Bibliography and Epitome

Potentiating Effect of Alcohol on Tranquillizers and Other Central Depressants

Extinction of a learned response under shock-avoidance conditions involving a two-choice discrimination situation was studied in rats.

In a newly-designed apparatus they have measured anxiety reduction, discrimination loss,

and inability to respond, as operationally defined. Phenaglycodol, meprobamate, and alcohol decreased anxiety and discrimination and increased the inability to respond. When the drugs were combined with alcohol, however, anxiety was potentiatingly reduced by meprobamate, chlorpromazine, and pentobarbital. Loss of discrimination by alcohol was potentiated by meprobamate, chlorpromazine, phenaglycodol, and pentobarbital. The complete inability to respond as induced by alcohol was also potentiated by meprobamate, phenaglycodol, and chlorpromazine.

(Authors' Abstr.)

Evaluation of Certain Drugs in Geriatric Patient

No statistically significant differences in beneficial effects were demonstrated when the changes induced by chlorpromazine, reserpine, or pentylenetetrazol were compared with effects of a placebo in senile female patients studied at the Rochester State Hospital.

In isolated instances of drug therapy, sustained improvement was observed to a degree not seen in the group of patients receiving a placebo. These isolated cases were fairly evenly distributed among the groups receiving the drugs under study. An initial improvement during the first six weeks of drug therapy observed in eight patients was followed by a regression to control levels when drug therapy was continued for an additional six weeks. Therefore, initial favourable responses must be viewed with caution.

Patients with the least degree of organic damage seemed to respond better than patients with advanced deterioration. However, the number of patients showing evidence of mild deterioration was small. A tendency to lower the level of functioning in many patients was observed with each of the medications, as compared with spontaneous deterioration observed in the group given a placebo. This tendency was statistically significant in the patients who received chlorpromazine, while the trend was not statistically significant for patients treated with reserpine or pentylenetetrazol.

Undesirable side-effects were most prevalent in the patients who received chlorpromazine. The side-effects included inertia, skin reactions, jaundice (in one case), and pallor. The most frequent side-effects encountered with reserpine included inertia, dryness of the mouth, and diarrhoea. Convulsions occurred in two patients and myoclonus in two patients who received pentylenetetrazol.

In general, it may be concluded that the use of chlorpromazine, reserpine, and pentylenetetrazol (Metrazol) will not effect any significant improvement in the groups of senile patients found in state hospitals.

Urinary "Epinephrines" in Patients with Mental and Emotional Disorders

Studies on the urines of patients with a variety of psychiatric disorders revealed increased excretion of urinary "epinephrines", i.e. epinephrines and/or substances related to it, in most of them. The range of values was the same in the various diagnostic categories and was not influenced by administration as such of tranquillizing drugs. However, improvement, by whatever means effected, was accompanied by lowered excretions.

The urines of depressed and/or psychotic patients contained an unstable fraction that had properties similar to those of adrenolutin: Reaction of this fraction with 2,3-naphthalenediamine yielded a compound with an absorption spectrum similar to that of the compound formed in the reaction between pure adrenolutin and 2,3-naphthalenediamine. Available evidence indicates that the urines studied contained a mixture of epinephrine and an adrenolutin-like substance. Since the latter substance constituted much or most of the urinary "epinephrines" excreted by psychotic patients, it appears that the quantity of catecholamines excreted by psychotic patients is much less than that by patients with anxiety neurosis.

The possible significance of these findings in interpreting the origin of certain mental symptoms is discussed.

(Authors' Abstr.)

AUGUST 1959

Parents of Schizophrenics, Neurotics and Normals

This study has concerned itself with testing the hypothesis that the degree of personality pathology manifested by a patient is a function of the degree of pathology characterizing his parents. The parents of 20 normal men, 20 neurotic men, and 20 schizophrenic men were compared with one another by means of a battery of techniques which included measures not only of individual functioning but also of spouse interaction patterns. It was found that parents of normal men are individually less maladjusted than parents of neurotics and parents of schizophrenics.

