. of natural schizophrenia. The latter is characterized with auditory hallucinations, psychopathology, developmental lags and an array of compensations, decompensations, rationalizations, defense, anxiety, fear, insecurity, etc. which may be the result of a genetically predisposed nature, subject to the crises and vulnerability of life experiences. The several factors involved in natural schizophrenia have been considered in a chapter on the multithemic etiology of schizophrenia in a book on "*Schizophrenia - Current Concepts and Research*" by Sankar.

Bleuler (87) pointed out that medico-historical facts opposed identification of LSD intoxification with schizophrenia. The comparison between the two is valid within very narrow limits (88). Hollister (89) compared the clinical syndromes from psychotomimetic drugs with schizophrenic reactions. Somatic and perceptual effects attended with few psychopathologic symptoms characterized the effects of LSD. Disorientation, distorted thinking, paranoid ideation, auditory, gustatory,olfactory or tactile hallucinations were uncommon with LSD. JB-329 yielded a characteristic picture of toxic delirium.

There have been several reports (90) where subjects with a history of chronic LSD use, have been hospitalized. These patients differed from others in the same age group in a history of drug abuse, chaotic sexual behavior, responding to intrafamilial conflict with antisocial and dissocial behavior and poor work histories. In Hensala's group (90) of hospitalized LSD-users, there were no professionals who have been hospitalized except one teacher. The problem of pinpointing the effects of LSD resulting in schizophrenia

requiring hospitalization is complicated by the endogenous psychopathology, multiple-drug use, and chaotic life style of the patient.

The therapeutic aspects of other lysergates and psychedelics has received some, but inadequate, attention. Turner and Merlis (91) used the non-hallucinogenic analog, BOL-148, in the treatment of chronic schizophrenic subjects. No evident effect on the psychosis could be found, perhaps suggesting that the psychotomimetic activity is part of the therapeutic picture. UML has been used not only in migraine, but also on adult and childhood psychotics. However, even though UML was not found to alter the condition of eighteen chronic schizophrenic patients by Marie, *et al.* (92), such a treatment of hospitalized, disturbed children was reported to be beneficial by Bender, *et al.* (93).

Dimethyltryptamine was also tested on twenty-four female patients (94). This treatment either delayed or decreased the vegetative symptoms in schizophrenics. Administration of LSD (95) reversed the akinetic-abulic syndrome induced by prolonged treatment of patients with chlorpromazine and reserpine.

LSD, combined with apomorphine was of diagnostic and therapeutic value (96) in alcoholism. Itil (97) used a combination of LSD and Ditran in order to determine whether the prognosis of chronic schizophrenic patients could be influenced by altering "stable" hypersynchronous EEG patterns. They found that EEG desynchronization was accompanied by activation of psychic symptomalogy and rendered the patients more responsive to usual psychotropic drugs. Similar treatment of schizophrenia with the tranquillizers after activation of the psychic systems by psychotomimetics was studied by Shirvaikar and Kelkar (98). LSD was given daily in the morning followed by thioridazine in three doses during the rest of the day for one week. No conclusive results were obtained and excessively chronic cases were considered unsuitable for this form of treatment.

Small doses of LSD coupled with intravenous Ritalin (99) were administered to 350 outpatients. Conditions like emotional immaturity, excessive anxiety, psoriasis, etc.

could be helped by this treatment. Sankar and Grover (unpublished) found involvement of serotonin in psoriatics who were benefited by reserpine therapy. Treatment with a combination of LSD-25 with Ritalin, or the drug alone, were found to be beneficial (100) in a group of patients undergoing ambulatory psychotherapy. Martin (101) found that Ritalin and sodium amytal could be used as alternatives to LSD as adjuncts to psychotherapy. This treatment is potentially valuable, but is dangerous also and is accompanied by problems of withdrawal. Oral intake of sodium amytal followed by intravenous injection of Ritalin or methedrine was also found successful (102). The above studies point out the possible therapeutic value of Ritalin, methedrine, Ditran, etc. and combination therapies which warrant further studies.

One of the main areas where LSD has been found beneficial, besides in psychotherapy, is in treatment of alcoholics. Smith (103) reported in 1958 that LSD or mescaline in conjunction with psilocybin benefited refractory alcholics with character disorders. Borderline or actual psychotics did not benefit. Rolo, Krinsky, and Goldfarb(104) used LSD as an adjunct to psychotherapy in alcoholics with a history of alcoholism dating from eight to over twenty years. This chemo-psycotherapeutic approach allowed expectation of favorable results. Savage (105) showed that LSD may help the alcoholic because of transcendental, mystic peak experience. A review of the use of psychedelics on 159 chronic alcoholics and 80 control subjects who did not receive LSD showed (106) that the psychedelic drugs could be effective agents in the treatment of recalcitrant alcoholics. Many of these studies were done in Canada. Smith continued (107) his studies on LSD in alcoholics and found it to be reasonably safe and free from complications if properly used.

