FURTHER STUDIES IN THE THERAPEUTIC VALUE OF LYSERGIC ACID DIETHYLAMIDE IN MENTAL ILLNESS

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This paper follows a preliminary communication to this Journal two years ago (Sandison, Spencer and Whitelaw, 1954) and gives an account of the fuller experience gained up to the present time with lysergic acid diethylamide in the treatment of mental illness.

1. The results of a two-year follow-up of the 36 patients originally reported upon in 1954.
2. The results of treatment in all the patients (94) treated up to March, 1956. These have been followed up for a minimum of six months (September, 1956).
4. Description of a technique for treating psychotic patients with a combination of LSD and chlorpromazine.
5. A discussion of the present position of LSD in relation to psychiatry.

SUMMARY OF SOME RECENT LSD STUDIES

During the past three years increasing interest has been shown in LSD and allied substances. Studies have been carried out with lysergic acid monoethylamide, mescaline, methedrine, adrenochrome and 3,4,5-trimethoxyphenylaminopropane (T.M.A.). All these substances have certain chemical features in common, and their psychic properties are similar in that when given in suitable doses they all produce hallucinations, changes in time and space perception and an awareness of material from the unconscious mind. Research into the action of these drugs has in recent years been directed into three main channels. First, studies of their effects on normal individuals in whom they induce a so-called model psychosis. As a result of these studies, valuable light has been thrown on the mechanism of the schizophrenic process. Second, some of the drugs, particularly LSD, have been used for the treatment of the psychoneuroses and on a smaller scale and in a more experimental manner for the treatment of the psychoses. Third, they have been used alone or in conjunction with other drugs in an attempt to unravel the complex biochemical disorders which may be associated with mental illness.

A considerable number of interesting papers have been published on the first and the third of these projects, but here we shall refer chiefly to the work of those authors who have reported on the use of LSD for the treatment of mental illness.
As far back as 1936 Guttman and Maclay suggested small doses of mescaline as an empirical therapy for derealization and personalization. Mayer-Gross (1951) appears to have written the first English paper which compares the clinical action of mescaline and lysergic acid diethylamide and suggests the possible uses of these drugs in treatment. Savage (1952) studied the effects of LSD in five normal controls and fifteen depressed patients. In the latter group three patients recovered and four patients improved after one month of LSD treatment in which 20–100 µg. were given daily by mouth. Four patients showed no improvement. Benedetti (1951) gave two doses of 50 µg. LSD within two hours of each other to a chronic alcoholic patient with marked psychocatharsis. Frederking (1953/54; 1955) used both LSD and mescaline for the treatment of neurotic patients who were refractory to psychoanalysis. Twenty-four cases were described and the therapeutic effect of LSD was considered better than that of mescaline. The paper is of interest to us as the author describes many LSD experiences which bear great similarity to the ones we ourselves reported in 1954. For example, he states that the LSD phenomena are either purely symbolical in character or they represent childhood memories, the latter often appearing in symbolized form. Many of these memories are accompanied by more or less violent emotions corresponding to the patients' problems. The recollections can go back as far as very early childhood, sometimes even to the moment of birth. The patient is able to remember to a large extent the experiences evoked during his intoxication and they can be discussed with him a few days later. Considerable caution is indicated in cases of extreme anxiety and of suspected schizophrenia. Sloane and Doust (1954) gave LSD to eleven healthy controls, twelve patients with predominant depression and seven patients with schizophrenia. These authors thought there were slight, clinically apparent changes attributable to LSD which were difficult to verify objectively. Anderson and Rawnsley (1954) gave 10–600 µg. of LSD by mouth on 58 occasions to four normal subjects and nineteen psychiatric patients. In six cases LSD produced long-lasting favourable changes in the clinical picture. Abramson (1955) used LSD rather differently as an adjunct to psychotherapy, giving small doses, e.g. 20–40 µg. to a patient already undergoing analysis. Following ingestion of the drug, the author stayed with his patient for a continuous period up to four hours in length recording the material and discussing it with the patient. A satisfactory elimination of the patient's fear of homosexuality was achieved. An earlier paper, by Busch and Johnson (1950) should again be quoted as our original work was partly inspired by their findings and also the more recent work of Katzenelbogen and Ai Ding Fang (1953) should be mentioned. In England, Ling (1955) has successfully used LSD for the treatment of the psychoneuroses, while Davies and Davies (1955) have used it as an aid to psychotherapy in mental defectives. Martin (1955) has reported excellent results in psychoneurotics treated as out-patients in a day hospital, controlling after-reactions with chlorpromazine and barbiturates.