There were no apparent differences in this respect between parents of neurotics and parents of schizophrenics. It was further shown that both patents of normals and parents of neurotics may be distinguished from parents of schizophrenics by having closer, more harmoniously intercommunicating spouse relationships.

(Authors' Abstr.)

Disappearance Rates of Infused Epinephrine and Norepinephrine from Plasma

Increased adrenal-medullary and sympathetic-nerve secretions were simulated in a group of schizophrenic subjects and normal volunteers by means of intravenous infusions of epinephrine and norepinephrine. A study of the plasma concentrations attained by the infused catecholamines demonstrated that the rates of utilization of circulating epinephrine and norepinephrine were equivalent for the two groups.

(Authors' Abstr.)

SEPTEMBER 1959

Production of High-Energy Phosphate Bonds in Schizophrenia

The levels of adenosinetriphosphate (ATP), adenosinediphosphate (ADP), adenylic acid (AMP), and fructose-1,6-di-phosphate (F1,6P) and the specific activities (radioactivity per minute per milligram) of ATP, ADP, and F1,6P were measured in the erythrocytes of 10 control subjects and of 10 acute and 10 chronic schizophrenic patients. These determinations were made under basal conditions and after 10 units of intramuscular insulin in a controlled setting.

Comparisons of mean levels of the substances mentioned above revealed no significant differences among any pairs of means, except that the AMP level of chronic schizophrenic patients under basal conditions was significantly lower than that of the control subjects.

Under basal conditions the ATP specific activity of chronic patients was significantly higher than that of the control subjects and acute patients. The ADP specific activity of the chronic schizophrenic group was also higher than that of the other two groups.

Insulin stress increased the specific activity of ATP in the control and acute schizophrenic groups, but decreased it significantly in the chronic patient group. The response to insulin of the chronic schizophrenic group was significantly different from that of the other two groups. The changes in ADP specific activity mirrored the changes in ATP.

Under basal conditions the F1,6P specific activity was significantly lower in the control subjects than in either schizophrenic group. The acute and chronic groups did not differ. Thus, this was the single measure which differentiated schizophrenic from non-schizophrenic subjects. Under insulin stress there was an increase in F1,6P specific activity for the control subjects and a decrease for both schizophrenic groups. These differences in response to insulin were significant.

All the substances measured are involved in biologic energy-transfer systems. Various alternative hypotheses were presented in explanation of the findings. The most likely hypothesis is that in schizophrenia there is a disturbance in the regulation of biologic energy formation and utilization. Further studies are in process to substantiate this evidence and to clarify a pathophysiologic mechanism of schizophrenia.

(Authors' Abstr.)

Effect of Repeated Doses of Insulin on Excretion of Pyrocatecholamines

In summary, it has been demonstrated in mental patients undergoing therapy that repeated administration of insulin results in a markedly diminished response to this hormone, as measured by the output of epinephrine in the urine.

(Authors' Abstr.)

Acquired and Crossed Tolerance to Mescaline, LSD-25 and BOL-148.

It was possible to prove that tolerance to lysergic acid diethylamide (LSD-25) develops very rapidly in man. Tolerance to mescaline also occurs but less rapidly. Subjects tolerant to LSD-25 are very resistant to mescaline effects. Tolerance to mescaline, likewise, seems to be related to a certain resistance to LSD-25 effects. Prolonged administration of 2-bromo-d-lysergic acid diethylamide (BOL-148) does not cause the subject to be resistant to LSD-25. Tachyphylaxis effects to LSD-25 are not visible in man.

(Authors' Abstr.)

The Protein Metabolism in Anorexia Nervosa

A case of anorexia nervosa has been studied for 112 days, with particular reference to the protein metabolism. It is found that administration of large quantities of carbohydrate (61–70 Cal/kg. of body weight) sufficed to reduce the protein loss to a minimum of 0·025 gm. N per kilogram, i.e. 0·16 gm. of protein per kilogram.

In this case, a positive nitrogen balance was obtained, with ingestion of 0·31 gm. of protein per kilogram, or 0·05 gm. N per kilogram, with a caloric intake of 40 Cal/kg.