Cheek and her associates (108, 109, 110) devised a setting comparable to *Alcoholics Anonymous* and controlled their variables in a rigorous manner. Studying both the patient and the family, they devised a questionnaire and rating system. Participation by the husband and wives was involved. They concluded that at three months the LSD

group showed much greater improvement in terms of sobriety, work and family adjustment. However, at the end of six and twelve months, some of these advantages dimished considerably, even though "essential-reaction" measure was significantly related to outcome in the LSD group, but not in the control group. They found it important to prepare the spouses of the alcoholics to the period after LSD treatment. The wives of the subjects on LSD were vociferous in their requests for concurrent help. Cheek and Holstein (110) studied the relation between dosage levels of LSD, group differences and social interactions. They found increased negative social-emotional behavior in aggressive reformatory inmates, while two alcoholic groups rose in positive social-emotional behavior. The schizophrenics seem to rise in both positive and negative behavior with increasing doses of LSD.

The rehabilitation of the alcoholic in a multi-disciplinary approach is important (111,112), besides pharmacotherapy, psychotherapy etc. Claims made for the beneficial nature of psychedelic therapy and alcoholism have been questioned (113). Approximately one-third of the alcoholics will remain sober after the therapy while another one-third will be benefited (114).

A study of the alcoholism treatment program at Topeka Veteran's Administration Hospital showed (115, 116) that out of 79 patients treated with LSD, 15 were abstinent. The self-destructive nature of alcoholism and arrests decreased while employment and attendance at the *Alcoholics Anonymous* groups increased. The most successful results were obtained with the therapeutic set and informal setting. The values of alcoholics (117) changed after psychedelic therapy. Religious values showed a significant increase while values classified as economic, social, political, theoretical, aesthetic did not change significantly. Alcoholics volunteering for LSD treatment appeared (118) to be more aware of their emotion and behavioral difficulties and found less pleasure in drinking with a willingness to try a new treatment. Besides LSD (120), chlordiazepoxide and phenothiazines have also been used (119) in the drug therapy of alcoholism. Disulfiram has been a classical drug for treatment of alcoholism by its ability to inhibit the further

metabolization of alcohol, giving rise to unpleasant consequences after consumption of alcohol. Anxiety may lead to drinking, which may thus be partially an escapist defense mechanism from an acute psychotic breakdown.

There are several possible escape mechanisms from acute psychotic breakdowns. These include obsession, compulsion, alimentary tract ulcers, cardiopathies, etc. The occurrence of non-psychiatric disorders may thus be beneficial in the prevention of acute psychiatric disorder! Claims have been made to lowered incidence of non-psychiatric diseases in psychiatric patients.

Music therapy in conjunction with psychedelic therapy has been recommended (121) to treat alcoholism. A study of the treatment of 33 chronic alcoholics with LSD showed (122) that 17 of these subjects were benefited by the treatment. Short-term treatment with LSD or with sodium amylobarbital-methedrine (SAM) was found to be useful. SAM produced a different quality of response from LSD (123). A successful post-treatment adjustment (125) was more closely associated with the pretreatment employment level, marital status, etc.

The long-term gains through the use of LSD have been questioned (124, 125). Patients evaluated (124) on the Eysenck Personality Inventory, the Ipat Objective Anxiety Scale, the MMPI, the Lorr Multi-dimensional Rating Scale, etc. showed no significant difference between the control group and the LSD group. Faillace, Vourlekis and Szara (126) found the use of hallucinogenic drugs in the treatment of alcoholism to be of limited value. Similar lack of beneficial effects which could be attributed to the LSD treatment has been reported (127). Baker (128) treated 150 non-psychotic, psychiatric patients with LSD. Phobic neurotics, hysterics, and bipolar manic-depressive psychotics were helped by LSD, but treatment of 30 alcoholics with LSD showed no enhancement of the effectiveness beyond regular treatment by LSD. Alcoholics responding favorably to treatment showed under LSD, a will to live, lack of ambivalence to their neuroses and a good correlation between words and actions. Hollstein, *et al.* (129) found that LSD produced slightly

better results in the alcoholics during the earlier phase of treatment. After six months, the results were comparable for the LSD and the amphetamine groups. Such beneficial nature of LSD in the first three months before tolerance could be built up, has been pointed out above.

Ludwig, *et al.* (130) found that LSD treatment was in no way better than milieu therapy and other therapeutic modalities. They concluded that the dramatic claims for the usefulness of LSD in alcoholism were unjustified. This story was clearly highlighted by *"Chemical and Engineering News"* (131) under the heading, "LSD Therapy-No Help for Alcoholics". Smart and Storm (132) also concluded that there was no solid evidence for the efficacy of treatment of alcoholism with LSD.

As with all subject matter in the story of LSD, there was a curious, initial investigation followed by a rapturous, psychedelic admiration terminating in a disillusionment. These periods in the history of LSD are clearly marked chronologically with the law and the abuse of the drug. Granted that a lot of emotion had gone into the studies on LSD, more attention should be paid to its usefulness where a transcendental peak experience could be properly interrelated with practical benefits. Its use in breaking down autistic barriers and an orderly structure of emotion and feeling ending but in psychopathology (giving rise to disorder) could benefit a certain number of patients.

The ability of LSD to enhance the mystical self-understanding of a person has never been better put to use than in terminal cancer patients. Unfortunately, one form of cancer, malignant carcinoid, is characterized by increased urinary excretion of 5-hydroxyindole acetic acid. LSD and UML have been established to be serotonin antagonists. However, no marked benefit resulted (133) by the use of UML-491 in two patients with carcinoid tumors metastasing to the liver. One of these patients responded favorably with relief of flushing and respiratory defects, but little improvement in the gastrointestinal cramping.