**TWO-YEAR FOLLOW-UP IN THE THIRTY-SIX PATIENTS REPORTED ON IN 1954**

In 1954 we classified the results of treatment as "Recovered", "Greatly Improved", "Moderately Improved" and "Not Improved". These terms will now be defined and the definitions have been followed in assessing all the cases reported in this paper.
Recovered—Able to discontinue treatment and resume normal life at an equal or superior level to that attained before the illness began. The patient must be able to enjoy normal social relationships and family life and must be free of symptoms.

Greatly Improved—Able to discontinue treatment and to resume normal life, including return to full work. Some personality disorders permitted in this category which may result in an occasional return of symptoms which are not sufficiently severe to disturb social or family life.

Moderately Improved—Some dependence on psychiatric treatment but return to full work, possibly at a lower level than before illness. Some persistence or recurrence of symptoms permitted, which may disturb social or family relationships but not sufficiently to require readmission to hospital.

Not Improved—Symptoms remain as disabling as when the patient first attended clinic or hospital.

There is a fairly wide difference between the “Moderately Improved” and “Not Improved” categories, and in intermediate states patients have been placed in the “Not Improved” group.

The following table summarizes the present condition of the 36 patients reported on in 1954.

<table>
<thead>
<tr>
<th></th>
<th>Recovered</th>
<th>Greatly Improved</th>
<th>Moderately Improved</th>
<th>Not Improved</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>Females</td>
<td>2</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>14</td>
</tr>
</tbody>
</table>

Omitted from series (inadequate treatment) and responded to other methods: 1
Inadequate follow-up: 2
Refused to continue after one treatment (but has now resumed): 1
No reply to any follow-up: 2

Total: 36

It may be noted that whereas 21 patients were grouped in the “Improved” categories in 1954, 19 are now so assessed. This may be accepted as evidence of the relatively low relapse rate. It should be pointed out that 27 out of the original 36 patients required mental hospital in-patient treatment when we first saw them, and at the time of writing, as far as we are aware and excluding the 4 cases inadequately followed up, not one of these patients is in a mental hospital.

The Results of Treatment in the Ninety-four Patients Treated up to March, 1956

These patients include 30 of the original 36 patients treated in 1953 and 1954 (Table 1), excluding the 6 patients in whom the follow-up was unsatisfactory. This means that a further 64 patients were treated up to March, 1956, and these have now been followed up for at least six months to September, 1956. The results are given in the following table.
### Table II

**Results of Treatment in Whole Series**

<table>
<thead>
<tr>
<th></th>
<th>Recovered</th>
<th>Greatly Improved</th>
<th>Moderately Improved</th>
<th>Not Improved</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>8</td>
<td>11</td>
<td>5</td>
<td>19</td>
<td>43</td>
</tr>
<tr>
<td>Females</td>
<td>13</td>
<td>9</td>
<td>15</td>
<td>13</td>
<td>50</td>
</tr>
<tr>
<td>Female</td>
<td>No reply</td>
<td>follow-up (recovered at time of discharge)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table III