During the periods of starvation, the nitrogen excretion is found to be considerably greater, amounting to 0·18 gm. N per kilogram, i.e. 1·1 gm. of protein per kilogram of body weight.

The patient had a subnormal temperature and considerably decreased basal metabolism.

The importance is stressed of providing nourishment that is as adequate as possible in anorexia nervosa. Protein deficiency is best prevented by administration of large quantities of carbohydrate, as well as the largest possible amount of adequate protein.

(Authors' Abstr.)

VOL. 1 A.M.A. ARCH. NEUR. JULY, 1959

AUGUST 1959

SEPTEMBER 1959

VOL. 64 AM. J. MENT. DEFIC. JULY, 1959

VOL. 29 AM. J. ORTHOPSYCHIAT. APRIL, 1959

JULY

VOL. 116 AM. J. PSYCHIAT. JULY, 1959

AUGUST 1959

The Physiological Basis of the Treatment of Delirium Tremens

The current study involved the analysis of 700 cases of D.T., including a review of the causes of death of the 17 patients who succumbed to this illness. Forty-five patients were subjected to a study of their water and electrolyte disturbance.

Delirium tremens was found to be a combination of a physiological disturbance and an emotional stress in an individual whose relation to reality is, at best, tenuous. The particular mental event precipitating delirium was felt to be the "pharmacothymic crisis". The physiological disturbance was found to be varied and consisting of one or more of the following syndromes: (1) Dehydration; (2) Low serum magnesium; (3) Low salt syndrome; (4) Brain swelling. The last two, as well as the lack of resistance to infection, frequently found in delirium tremens, were assumed to be due to an inability to respond to stress. Owing mainly to a chronic vitamin deficiency, the alcoholic is unable to respond with the formation of desoxycorticosterone-like, prophlogistic mineral-corticoids.

Methods of clinical diagnosis of the several physiological disturbances involved in delirium tremens were discussed, and suggestions were made to revise the management of this syndrome accordingly.

(Author's Abstr.)

SEPTEMBER

The Administration of BAS, 5-HTP, and Marsilid to Schizophrenic Patients

The administration to 5 chronic schizophrenic patients of BAS alone, of BAS and 5-HTP combined, and of BAS and 5-HTP in conjunction with Marsilid was not therapeutically useful. The fact that the patients did not react to the presumed increase in brain serotonin casts doubt upon the hypothesis that too little or too much serotonin is causally related to schizophrenia.

BAS appears to be a monoamine oxidase inhibitor. The conversion of 5-HTP to 5-HIAA was thus prevented resulting in an accumulation of serotonin in urine.

(Authors' Abstr.)

OCTOBER

Serum Toxicity in Various Psychiatric Disorders

The serum of schizophrenic, alcoholic, and mongoloid patients had no inhibiting effect on the respiratory activity of surviving rat brain. The serum of patients treated with chlorpromazine enhanced the respiratory activity. A slight tendency to elevated values found in recently admitted schizophrenic adults who were not taking chlorpromazine may be due to prior medication before admission. Phenylketonuric serum depressed brain oxidations, though a similar effect was induced by racemic phenylalanine in concentrations above 40 mg. per cent. as well as by other essential amino acids. It has been suggested that the depressant action of various amino acids may be due not to a direct effect of the amino acids, but to aldehyde formation. It has also been known for a long time that a number of toxic amines such as tyramine, phenylethylamine, mescalin, indole and skatol, all inhibit brain oxidations.

The observed phenomenon may explain the general depression of brain oxidations found *in vivo* in phenylketonuria by Himwich and Fazekas. The low cerebral metabolic rate found in mongoloid children *in vivo* by these authors may be due to the brain pathology associated with the condition.

(Author's Abstr.)

Clinical Findings in the Use of Tofranil in Depressive and Other Psychiatric States

1. Preliminary observation would indicate that Tofranil is a useful drug in the treatment of depressive states. It is not a tranquillizer and, therefore, is of little value in other conditions. It is a promising drug which can be used as an anti-depressant. However, its indication and scope must be studied for a longer period to determine what symptoms respond best to it.