An interesting study by Rassidakis, *et al.* (134) showed that the number of mental patients who die from malignant

neoplasms is proportionately much less than the number in the general population. The death rate from malignant neoplasms was 15% in the general population and 4.9% in psychiatric populations in Greece in 1967. Similar statistics were found in England, Wales and Scotland also. The authors correctly questioned the possible pitfalls in this observation.

Sackler (135) wrote that schizophrenics have fewer heart attacks, and are usually spared from the miseries of peptic ulcer, ulcerative colitis and asthma. If there is less cancer in the schizophrenic, production of schizophrenia may help the cancer patient! This is a rather challenging speculation, suggestive of the beneficial nature of the production of an acute psychotic state with LSD.

Administration of 2 micrograms of LSD or of 2.5 milligrams of pargyline per 100 g. body weight of rats, inhibited the growth of chemically-induced mammary carcinomas (136). However, discontinuation of the treatment produced a rapid increase in the size and number of the tumors. These effects could be due to the decrease in serum prolactin levels by pargyline and LSD. Haloperidol which increased serum prolactin levels had the opposite effect.

As has been mentioned above, psychedelic therapy with LSD of terminal cancer patients by Pahnke, *et al.* (137) has been productive to increased insight, acceptance and tolerance in the patient. The question of an illuminated emotional benefit as opposed to clinical oncological improvement should be studied more carefully in a better perspective.

The professional use of LSD has not been confined to psychotherapy and pharmacotherapy of behavioral disorders only. LSD, as has been pointed out in the chapter on "Endocrine Relations", interacts closely with the thyroid hormone system. Further, Salerno and Tallaferro (138) obtained favorable results in four cases of amenorrhea by treatment with mescaline or LSD. Homosexuality in twelve males was benefically treated with LSD (139). In this particular case, as also in the studies by Martin (140) and by Geller and Boas (141), the psychophysiological and psychopathological involvement was deeper than any

biological involvement. Geller and Boas (141) treated marital and sexual problems in men and women. They pointed out that LSD was not an aphrodisiac and could act, when it does, as an emotional relaxant and strong stimulus in sexual encounter. On the other hand, Szanto, *et al.* (142, 143) found that LSD and UML could augment thyroid function.

Involvement of LSD with the physiological and biochemical functions of the bioamines has been described earlier. In view of these interrelations, LSD could be expected to be of possible, though not proven, therapeutic value in disorders involving some biogenic amines. Oh and Evans (144) found that pretreatment of eyes in rabbits by injecting LSD moderately decreased the number of rosettes produced by New Castle Disease virus. The formation of these rosettes is an indicator of the virus' ability to induce corneal lesions. In studies on the influence of LSD on allergic encephalomyelitis (145), it was found that simultaneous administration of LSD with brain-adjuvant emulsion decreased the incidence of paralysis and mortality rate in guinea pigs. The venom from saw-scale viper can increase capillary permeability in the rat. This increased permeability is mediated through a release of (146) histamine and serotonin. Antivenom and antiserotonin drugs, like LSD,etc. could block the increased capillary permeability.

An increase in the urinary excretion of 5-hydroxyindole acetic acid in dumping syndrome was prevented (147) by the administration of LSD prior to concentrated glucose. UML also could (148) normalize the increased blood glucose and potassium levels and heart rate induced by oral administration of glucose in patients with dumping syndrome. However, UML had little effect on the urinary excretion of the 5-hydroxyindoleacetic acid. It is conceivable that analogs of LSD could be synthesized which may possibly have value as anticholinergic, antihistaminic, vasoactive, etc. compounds.

Chronic headache (149) is closely related to vasodilation of the cranial arteries and traction of the blood vessels,

sustained contraction of skeletal muscles of head and neck, etc. Pharmacologic treatment of headache could consist of raising the pain threshold (analgesia), interrupting the mechanism producing pain and also by reducing emotional tension and anxiety associated with the pain. Migraine headaches could be caused by several conditions including psychogenic, endocrine, hereditary, allergic or by combinations of several factors. Several substances have been used in the treatment of the many forms of headache which is the most difficult to pinpoint in regard to etiology or therapy. Ergotamine has been used in several forms of headache, especially migraine. UML-491 has been often successfully used in the prophylaxis and therapy of migraine. Thus notable improvement was found (150) in 18 cases of migraine and two Horton's histaminic cephalalgia on treatment with UML. Various types of headaches (151) have been treated with UML. The beneficial effects were found to occur within a day or two, and disappear equally fast. Withdrawal could cause significant flareups of the headache.

Raynaud's phenomenon or Raynaud's disease presents a symptomatology of intermittent pallor or cyanosis of the extremities, precipitated by cold and with patency of the large peripheral vessels. Primary Raynaud's disease, associated with a disease, is comparatively rare, but Raynaud's phenomenon can occur secondary to diverse pathological conditions. In this way, Raynaud's phenomenon is highly non-specific, but is based on vasomotor circulatory conditions. The vasoconstrictor properties of serotonin could be closely related to Raynaud's phenomenon (152). Eleven patients with diagnoses of primary Raynaud's disease, and several patients with Raynaud's phenomenon were treated with UML and/or other drugs. The processes involved in the production of Raynaud's phenomenon involved biogenic amines, especially serotonin, and are thus susceptible to clinical alteration by UML. No definitive conclusions could be drawn.