**Diagnosis and Results of Treatment in Whole Series**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Recovered</th>
<th>Greatly Improved</th>
<th>Moderately Improved</th>
<th>Not Improved</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary anxiety neurosis</td>
<td>8</td>
<td>6</td>
<td>3</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>Anxiety neurosis associated with alcoholism, schizoid or immature personality</td>
<td>2</td>
<td>3</td>
<td>—</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>Phobic anxiety</td>
<td>1</td>
<td>1</td>
<td>—</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Anorexia nervosa</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Obsessional neurosis</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Hysteria (all forms)</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Psychoneurotic depression</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>13</td>
</tr>
<tr>
<td>Sexual neurosis: Homosexuality</td>
<td>1</td>
<td>—</td>
<td>—</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Transvestism</td>
<td>2</td>
<td>—</td>
<td>1</td>
<td>—</td>
<td>3</td>
</tr>
<tr>
<td>Impotence</td>
<td>1</td>
<td>—</td>
<td>2</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Psychopathic personality</td>
<td>—</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Convalescent schizophrenia</td>
<td>2</td>
<td>—</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>No reply to follow-up</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1</td>
<td>93</td>
</tr>
</tbody>
</table>

The follow-ups have been carried out at intervals of about six months since the completion of treatment. Wherever possible personal interview was relied upon and this was carried out in all cases except those that lived at a considerable distance from the hospital. The only patient who could not be traced had moved to Liverpool.

It will be noted that, out of 94 patients, 61, or 65 per cent., are recorded as recovered or improved. This compares favourably with other methods of treating the severe neuroses and we must again emphasize the fact that all our earlier cases and most of the later cases had failed to respond to conventional methods of therapy.
THE CAUSES OF FAILURE

In 1954 we thought that chronicity was an important factor in failure, although several cases were recorded in which a longstanding neurosis had improved. The following table analyses the possible causes of failure in the 32 cases recorded as "Not Improved".

TABLE IV
Relationship between "Improved" and "Not Improved" groups
and accepted factors affecting recovery

<table>
<thead>
<tr>
<th></th>
<th>Recovered and Improved Group</th>
<th>Not Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of illness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 or more years</td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>Latent or actual psychosis</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Hysterical illness</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Inadequate personality</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Total 29</td>
<td></td>
</tr>
</tbody>
</table>

N.B.—The total number of "Not Improved" cases is 32. Three patients in this group do not belong to the four categories listed. Similarly, only 28 out of the 61 patients that recovered fall into these categories. Thus a much greater proportion of the "Not Improved" cases are associated with factors which are generally accepted as carrying a poor prognosis compared with the "Recovered" and "Improved" categories. Nevertheless, 28 patients with poor prognostic features were materially influenced by LSD treatment.

COMMENTS ON THE RESULTS

Therefore the outstanding causes of failure are the presence of actual or latent psychosis and "inadequate personality". The latter assessment is notoriously difficult to make, but we are now achieving more success in estimating personality traits by the use of a formal social history, details of which may be published later. We must stress the need for taking a very careful history before submitting patients to LSD treatment. In the various diagnostic groups the proportion of successes to failures is reasonably uniform. The surprising success in the psychopathic personalities must now be added to our continued success with the obsessional neurotics, as reported in the earlier paper. These two categories deserve special comment.

Psychopathic Personality

Of the many problems which beset the therapist in treating psychopaths, perhaps the most obvious is the patient's inability to identify himself with the aims of the therapist. He will frequently appear to take a great interest, for example, in group therapy, in which he will participate freely and often with apparent insight, saying that he is learning much about himself and his social shortcomings. But again and again, he relapses and fails to integrate anything he has learned. To lysergic acid, however, the attitude of the psychopath is different. We have found that our psychopaths do take this treatment seriously. The upsurge of inner psychological material compels these patients to do something about themselves and they develop an interest in the treatment which in itself overcomes their desire to satisfy their libido in antisocial ways. It is no doubt true that some natural maturation occurs in time in most psychopaths and LSD treatment appears to enhance rapidly this natural development of character without all the dangers of "learning the hard way".
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It will be appropriate to mention at this point that it is not only in psychopath that maturation and unfolding of the personality occurs during LSD treatment. In many of our patients we have observed changes of character in terms of increased drive and initiative, greater independence and a more mature outlook which occurred early in the treatment, often before symptoms began to be relieved. This was particularly noticeable in the sexual neuroses, which many would regard as forms of character disorder. We would therefore suggest the wider use of LSD in the treatment of psychopathic states and character disorders.