2. The effect of Tofranil in many patients can be increased by the concomitant use of a tranquillizer or a stimulant. In a number of patients Tofranil, by removing the depressive elements, frees and exaggerates anxiety.

3. It can be used in combination with electric shock or after electric shock as a maintenance dose.

4. It is of little value in the treatment of schizophrenics and in paranoid types may often aggravate the condition and break down an unstable equilibrium to which the patient has become adjusted.

5. The combined use of Tofranil and a tranquillizer is helpful in certain psychoneurotic states, associated with anxiety or with reactive depressions.

6. It is of value in the treatment of depressions occurring in the older age group.

7. High doses are unnecessary and the effective range is somewhere between 75 and 150 mg. per day.

8. For the most part, side-effects are minimal, particularly in the younger age group. As one approaches the older age group, the frequency of such side-effects increases, but usually they are more uncomfortable than serious. In patients over 60 there may be a tendency to sudden falls which occur without warning. It is recommended that in older patients the dosage be limited to 75 mg. or less.

9. Side-effects can usually be reduced in frequency or intensity by a reduction in the dosage.

10. Long-term use of the drug is apparently necessary as patients may relapse, at least in the early stages when the drug is prematurely removed. Since the drug is rapidly excreted, it is necessary to give the medication 3 times a day.

(Author's Abstr.)

Sensory Deprivation and Schizophrenia; Some Clinical and Theoretical Similarities

It would seem, in fact, that they now have an experimental model of the schizophrenic syndrome superior to the "model psychoses" induced with mescaline or LSD. Not only will perceptual interference reproduce more closely the primary symptoms of schizophrenia, but these disturbances are caused entirely by external manipulation, without the confusion of a toxic psychosis. While of course they cannot assume that approaches such as these will give them valid answers to all their questions, the author believes they have here an important instrument to help them bridge the gap between the laboratory and the clinic.

(Author's Abstr.)

VOL. 24 BULL. LOS ANGELES NEUR. SOC. JUNE, 1959

Multiple Sclerosis as an Incidental Complication of a Disorder of Lipid Metabolism: I. Close Resemblance of the Lesions Resulting from Fat Embolism to the Plaques of Multiple Sclerosis

The first phase of this trilogy of studies on the possible genesis of the lesions of multiple sclerosis in a disorder of lipid metabolism is concerned with a case of delayed death incident to fat embolism of the brain. In addition to the expected widespread petechial haemorrhages, there were also found multiple, irregular foci of demyelination and focal necrosis whose gross appearance and distribution were quite reminiscent of the lesions of multiple sclerosis. To further strengthen this impression were the characteristic changes in the foci of demyelination as observed in the microscopic preparations. All of these lesions were apparently the result of lodgment of globules of fat in the small arterioles and capillaries of the white matter of the brain. The total picture presented by these lesions suggested the possibility that the lesions of multiple sclerosis might also be the result of the deposition in the brain of some lipid globules freely circulating in the blood stream. By the lodging of these lipid particles in the small blood vessels of the central nervous system, a clinical picture of this disease could thereby be produced. Additional studies on this point will point out contributing evidence which may lend support to this conception.

(Author's Abstr.)

Multiple Sclerosis as an Incidental Complication of a Disorder of Lipid Metabolism: II. A Survey of the Geographical, Clinical and Biochemical Evidence: The Significance of Endogenous Fat Embolism