The mode of action of UML in vascular headaches (153) involved peripheral vasoconstriction and anti-inflammatory

properties. Wolff and his associates (154) have done extensive work on headache. They concluded that the therapeutic efficacy of UML-491 in migraine depended on its ability to modify the effects of vasoconstriction and vasodilation in migraine. Vascular headaches in 171 patients were treated by Friedman and Losin (155) by UML. They noted reduction in the severity and frequency of the headaches in 65% of the patients with migraine. This figure was significantly higher than in a control group not receiving UML. 71% of patients with cluster headache benefited from UML. Vascular headaches could be treated with UML, but not headaches due to neuromuscular tension (156). UML was found to be beneficial in 77% of 159 subjects with histaminic cephalalgia, being both safe and effective (157). However, therapy with UML did not help (158) 25 chronically ill allergic patients. Curran, *et al.* (159) reviewed the nature, usefulness and side effects of UML.

Sicuteri (160) has been among the earliest in the use of lysergates for migraine headaches. Of all these derivatives, UML was found to be the most potent agent. However, he stated that UML - like other derivatives of lysergic acid - has *no antihistamine* effect. This is certainly subject to question. The usefulness of UML in migraine headaches, cluster headaches (histaminic cephalalgia), but not in common vascular tension headaches was shown repeatedly(161). Abrupt discontinuation of treatment may give rise to "rebound headaches". 1-Methyl-N-carbobenzyloxy-dehydrolysergamine was slightly less effective (162) than UML, but was better tolerated.

Ostfeld (163) pointed out that serotonin was more likely a candidate for "pain substance" than histamine or acetyl choline in migraine headache in certain patients. UML being a highly potent antiserotonin could be of beneficial effect in such a case. However, as has been stated above, some of the adverse effects of UML may have to be carefully watched in the therapeutic program of migraine with UML.

Other uses for LSD and its derivatives could be varied. For example, Lieberman (164) discussed the use of psychochemicals as weapons. Besides lethal nerve gases such as Sarin (GB), mustard gases, tear and vomit gases, the use of

substances like LSD could be conceived as deterents to the efficacy of an enemy. It was reported than Gen. Creasy testified that "provided sufficient impetus is put behind it, I think the future lies in the psychochemicals". Cohen (165) also considered such possibilities. The use of psychochemicals in brain washing, coercive persuasion, etc. (166) could also be part of future research inasmuch as our behavior is mostly patterned after reward and punishment.

Several claims have been made for increased creativity induced by LSD. For example, Arana-Gallegos (167) found dedication to the task and intralease were abundant in schizophrenics treated with LSD. Amphetamine, nicotine, benactyzine, and LSD produced (168) amelioration of performance in rats that were slow in acquiring an escape conditioning. In a pilot study, Harman, *et al.* (169) found that psychedelic agents under carefully structured regimen, could facilitate creative problem solving. LSD and similar chemicals (170) were reported to have enhanced the ability to solve many specific architectural problems. Reversal learning was facilitated by a single injection of LSD in the rat (171). Fischer and Scheib (172) reviewed some of the effects of hallucinogenic drugs on creative performance. Zegans, Pollard and Brown (173) concluded that the administration of LSD to a relatively unselected group of people is not likely to enhance their creative ability.

Krippner (174) recounts the story of Oliver Wendell Holmes, Sr., who enjoyed sensations of transcendent beauty and divine wisdom under presurgical ether. Determined to perpetuate this experience for posterity, Homes went through a second ether session and wrote in a shaking hand, "Oh, Lord, what a stink!". Coleridge, Poe, De Quincey, Berlioz, Browning, Carlyle, Tennyson, Dickens, Keats, Sir Walter Scott, and others have used opium. None of these writers have been transported into a higher order of creativity due to the opium. However, further research on the use of psychedelic drugs in artistic creativity, in music, and other related fields deserves well-structured, careful research. Krippner (174) pointed out the influence of drugs on lyrics. The usual boy-girl theme could often be replaced

by a man-cosmos theme, pointing out the cosmic perspectives induced by psychedelics. The poet, John Sinclair, was sentenced in 1969 to ten years' imprisonment following conviction for the possession of two marijuana cigarettes as was Aldcroft in 1967.

It may thus be seen from the above material that LSD and its congeners could be of use in aiding psychotherapy, in breaking down autistic barriers by pharmacotherapy, in vascular headaches, in migraine, and perhaps in enhancing the learning and creativity in a select population. However, the abuse of LSD by "unselect populations" has been the main stay and thrust in throwing LSD into a no-man's land. More harmful drugs, which have not been abused, have not suffered the same serious fate. Less harmful drugs, like meprobamate, have suffered the same penalty because of their *abuse*. The key word here is "abuse", but not possible "usefulness". If the abuse of LSD were less widespread, perhaps LSD would not have been recalled by Sandoz and forbidden by governments.

LSD is unique among all the lysergates in its hallucinogenic creativity. No other known compound, lysergate or otherwise, has its potency. Thus research on LSD should not be hindered, but carefully structured. The use of LSD as a tool for research has been pointed out by Max Rinkel (175), by Dahlberg (176), by Denson (177), by Gelder (178), and several others. Basic research on mechanisms of hallucinations, on psychobiology, on biogenic amines, and research in clinical areas involving these substances has been greatly benefited by the work on LSD. Abramson (179) has pointed these several aspects of LSD and has also written a chapter in this book stating his views.