**Obsessional Neurosis**

Obsessional neurotics respond poorly to previous methods of treatment and as a result of their lack of response to psychotherapy, the tendency in recent years has been to treat them by electroplexy, insulin, leucotomy or by chemical shock as with acetyl choline. Each of these methods has met with some success, but the results are less good in patients with developed obsessive-compulsive syndromes. The psychotherapeutic problem seems to lie in the excessive psychological resistance encountered in these patients and therefore they appear ideally suited to LSD therapy. This is found to be the case. The obsessional neurotics in our series do manage to produce material other than their obsessions and progress can be made, although larger doses of LSD and more prolonged treatment is required than with other types of case.

Hand-washing obsessional seem to respond particularly well to LSD as in their cases a well-marked sexual psychopathology is nearly always present; frequently the neurosis seems to have commenced with a definite incident of sexual trauma in childhood, the memory of which has been deeply repressed. In the authors’ experience, LSD is the only drug which will bring this particular type of repressed memory into consciousness.

**FURTHER OBSERVATIONS ON THE TECHNIQUE OF LSD TREATMENT**

In our previous paper we described the technique which we were using at that time in some detail and included some notes on instructions which should be given to the nursing staff looking after the patient. Whilst our general instructions to nurses still hold good, there have been some alterations in the management of the patient, the most important of which is the use of drugs such as barbiturates and chlorpromazine to modify the LSD reaction. In the earlier stages of the clinical studies we avoided as far as possible using any other drugs as we wished to demonstrate that the LSD alone was responsible for the phenomena observed. We find now that the usefulness of LSD treatment can be increased by the use of these drugs.

It has been found that LSD has two great disadvantages; it may cause excessive anxiety and it is liable to produce a repetition of the acute phase of the experience days or even weeks after the initial doses. It is probable that repeated and larger doses of LSD produce the most severe and prolonged after-effects, but we have seen this phenomenon well marked in patients who have had no more than 50 μg. weekly. One patient who had sixteen doses, the maximum of which was 150 μg. reports that she still has an occasional return of the LSD phenomena more than two years after cessation of treatment. The use of auxiliary drugs is therefore directed towards two ends. The first is to reduce the length of the psychic disturbances which occur on the day of
administration of LSD and to diminish the anxiety resulting. This is best accomplished by a short-acting barbiturate such as pentobarbitone given orally in doses up to 44 gr. (0·3 g.) three to six hours after the administration of LSD and if necessary six hours later. Second, drugs are given to avoid repetitions of LSD experiences, which may occur some hours or days after the treatment. For this purpose we have used chlorpromazine tablets, 25—50 mg. three times a day, and more recently Frenquel, but the value of this latter drug is still in doubt. The chlorpromazine is usually given for 5 days after treatment and is stopped on the day preceding the next treatment. These techniques have made it possible to treat a larger number of patients without admission to hospital than we hitherto thought possible. We still, however, feel that it should be possible to admit any patient undergoing LSD treatment to a hospital bed under observation for at least a night if the occasion should arise.

We have referred above to excessive anxiety as one of the by-products of LSD treatment. In cases of anxiety neurosis the symptoms may therefore become considerably worse under treatment, and the patient may become actively suicidal. This should not necessarily be taken as an indication to stop the treatment provided that useful psychological material is emerging. In our experience, marked suicidal urges have particularly occurred during the treatment of anxiety neurosis, and are not necessarily confined to patients who had depressive or suicidal ideas before treatment was commenced. One patient attempted to strangle herself at the height of the LSD reaction, whilst three others have expressed urgent wishes to be allowed to go and throw themselves in the nearby river, and had to be restrained from so doing. By "restraint", we mean moral persuasion rather than physical restraint, and patients in this condition can usually be persuaded to take pentobarbitone, after which the suicidal tendencies subside and are not necessarily present between treatments.

In our previous paper, we mentioned the possibility of precipitating a psychosis as an important complication of treatment. Now that we have treated a large number of patients of diverse types we feel that this risk has been overemphasized. We believe now that among the risks of treatment, the emphasis should be shifted to the possibility of suicide.