In the first of the three papers of this series concerned with the possible aetiology of multiple sclerosis in some disturbance of lipid metabolism, the structural changes in the brain in a case of delayed death after cerebral fat embolism are described. The multiple and widespread embolic lesions consisted of variously-sized and irregularly-contoured foci of demyelination and necrosis as well as the anticipated petechial haemorrhages. Both grossly and microscopically, these lesions were so strikingly reminiscent of the residual plaques of multiple sclerosis that they not only suggested a mechanism of lesion formation (central infarction) but also pointed to a possible underlying cause (a disturbance in lipid metabolism). This second study consists of a three-fold investigation into the fields of geographical distribution of multiple sclerosis, the possibly significant clinical findings, and of the chemical evidence of alterations in the serum lipids which might explain the occurrence of the lesions of multiple sclerosis as well as the pathogenesis of endogenous (non-traumatic) fat embolism. Geographically speaking, multiple sclerosis seems to be more common in countries or areas (northern Europe, the low countries, Germany, Austria, and Switzerland) where the dietary intake of fat is high while, to the contrary, it is relatively rare in those areas (the Orient) in which the quantitative intake of fat is low. Whether the use of saturated versus unsaturated fat plays any important role in this regard is not yet known. From a clinical viewpoint, evidence of a disturbed lipid metabolism in patients with multiple sclerosis is less convincing. Other than for an occasional complaint of a relative intolerance of a heavy fat meal or digestion of fatty foods, about the most suggestive feature of multiple sclerosis in this respect is the progressive deterioration in weight, to terminate in a marked loss in the fatty tissues of the body. The unverified statement that patients on a low-fat diet have fewer and less severe exacerbations

of the disease may also prove to be significant. Experimental support for this possibility lies in the occurrence of a high chylomicron index in the blood serum in the cases of multiple sclerosis (Thienes). There is extant evidence which suggests a mechanism for the formation *in vivo* of endogenous lipid particles large enough to obstruct the small aryerioles and capillaries of the brain. This mechanism of endogenous fat embolism could, therefore, furnish a source for obstructing micro-embolisms of the white matter capable of producing the plaques of multiple sclerosis. Evidence which would further support this conclusion may be found in a plan of successful treatment during the acute exacerbations of the disease by dissolution of the occluding lipid particles through action of lipases. This aspect of the problem will be considered in the third paper of the series.

(Author's Abstr.)

Multiple Sclerosis as an Incidental Complication of a Disorder of Lipid Metabolism: III. Treatment by Heparin of Acute Exacerbations of the Disease.

This, the third and last paper in a series of studies on multiple sclerosis, attempts an evaluation of a new concept as to causation of this disease. This study has to do specifically with the treatment of the acute exacerbations of this disease with Heparin. This medication is recommended on the theory that the acute phases of multiple sclerosis are the result of lodgment of lipid particles in the arteriocapillary system of vessels of the white matter of the central nervous system. Because even small doses of Heparin are credited by biochemists with the ability to stimulate lipase activity, which should result in an increased breakdown of neutral fats, this substance has been tried in an effort to promote the dissolution of lipid thrombo-embolisms which, according to this hypothesis, are already obstructing these vessels. The apparently favourable results achieved by the present writer in a preliminary trial of repeated intravenous administration of small doses of this medication seems to warrant its further investigation at the hands of others. A regimen is suggested for this purpose.

(Author's Abstr.)

SEPTEMBER

VOL. 20 DIS. NERV. SYST. JULY, 1959

Spectrophotometric Studies on Urinary Constituents of Schizophrenic Subjects

1. A urine test is described which has permitted the correct prediction of diagnosis of schizophrenia with results which agree 85 per cent. of the time with the clinical diagnosis of this disorder.

2. Preliminary studies suggest that this test reflects a difference in metabolism of the amino acid, tryptophane.

(Authors' Abstr.)

Dartal in Treatment of Hospitalized Schizophrenic Patients

The results obtained in a controlled experiment to test the effect of Dartal on hospitalized schizophrenic subjects is here reported: One group of subjects received placebos, another group received a commonly-used tranquillizer while a third received Dartal. Although it is immediately apparent that neither Dartal or the commonly employed tranquillizer are cures for the schizophrenic process a favourable response occurred in the overall behaviour of the

patients receiving Dartal which was greater than in the placebo group and in the group which was given the other tranquillizer.