The present author, who has worked in several basic science areas of psychotomimetics and has collaborated with Bender in the use of LSD in breaking down autistic barriers, also believes that basic research on LSD and its derivatives should be further encouraged. He also believes that any pharmacotherapeutic use of LSD is limited to three to six months after initiation of the use. Any progress the patients may make should be carefully aided and planned within this

rather short term of therapy. The problem is confused by the abuse of LSD and the abuse of multiple drugs in questionable groups of the population. This should not be so.

REFERENCES

1. Busch, A.K., and Johnson, W.C. *Dis. Nerv. Sys. 11*, 241 (1950).

2. Lewis, D.J., and Sloane, R.B. *J. Clin. Exper. Psychopathol. 19*, 19 (1958).

3. Katzenelbogen, S., and Fang, AD. *Dis. Nerv. Sys. 14*, 85 (1953).

4. Abramson, H.A. *J. Psychol. 39*, 127 (1955).

5. Abramson, H.A. *J. Psychol. 41*, 199 (1956).

6. Abramson, H.A. *J. Psychol. 42*, 51 (1956).

7. Abramson, H.A. In: *A.P.A. Lysergic acid diethylamide and mescaline in experimental psychiatry*, Grune and Stratton, New York, 51 (1956).

8. Abramson, H.A. *J. Nerv. Ment. Dis. 125*, 444 (1957).

9. Grof, S. *J. Psychedelic Drugs. 3*, 52 (1970).

10. Pahnke,W.N., Kurland,A.A., Unger, S., Savage, C., and Grof, S.P. In *Hallucinogenic Drug Research* (Ed). Gamage, J.R. and Zerkin, E.L. Stash Press, 1970, p.48.

11. Unger, S.M. In: Solomon, D. *LSD: The Consciousness-Expanding* Drug, New York, G.P. Putnam's Sons, 257 (1964).

12. Abramson, H.A. *J. Psychol. 51*, 33 (1961).

13. Abramson, H.A. *J. Asthma Res. 5,* 29 (1967).

14. Eisner, B.G., and Cohen, S. *J. Nerv. Ment. Dis. 127,* 528 (1958).

15. Frederking, W. *J. Nerv. Ment. Dis. 121,* 262 (1955).

16. Giberti, F., and Gregoretti, L. In: Bradley, P. *Neuropsychopharmacology,* Amsterdam, Elsevier Pub., 576 (1959).

17. Divry,P., Bobon, J., and Collard, J. In: Bradley,P. *Neuropsychopharmacology,* Amsterdam, Elsevier Pub. 542 (1959).

18. Chandler, A.L., and Hartman, M.A. *Arch. Gen. Psychiat. 2,* 286 (1960).

19. Ling, T.M., and Buckman, J. *Proc. Royal Soc. of Med. [London] 53,* 927 (1960).

20. Leuner, H., and Holfeld, H. *Psychiat. Neurol. 143,* 379 (1962).

21. Butterworth, A.T. *Psychiat. Quart. 36,* 734 (1962).

22. Ditman, K.S., Hayman, M., and Whittlesey, J.R.B. *J. Nervosa Superior [Prague] 5,* 218 (1963).

23. Hausner, M., Dolezal, V., and Saposnikova, O. *Activitas Nervosa Superior* (Prague) *5,* 218 (1963).

24. Terrill, J. *J. Nerv. Ment. Dis. 135,* 425 (1962).

25. Baker, E.F.W. *Can.Med. Ass.. J. 91,* 1200 (1964).

26. Whitaker, L.H. *Med. J. Australia 51,* 36 (1964).

27. Terrill, J., Savage, C., and Jackson, D.D. In: Solomon, D. *LSD: The Consciousness-Expanding Drug,* New York, G.P. Putnam's Sons, 174 (1964).

28. Savage, C., Savage, E., Fadiman, J., and Harman, W. *Psychol. Rep. 14,* 111 (1964).

29. Mogar, R.E. and Savage, C. *Psychotherapy: Theory, Research & Practice 1,* 154 (1964).

30. Savage, C., Fadiman, J., Mogar, R., and Allen, M.H. *Intern. J. Neuropsych. 2,* 241 (1966).

31. Rolo, A., Krinsky, L.W., Abramson, H.A., and Goldfarb, L. *J. Psych. 58,* 237 (1964).

32. Derblowsky, U. *Zeit. Psychosom. Med. Psychoanalyse* [*Gottingen*] *16,* 33 (1966).

33. Spencer, A. M. *Brit. Med. J.* [*London*] *5504,* 49 (1966).

34. Spencer, A.M. *Intern. J. Neuropsychiat. 2,* 60 (1966).

35. *Medical World News 8,* 50 (1967).

36. Taus, L. *Activitas Nervosa Superior* [*Prague*] *9,* 380 (1967).

37. Cutner, M. *Psychother. Psychosom. 15,* 14 (1967).

38. Mechaneck,R., Feldstein,S., Dahlberg,C.C.,and Jaffe, J. *Comp. Psychiat. 9,* 490 (1968).

39. Kurland, A.A., Savage, C., Shaffer, W., and Unger, S. In: Debold, R. *LSD, Man & Society,* Middletown, Conn. Wesleyan University Press, 20 (1967).