Smaller differences in technique consist of a fairly rigid adherence to once weekly treatment, the use of somewhat smaller doses than hitherto (50—200 μg.), and where possible, an intensification of the psychotherapy which forms of course the essential basis of the treatment. We have had experience with a small number of cases in which LSD was given at weekly intervals with the minimum of supervision by the therapist. Most of these patients produced a great deal of material which they wrote down but which they failed to integrate and the results were poor. We can therefore favour a plan of treatment which does not extend beyond four months. This allows about two weeks of initial interviews, eight or ten weeks for the active treatment of the patient with LSD, and during the remaining time the patient's material is the subject of further observation and analysis. In some cases, the psychotherapy and self-analysis may have to be extended for a longer period. Apart from a few exceptional cases in which it becomes clear at the end of the four months that there is no alternative to a full-scale psychological analysis with or without LSD, most of those patients who had not improved after four months' intensive treatment are not likely to benefit. Exceptions to this rule do, of course, occur but no definite guidance can be given for their selection, as the judgment of the clinician must be used in each case.
LSD AND CHLORPROMAZINE IN COMBINATION
A SPECIAL TECHNIQUE FOR THE TREATMENT OF
PSYCHOTIC PATIENTS

It has been generally conceded that LSD has little therapeutic influence on psychotic patients and that its effect is to accentuate existing psychotic symptoms. The work of Denber (1955) has drawn attention to the possibility of the use of mescaline modified by a single dose of chlorpromazine in the treatment of schizophrenia. This worker administered 0.5 g. of mescaline sulphate intravenously followed 1 to 1.5 hours later by 50 mg. of chlorpromazine hydrochloride intramuscularly. This treatment was given to 57 psychotic patients, on one occasion only to 27 patients and between 1 and 16 occasions to the remainder. Forty of the patients were suffering from an acute psychotic illness and 18 of these showed a complete remission, and 7 showed a partial improvement, while only 7 of 17 chronically ill patients showed any improvement at all. The patients in this series are reported to have produced much psychological material during the mescaline stage of the treatment which was discussed therapeutically in the state of relaxation later induced by the chlorpromazine. The results of this investigation were sufficiently interesting to prompt us to treat psychotics by a similar technique using an LSD-chlorpromazine combination.

We felt that the efficacy of such a method would be difficult to assess in acute psychotics, of whom approximately 40 per cent. remit spontaneously and in whom the effects of the chlorpromazine and psychotherapy alone would be difficult to discount. We therefore selected 10 psychotic patients of various diagnostic groups with well-preserved personalities who had been ill and confined to hospital for 1 to 2 years and in whom other methods of treatment had failed. The series of 14 patients was completed by 4 schizophrenic patients who had been ill for more than 2 years with reasonably well-preserved personalities. These patients were given 50—100 µg. LSD in the morning and precisely 2 hours later received 50 mg. chlorpromazine intramuscularly. This treatment was repeated weekly and an average of 5 treatments was given to each patient. During both phases of treatment the physician spent some time with the patient, recording material, but this was only rarely interpreted. The most striking result of the LSD phase was the increased emotional facility of the patients, often with outbursts of weeping and evident anxiety, which were not normally encountered. Many of the patients became more emotional and aggressive following treatment and the aggressive behaviour lasted several weeks and required additional chlorpromazine to control it in 2 patients. This increase in aggressive behaviour was regarded as a favourable prognostic sign and did not occur in those who failed to get well.

SUMMARY OF TREATMENT BEFORE GIVING LSD-CHLORPROMAZINE

Two patients had E.C.T. only before treatment, 7 patients E.C.T. and deep insulin treatment, 2 E.C.T. and prefrontal leucotomy, and 1 E.C.T., insulin and leucotomy, whilst 2 received E.C.T. and chlorpromazine.

Table V shows the results in the different diagnostic groups.