It is apparent that Dartal does not alter the course of the schizophrenic process although it does favourably influence a number of the individual signs and symptoms, i.e. associations, attention, awareness, feeling, mimetic expression, motor activity, speech and interest in work. It is of pertinence to note that three functions which are considered by most psychiatrists to be cardinal manifestations of the schizophrenic process, namely associations, attention and awareness were favourably altered by Dartal with a change approaching the individual norm or baseline. No change in these functions occurred in the group receiving placebos or the group receiving the other active compound.

No deleterious side-effects on blood pressure, liver function or blood forming organs were encountered in the patients receiving Dartal. Two patients receiving Dartal did show what was interpreted as a toxic manifestation consisting of a clinical picture closely resembling a Parkinsonian syndrome. However, this reaction completely disappeared after the drug was discontinued for 48 hours and did not again become manifest when the compound was resumed at a lower dose level.

The results here reported are based on a study of a numerically small group of subjects. There may be some variation in these results when large groups are similarly studied.

(Authors' Abstr.)

Convulsive Therapy Without Curarization in Severe Somatic Complications

The literature was reviewed to emphasize that for more than 15 years E.C.T., *per se*, without pre-medication, was found to be a safe and relatively simple procedure even when severe somatic or skeletal conditions complicated the psychiatric picture. Five cases of severe combined conditions were reported to illustrate this relative safety of unpremedicated E.C.T. where the skeletal, cardiorespiratory, and neurologic status were distinctly vulnerable. It was felt that in these cases curarization might have added to the treatment risk. Additional cases were presented to illustrate that curarization complicated the E.C.T. procedure and in three instances did not prevent the onset of post-treatment coronary thrombosis. These features were discussed in relation to further researches with electrocerebral therapy and in maintenance electroconvulsive therapy of chronic, relapsing psychoses.

The experience and responsibility of the individual psychiatrist should be the determining factor in the management of E.C.T. rather than general or "legal" subjection to complex curarizing anaesthesiologic procedures.

(Authors' Abstr.)

AUGUST (1)

Deprol in Depressive Conditions

Several new drugs have been introduced recently for the treatment of depressive conditions. Deprol, a combination of meprobamate and benactyzine, interested us because of the previously observed fact that meprobamate alone already possesses certain anti-depressive properties; particularly when administered in dosage higher than usually used in the treatment of anxiety conditions, and when given to patients who exhibit a certain amount of anxiety and tension, even if their psychomotor activity is slightly retarded. The addition of benactyzine is considered to be beneficial as it seems to relieve the ruminative obsessive aspects of the depressive mood.

In the series of patients suffering from varying degrees of depression, Deprol, in conjunction with milieu and various forms of psychotherapy, did benefit a considerable number of patients. The improvement under Deprol consisted mainly in lessening of general depressive mood without euphoria, producing more interest in the surroundings (libido extension), lessening of fear, apprehension, panic and anxiety and marked reduction of irritability, crying spells and insomnia. Patients who manifested marked delusions and hallucinations were least influenced. In a great number of the patients Deprol definitely facilitated psychotherapy while it was much less effective without it.

(Authors' Abstr.)

AUGUST (2)

Introductory Remarks

Today psychiatrists are about to take a good look at various phases of knowledge on nialamide. All research in medicine is designed to benefit the patient. The practitioner, who ultimately dispenses the agent, is an integral part of the process. Without him, medical research would be pure research and not applied research, as it is intended to be.

Those who have carefully and painstakingly assembled this knowledge, are the most prominent and erudite in their field and everyone is very grateful for their help and philanthropy.

The Eastern Psychiatric Research Association, officially incorporated four years ago, has a membership of nearly 200. This membership, among whom is the President of the American Psychiatric Association, Dr. William Malamud, is made up mainly of practising and research psychiatrists. The chief aim of the Eastern Psychiatric Research Association is the fostering of clinical studies on therapeutic methods, drugs and apparatus in psychiatry; and the presentation and publication thereof. Clinical study is there used in its broadest sense and includes not only the study of the effect of an agent on the patient's clinical condition but also chemical, pharmacologic and cognate investigations, all leading to a sound understanding of the agent, its indications and clinical effects, its chief site of action, its absorption, fate and excretion and its side actions.