40. Kast, E. *Psychiat. Quart., 1,* October 1967.

41. Unger, S. *New Outlooks in Psychology,* New York, Philosophical Library, 257 (1968).

42. Lyle, W.H. *Correctional Psychologist 3*, 6 (1968).

43. Ditman, K.S. In: Ungerleider, J. *The Problems and Prospects of LSD*, Springfield, Ill., Charles C. Thomas, 45 (1968).

44. Fisher, G., Martin, J. *Voices 5*, 67 (1970).

45. Kurland, A.A. *Medical Trubune 11*, 15 (1970).

46. Savage, C. *J. Nerv. Ment. Dis. 125*, 434 (1957).

47. Day, J. *J. Nerv. Ment. Dis. 125*, 437 (1957).

48. Fisher, G. *Psychedelic Rev. 1*, 208 (1963).

49. Gucker, D.K. *J. Psychol. 55*, 401 (1963).

50. Mogar, R.E. *J. Humanistic Psychol.*, 147 (Fall 1965).

51. Bieberman,L. *"Session Games People Play"*, Psychedelic Information Center, Cambridge, Mass. (1967).

52. Caldwell, W.V. *LSD-Psychotherapy*, New York, Grove Press (1969).

53. Cohen, S. In: Cohen S. *The Beyond Within: The LSD Story*, second ed., New York, Atheneum, 180 (1970).

54. McGlothlin,W.H. and Arnold, D.O. *Arch. Gen. Psychiat. 24*, 35 (1971).

55. Hoch, P.H., *J. Nerv. Ment. Dis. 125*, 442 (1957).

56. Faillace, L.A. *Comp. Psychiat. 7*, 13 (1966).

57. Hollister, L.E., Degan, R.O., and Schultz, S.D. *J. Ment. Sci. 108*, 99 (1962).

58. *Medical World News 7,* 36 (1966).

59. Leuner, H. *Nervenarzt,* (Berlin) *39,* 356 (1968).

60. Caldwell, W.V. In: Caldwell, W. *LSD-Psychotherapy,* New York, Grove Press, 101 (1969).

61. Persyko, I. *J. Nerv. Ment. Dis. 154,* 299 (1972).

62. Vanggaard, T. *Acta Psychiat. Scand. 40,* 427 (1964).

63. Sandison, R.A., Spencer, A.M., and Whitelaw, J.D.A. *J. Ment. Sci.* [*London*] *100,* 491 (1955).

64. Sloane, B., and Doust,J.W.L. *J. ment. Sci.* [*London*] *100,* 12 (1955).

65. Cholden, L.S., Kurland, A., and Savage, C. *J. Nerv. Ment. Dis. 122,* 211 (1955).

66. Martin, A.J. *Intern. J. Soc. Psychiat. 3,* 188 (1957).

67. Abramson, H.A., Hewitt, M.P., Lennard, H., Turner, W.J., O'Neill, F.J.,and Merlis, S. *J. Psychol. 45,* 75 (1958).

68. Shagass, C., and Bittle, R.M. *J. Nerv. Ment. Dis. 144,* 471 (1967).

69. Shagass, C., and Bittle, R.M. *Appl. Therap. 10,* 467 (1968).

70. Taus,L. *Ceskoslovenska Psychiatrie* [*Praha*] *64,* 260 (1968).

71. Kato,K. *Intern. Pharmacopsychiat.* [*Basel*] *1,* 112 (1968).

72. De Ropp, R.S.. In: De Ropp, R. *Drugs and the Mind,* New York, Grove Press, 202 (1961).

73. Pfeiffer, C.C., Jenney, E.H., Murphree, H.B., and Goldstein, L. *Pharmacologist 4,* 166B (1962).

74. Kornetsky, C., and Mirsky, A.F. *Psychopharmacologia 8,* 309 (1966).

75. Smythies, J.R., *Biological Psychiatry: A Review of Recent Advances,* New York, Springer-Verlag, 25 (1968).

76. Browne, S.E. *Brit. Med. J.*(London) *No. 5504:49* (1966).

77. Rojas Bermudez, J.G., *Acta Neuropsiquiat. Argent. 6,* 497 (1960).

78. Massoni, R.S. *med. Pract.* (Buenos Aires) *18,* 5 (1964).

79. Bender, L. *Dis. Nerv. Sys. 27,* 39 (1966).

80. Rolo, A., Krinsky, L.W., Abramson, H.A. and Goldfarb, L. *Intern. J. Neuropsychiat. 1,* 552 (1961).

81. Abramson, H.A. *J. Asthma Res. 5,* 139 (1967).

82. *Science News 89,* 378 (1966).

83. *New York Times* p. 74 (May 8, 1964).