All of the patients regarded as recovered or improved were able to leave hospital and are making satisfactory social adjustments. Of the failures, 4 were able to leave hospital for a few months, but relapsed and had to return. These patients have now been followed up for periods varying from 5 to 12 months. Beyond noting that some of the recoveries were dramatic and unexpected, the
This table shows the results in the different diagnostic groups

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Recovered or Much Improved</th>
<th>Not Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia, all types, duration 1 to 2 years</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Chronic schizophrenia, duration over 2 years</td>
<td>nil</td>
<td>4</td>
</tr>
<tr>
<td>Paraphrenia, duration 1 to 2 years</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Endogenous depression, duration 1 to 2 years</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Recurrent stupor, (?) psychotic, 1 year in hospital</td>
<td>1</td>
<td>nil</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>7</td>
</tr>
</tbody>
</table>

authors prefer at this stage to avoid elaborating the results until more material has been collected. Larger follow-up studies may provide a suitable basis for a later communication.

THE PRESENT POSITION OF LSD IN RELATION TO PSYCHIATRY

Our clinical investigations during the past 3 years have convinced us that lysergic acid diethylamide produces psychological changes in sufferers from neurotic illnesses which can be used by the therapist to assist the patient to come to terms with the psychological problems and thus achieve a cure. It has become increasingly clear that the ingestion of LSD produces two types of reaction in the organism. The first, which occurs soon after the ingestion of the drug, consists chiefly of vegetative disturbances, characterized by variable disturbances of both sympathetic and parasympathetic systems, chiefly the latter. The second type of reaction occurs later, 1½ to 2 hours after ingestion and is characterized by "psychic" disturbances, when, for example, alterations of perception and awareness of the outer world are combined with psychological experiences of the deepest significance to the patient. These frequently involve the recovery of emotionally charged memories. It seems likely that the vegetative experiences are frequently accompanied by so-called toxic manifestations involving confused and sometimes bizarre alterations of the body image and of external objects. We believe that these vegetative and toxic changes are the ones that have been most frequently described by investigators working with normal volunteers. Our experience has been that during the first few treatments patients have chiefly experienced these vegetative symptoms to the exclusion of the psychological material which becomes predominant during later treatments. Patients who have had a number of treatments cease to be worried by the earlier "toxic" symptoms and seldom refer to them.

The nature of these later changes which are made use of by the therapist is still far from clear. That they involve the central autonomic nervous system and the mechanism of memory recall are made clear by the clinical material. On the question of memory, it seems that the problem of the human brain in this respect is not so much the storage of memory but its recall. Psycho-analytical theory suggests that human consciousness exists partly as a result of repressing memories and that memories charged with unpleasant emotional material become more easily repressed than others by predisposed subjects. The mechanism by which LSD produces memory recall and emotional release are
likewise obscure. It is tempting to compare some of the LSD manifestations with the temporal lobe syndrome, characterized by dreamy states, alterations of space and time perception, disturbances of body image, *déjà vu* phenomena and the vivid recall of earlier memories.

In an earlier paper (1954) one of us suggested that the recall of memory might go beyond the frontiers of personal memories and extend into racial or archetypal experiences which have been described by Jung as the racial or inherited memory. There is much experimental work to support this and Aldous Huxley (1954) also gives the notion credence in his work on mescaline. No further theoretical implications of this can be deduced at present, and in practice the archetypal experiences are more material for the analyst if he be minded to use it.

The picture would become clearer if we knew more about the fate of LSD after its ingestion in the body. Lanz, Cerletti and Rothlin (1955) have established that, in the mouse, the half-life time of LSD in the blood is 37 minutes, measured by testing the antagonism of LSD to serotonin on the isolated rat uterus. These authors also attempted to determine the distribution of LSD in the organism. The findings showed that LSD administered intravenously disappeared relatively rapidly from the blood and its presence could be detected in various organs such as the brain, liver and striated muscle. Stoll, Rothlin and Rutschmann (1955) have investigated the distribution and fate of carbon-labelled LSD in the animal body. They conclude that the greater part of the LSD undergoes chemical alteration and is excreted within a relatively short time via the liver and bile into the small intestine, and that, in contrast to LSD itself, the metabolites are water soluble. The LSD content of the liver is especially high, and the ratio for LSD in hepatic tissue and blood remains constant. Independently of the blood level, the LSD content of the brain, however, diminishes more rapidly. These findings, if applied to man, are of considerable significance because the intravenous injection of LSD does not produce any symptoms for 20 to 30 minutes, while the psychic symptoms are not fully developed for two or three hours. Assuming that LSD disappears rapidly from the brain and blood stream the late onset of the symptoms is difficult to explain and LSD phenomena occurring days or weeks after the initial dose are even more difficult to account for unless one postulates the production of a second substance. The nature of this secondary substance cannot be determined as yet, but it is tempting to suggest that LSD, effective as it is in extremely small doses, may initiate biochemical changes in the body which are unknown and which continue for at least some hours.