At the meeting of the American Psychiatric Association in Philadelphia, a round table discussion entitled "Integration of Somatic Therapies in Psychiatry" the author had occasion to say a few words on electroshock therapy (E.C.T.) and drugs. He made special reference to depressed patients, electroconvulsive therapy and psychic energizers. There is no need to relate the extremely favourable clinical reports on these drugs by many of the original investigators; and of the expressed opinion of some that at last, after 20 years, they see the end of E.C.T. Some of these clinicians have practically abandoned E.C.T. in favour of the psychic energizers. Is this wholesale shift of therapeutic agents justified? Many will answer in the affirmative. But are they sure of their answer? No one will dispute, that today the most efficient and reliable therapeutic agent available for relief of depression is E.C.T. This modality is far more effective than any drug presently available. Its results are quick and long lasting. This cannot be said of the psychic energizers psychiatrists have been using. They yield results slowly, the number benefited is considerably less than with E.C.T. and to prevent relapse the drug has to be given for months upon months.

Since the advent of succinylcholine a few years ago E.C.T. has become the safest treatment in psychiatry. With psychic energizers there has always been the threat of liver damage and possibly death. To guard against this, the patient is subjected to repeated blood counts, urine and liver studies. The long duration of the treatment and the repetition of these tests make the treatment more costly than E.C.T. More important than the cost, is the fact that the patients are not relieved quickly and are subjected to a longer period of suffering.

The originator of E.C.T., Dr. Ugo Cerletti, who was recently in America, expressed the opinion that E.C.T. was a trying treatment and that since its inception he had been attempting to find a substitute. He has experimented with injections of emulsions of shocked pigs' brains. His results have been encouraging but not conclusive. Psychiatrists have, for a long time, wished that some day they might have an injection or a drug which would give comparable results to E.C.T. in both percentage of cures and rapidity and duration of improvement. Until such a drug becomes available they should not delude themselves by being over enthusiastic about any agent less effective than E.C.T. They should not become second-rate therapists: second rate because they are afraid to use an agent known definitely to be superior and substitute in its stead a second-best agent. Psychiatrists do hope that nialamide, now to be discussed, will prove to be the agent which they are looking for. Should this not be so, it is hoped that these studies will lead them to discover specific indications for its use at least in certain patients. They should be careful and conservative in passing judgment on any therapeutic agent; for undeserved over-enthusiasm may guillotine any beneficial effect it may have.

(Author's Abstr.)

A Pharmacologic Summary of Nialamide

Nialamide has been found to be a potent, specific, relatively non-toxic antidepressant with important features from a clinical point of view, that is, no adverse effect on liver function or postural hypotensive activity.

(Author's Abstr.)

Transaminase Controlled Nialamide

This report is concerned with the use of nialamide in 23 patients with various mental disturbances. These include reactive depression, manic-depressive insanity, involutional melancholia, schizophrenia, psychopathic personality and barbiturate addiction.

On the basis of recent experience, it can be stated that nialamide is a good amine oxidase inhibitor which will induce remission of depression and apparently is free from serious side-effects.

Dosages with amine oxidase inhibitors were adjusted to levels that would not produce serious liver damage. This was done by means of sodium glutamic-oxaloacetic transaminase (SGO-T) determinations.

(Authors' Abstr.)

Nialamide for the Treatment of Anergy and Depression

The psychic stimulant, nialamide, in a study with 26 hospitalized patients was found to be therapeutically effective, comparable to previously investigated monoamine oxidase inhibitors. Nialamide was markedly effective in alleviating depression and/or anergy in 16 persons, restoring them to a higher level of psychic integration. Of the 16 cases, three were classed as recovered, five as much improved, and eight as improving. One patient showed sporadic improvement and nine were either unimproved or worse with nialamide. Side-effects were anxiety and akathisia in a total of four patients which were quickly relieved by concomitant administration of phenothiazines. Four patients experienced either a mild nausea and headache, transitory choreic movements, a syncopal attack or transitory diarrhoea. There was a slightly elevated BUN in one case. Later studies showed a transitory rise of alkaline phosphatase in one patient. There was no relief of pain in one case of angina pectoris. Evidence of postural hypotension was encountered in one patient. Nialamide appears to have little of any potentiating effect on other phrenotropic drugs. There were no serious untoward effects observed in this study. In addition to alleviation of the anergy and/or depression in 16 patients, there was a complete loss or marked lessening of delusional and hallucinatory content in nine of these.