84. Simmons, J.Q., Benor, D.,and Daniel, D. *Behavioral Neuropsychiat. 4,* 10 (1972).

85. Maccagnani, G., Bobon, J., and Goffioul, F. *Encephale* (Paris) *53,* 543 (1964).

86. Fisher, G. *Intern. J. Soc. Psychiat.* (London) *16,* 112 (1970).

87. Bleuler, M. In: Bradley, P. *Neuropsychopharmacology,* Amsterdam, Elsevier Publ., 161 (1959).

88. Elkes, J. In: Bradley, P. *Neuropsychopharmacology,* Amsterdam, Elsevier Publ., 166 (1959).

89. Hollister, L.E. *Ann. N.Y. Acad. Sci. 96,* 80 (1962).

90. Hensala, J.D., Epstein, L.J. and Blacker, K.H. *Arch. Gen. Psychiat. 16,* 554 (1967).

91. Turner, W.J., and Merlis, S. *Am. J. Psychiat. 114,* 751 (1958).

92. Maire, F.W., Collins, L.G., and Marks, J.B. *Intern. J. Neuropsychiat. 3,* 397 (1967).

93. Bender, L., Faretra, G., and Cobrinik,L. *Recent Advances in Biol. Psychiat. 5,* 84 (1963).

94. Boszormenyi, Z., and Szara, S. *J. Ment. Sci.* (London) *104,* 445 (1958).

95. Flugel, F., and Bente, D. *Deut. Med. Wochschr. 81,* 2071 (1956).

96. Lanter, R. Weil, J., and Roth, M. *Ann. Medico-Psychologiques* (Paris) *120,* 244 (1962).

97. Itil,T.M., Keskiner,A., and Holden,J.M.C. *Dis. Nerv. Sys. 30,* 93 (1969).

98. Shirvaikar, R.V., and Kelkar, Y.W. *Neurology-India* (Bombay) *14,* 97 (1966).

99. *Psychedelic Review 1,* 484 (1964).

100. Derbolowsky, U. *Zeitschr. Psychother. und Med. Psychol.* (Stuttgart) *16,* 33 (1966).

101. Martin, I. *Med. J. Aust. 2,* 1264 (1966).

102. Listwan, I.A. *Med. J. Aust. 1,* 305 (1967).

103. Smith, C.M. *Quart. J. Studies on Alcohol 19,* 406 (1958).

104. Rolo, A., Krinsky, L.W., and Goldfarb, L. *J. Psychol. 50,* 85 (1960).

105. Savage, C. *J. Nerv. Ment. Dis. 135,* 429 (1962).

106. No author. *Psychedelic Review 1,* 205 (1963).

107. Smith, C.M. *Quart. J. Studies on Alcohol 25,* 742 (1964).

108. Cheek, F.E., Osmond, H., Sarett, M., and Albahary, R.S. *J. Psychopharm. 1,* 56 (1966).

109. Sarett, M., Cheek, F., and Osmond, H. *Arch. Gen. Psychiat. 14,* 171 (1966).

110. Cheek, F.E., and Holstein, C.M. *J. Nerv. Ment. Dis. 153,* 133 (1971).

111. Polacsek, E., Barnes, T., Turner, N., Hall, R., and Weise, C. *Addiction Research Foundation Bibliographic Series, No. 3* (1972).

112. Fox, R. *Intern. J. Psychiat. 5,* 34 (1968).

113. Johnson, F.G. *Am. J. Psychiat. 126,* 481 (1969).

114. Geller, A., and Boas, M. In: Geller, A. *The Drug Beat,* New York, Cowles Book, 214 (1969).

115. Reinert, R.E. *Quart. J. Studies on Alcohol 26,* 674 (1965).

116. Godfrey, K.E. In: Catanzaro, R. *Alcoholism: The Total Treatment Approach,* Springfield, Ill. Charles C. Thomas, 237 (1968).

117. Ramsay, R., Jensen, S., and Sommer, R. *Quart. J. Studies on Alcohol 24,* 443 (1963).

118. Ditman, K.S., Moss, T., Forgy, E., Zunin, L., Funk, W., and Lynch, R. *Quart. J. Studies on Alcohol 31*, 414 (1970).

119. Milt, H. *Basic Handbook on Alcoholism*, Fair Haven, N.J., Scientific Aids Publications, 64 (1967).

120. Abuzzahab, F.S., and Anderson, B.J. *Intern. Pharmacopsychiat. 6*, 223 (1971).

121. Gaston, E.T., and Eagle, C.T., Jr. *J. Music Therap. 7*, 3 (1970).

122. O'Reilly, P.O., and Reich, G. *Dis. Nerv. Sys. 23, 331* (1962).

123. Johnson,F.G. , *Can. Psychiat. Ass. J.* (Ottawa) *15*, 493 (1970).

124. Denson, R., and Sydiaha, E. *Brit. J. Psychiat.* (London) *116*, 443 (1970).

125. Bowen, W.T., Soskin, R.A., and Chotlos, J.W. *J. Nerv. Ment. Dis. 150*, 111 (1970).

126. Faillace, L.A., Vourlekis, A., and Szara, S. *Comp. Psychiat. 11*, 51 (1970).

127. *Lakartidningen* (Stockholm) *64*, 1175 (1970).

128. Baker,E.F.W., *Addictions* [*Toronto*] *14*, 20 (1967).

129. Hollister, L.E., Shelton, J., and Krieger, G; *Am. J. Psychiat. 125*, 1352 (1969).

130. Ludwig, A., Levine, J., Stark, L., and Lazar, R. *Am. J. Psychiat. 126*, 59 (1969).

131. *Chem. & Eng. News 47*, 13 (1969).