While further research is called for in the fields of psychology and therapeutics, LSD must also be considered in relation to the problem of schizophrenia. In simple terms, attempts have been made for many years to discover a biochemical basis for schizophrenia. The belief that one single metabolic disorder leading to an over-production of an alien substance may be the cause of this psychosis continues to attract many workers. This theory is given strength by the similarity of the symptoms of a number of drug intoxications, including LSD, to genuine schizophrenia. Thus Fabing (1955) produced evidence that *a*(4-piperidyl) benzhydrol hydrochloride (Frenquel) blocked a schizophrenic dissociation state induced by LSD in a volunteer subject without blocking the viscerosympathetic components of the LSD reaction. He further claims that this compound has demonstrated interesting, though inconsistent, therapeutic properties in some schizophrenic dissociation syndromes. Similarly, serotonin metabolism has been invoked in support of the same theory in view of its
possible antagonism to LSD, as Woolley and Shaw (1954) have suggested. These authors believe that serotonin probably plays a role in maintaining normal mental processes; that metabolically induced deficiency of serotonin may contribute to the production of some mental disorders and that serotonin or a long-acting derivative of it may prove capable of alleviating disorders similar to schizophrenia. Montanari and Tonini (1955) have reported that two schizophrenic patients improved after treatment with serotonin, after chlorpromazine had failed to bring about a remission.

Our own limited experience with both Frenquel and serotonin has not led us to believe that acute hallucinatory psychoses in the schizophrenic group are materially affected by these drugs, but more work is needed to make any positive assertion on this point. In fact, one schizophrenic patient became more hallucinated after he had been given intramuscular serotonin. It is, however, necessary to explain why other substances which antagonize serotonin, such as Brom-LSD, are psychologically inert. (Cf. Cerletti and Rothlin (1955).) Some of our patients who had already taken LSD were given Brom-LSD some weeks later without any psychological changes occurring, whilst others who had never had LSD also experienced no change after taking Brom-LSD.

We therefore believe that there are many objections to a relatively simple biochemical explanation for schizophrenia, whilst on the other hand, there are undoubted links between the research work now going on in the field of LSD and allied drugs and their antagonists which promises exciting developments in the future. There is a great need for continued therapeutic research in this field.

SUMMARY

1. This paper presents an extension of the studies reported by the authors in 1954 which demonstrated the value of lysergic acid diethylamide in the treatment of mental illness. The 36 patients have been followed up for a further 2 years and the results are given. A further 64 patients have been treated since 1954 making a total of 100 in all. Of these 100 patients, 61 have recovered or improved, 32 failed to derive appreciable benefit and 7 were not assessed for reasons which are given. A wide variety of neurotic conditions were treated.

2. The significance of these results is discussed and the causes of failure are commented upon.

3. Special mention is made of the results in psychopathic personalities and obsessional neurosis.

4. A new technique for the treatment of psychotic illness, mostly schizophrenia, by means of an LSD-chlorpromazine combination is discussed. The results are given in 14 cases.

5. The position occupied by LSD in relation to therapeutics and biochemical research in psychiatry is examined.

6. The opinion is expressed that LSD treatment continues to be of the utmost value in psychotherapy, both in cases otherwise resistant to treatment and as a method of avoiding the prolonged time necessary for a full psychological analysis.

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