132. Smart, R.G., and Storm, T. *Quart. J. Studies on Alcohol 25,* 333 (1964).

133. Weaver, W.T., Metz, E.N., Anlyan, W.G., and Rundles, W.R. *Surgical Forum 12,* 330 (1961).

134. Rassidakis, N.C., Kelepouris, M., and Fox, S. *Intern. Ment. Health. Res. Newsletter.* P. 6

135. Van Dellen,T.R. *Daily News* p. 28 (March 20, 1973).

136. Quadri, S.K., Clark, J.L., and Meites, J. *Proc. Soc. Exp. Biol. and Med. 142,* 22 (1973).

137. Pahnke, W.N., Kurland, A.A., Unger, S., Savage, C., Wolf, S. and Goodman, L.E. *J. Psychedelic Drugs 3,* 63 (1970).

138. Salerno, E.V., and Tallaferro, A. *Semana Med.* (Buenos Aires) *110,* 47 (1957).

139. Martin, A.J. *Acta Psychotherap. Psychosomat. 10,* 394 (1962).

140. Martin, A.J. *Psychother. Psychosom. 15,* 44 (1967).

141. Geller, A., and Boas, J. In: Geller, A. *The Drug Beat,* New York, Cowles Book, 225 (1969).

142. Szanto, L., Reviczky, A.L. and Grynaeus, T. *Acta. Med. Acad. Sci. Hung. 19,* 169 (1963).

143. Szanto, L. and Reviczky, A. L. *Acta. Physiol. Acad. Sci. Hung. 30,* 233 (1966).

144. Oh, J.O., and Evans, C.A. *Virology 10,* 127 (1960).

145. O'Brien, D.J., Hughes, F.W., and Newberne, J. *Proc. Soc. Exp. Bio. Med. 111,* 490 (1962).

146. Somani, P. *Intern. Arch. Allergy Appl. Immunol. 21,* 186 (1962).

147. Wense, G. *Acta Conv. Med. Internae Hung., 3rd, Budapest,* 149 (1965).

148. Pistacchi, E., and Onetti, L. *Minerva Chir. 22,* 615 (1967).

149. Friedman, A.P. *Medical Times* August (1960).

150. Sicuteri, F. *Intern. Arch. Allergy Appl. Immunol. 15,* 300, (1959).

151. Graham, J.R. *New Eng. J. Med. 263,* 1273 (1960).

152. Halpern, A. Kuhn, P.H., Shaftel, N., Samuels, S.S., Shaftel, H., Selman, D., and Birch, H.G. *Angiology 11,* 151 (1960).

153. Dalessio, D.J., Camp, W.A., Goodell, H., and Wolff, H.G. *Arch. Neurol.* 4, (1961).

154. Dalessio, D.J., Chapman, L.F., Zilleli, T., Cattell, M., Ehrlich, R., Forouin, F., Goodell, H., and Wolff, H.G. *Arch. Neurol. 5,* 590 (1961).

155. Friedman, A.P., Losin, S. *Arch. Neurol. 4,* 241 (1961).

156. Abbott, K.H. *Dis. Nerv. Sys. 23,* 579 (1962).

157. Lovshin, L.L. *Dis. Nerv. Sys. 24,* 120 (1963).

158. Pinsker, W., and Thayer, K.H. *Ann. Allergy 21,* 200 (1963).

159. Curran, D.A., Hinterberger, H., and Lance, J.W. *Res. Clin. Stud. Headache 1,* 74 (1967).

160. Sicuteri, F. *Triangle,* Sandoz, p. 116.

161. Peterman,A.F. *Mind,* p.91 March (1963).

162. Franchi, G., and Fanciullacci, M. *Minerva Med. 60,* 4313 (1969).

163. Ostfeld, A.M *Scientific Exhibit at the American Med. Ass. Conv.* Miami Beach June 13-17, 1961

164. Lieberman, E.J. *Bull. At. Scientists,* 11 Jan. (1962).

165. Cohen, S. Unpublished Paper, Psychiatry Service, Wadsworth VA Hospital, Los Angeles, Calif, 14 pp. (1966).

166. Cohen, S. *Med. Counterpoint 1,* 47 (1969).

167. Arana-Gallegos,J. *Rev. Neuro-Psiquiat. 31,* 26 (1969).

168. Bignami, G., Robustelli, F., Janker, I., and Bovet, D. *Compt. Rend. 260,* 4273 (1965).

169. Harman, W.W., McKim, R.H., Mogar, R.E., Fadiman, J., and Stolaroff, M.J. *Psychol. Rep. 19,* 211 (1966).

170. Gjerstad, G. *Quart. J. Crude Drug Res. 12,* 1849 (1972).

171. King, A.R., Martin, I.L., and Seymour, K.A. *Brit. J. Pharmacol. 45,* 161 (1972).

172. Fischer, R., and Scheib, J. *Cinfinia Psychiat. 14,* 174 (1971).

173. Zegans, L.S., Pollard,J.C., and Brown,D. *Arch. Gen. Psychiat. 16,* 740 (1967).

174. Krippner, S. In: Gamoge, J.R., and Zerkin, E.L. *Hallucinogenic Drug Research. Impact on Science and Society,* Stash Press, 83 (1970).

175. Rinkel, M. *Recent Advances in Biol. Psychiat. 8,* 103 (1965).

176. Dahlberg, C.C. *Science 153*, 1595 (1966).

177. Denson, R. *Can. Med. Ass. J.* (Toronto) *101*, 53 (1969).

178. Gilder, S.S.B. *Can. Med. Ass. J.* (Toronto) *103*, 1347 (1970).

179. Abramson, H.A. *J. Asthma Res. 1*, 207 (1964).

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