From the data obtained in this exploratory study with nialamide, it is apparent that this monoamine oxidase inhibitor is a safe, fairly rapid antidepressive and alerting agent; plus beneficent effects on ideation and perception. It alleviated the symptoms in approximately 60 per cent. of hospitalized depressed and anergic patients without apparent relationship to the diagnostic category, the number of previous admissions, the duration of the present illness, the age of the patient, or the severity of the anergy or depression.

(Authors' Abstr.)

Effect of Amine Oxidase Inhibitors on the Conditional Psychogalvanic Reflex in Man

1. Successful response to treatment with amine oxidase inhibitors is associated with diminution in magnitude of the conditional psychogalvanic reflex responses without alteration in differentiation. In most cases the unconditional psychogalvanic reflex is diminished as well.

2. The neurophysiologic and psychophysiologic implications of this finding are discussed.

3. The diminution of the conditional psychogalvanic reflexes is related to dosage, duration of administration and treatment results.

4. Testing of the conditional psychogalvanic reflex is recommended as a means of evaluating adequacy of dosage with amine oxidase inhibitors.

(Authors' Abstr.)

Treatment of Depressive States in Ambulatory Patients

Nialamide, an amine oxidase inhibitor, is a new antidepressant which was prescribed for 100 ambulatory patients (ages 22 to 72) whose essential complaints were depressive symptoms. There were 32 manic-depressives, 17 involutional melancholics, 15 schizophrenics with depressive features and 36 neurotic depressives in this study.

Severely depressed individuals were started on nialamide 25 mg. three times a day and moderately ill patients were given 10 mg. three or four times daily. If after one week there was no improvement the dosage was increased by increments of 10 to 25 mg. a day until improvement occurred or until the dosage was 200 mg. daily.

Phenothiazine tranquillizers and barbiturates were combined with nialamide whenever the depression was accompanied by anxiety, agitation, panic, anorexia and insomnia, marked psychosomatic symptoms, paranoid colouring, or when the depression immediately followed physiological or psychological shock. This combined treatment also was prescribed routinely for all depressed schizophrenics.

Nialamide was given in conjunction with E.C.T. to 16 suicidal patients. This combined treatment was safe but did not reduce the number of shock treatments required.

Side-effects such as headaches (10 per cent.), dry mouth (4 per cent.), sweating (4 per cent.), dizziness (3 per cent.), constipation (3 per cent.), blurred vision (2 per cent.), hypotension (2 per cent.), epigastric distress (1 per cent.) and oedema (1 per cent.) occurred with doses in excess of 100 mg. daily. These were mild and did not necessitate the discontinuation of nialamide. This drug did not cause postural hypotension nor many of the other side-effects produced by other antidepressants.

At the end of eight weeks nialamide therapy 21 patients were improved and 30 were partially improved. Of the 49 treatment failures, 29 patients had a good prognosis and 20 had a poor prognosis. To achieve therapeutic benefit 50 to 75 mg. of nialamide daily was necessary. An occasional patient required as much as 150 mg. daily. Larger doses did not increase therapeutic benefit but were likely to produce side-effects.

Although therapeutically active, nialamide is somewhat less effective than other antidepressants used for the same target symptoms and assessed by similar criteria for benefit. On the other hand because nialamide is well tolerated by patients in every age group and particularly because it apparently does not cause postural hypotension it is safe for the treatment of ambulatory depressed patients by general practitioners and specialists other than psychiatrists.

(Authors' Abstr.)

Effectiveness and Tolerance of Nialamide for Geriatric Patients

Nialamide was studied in three groups of patients to establish dosage, effectiveness and safety. In depressed geriatric hospitalized patients, 25 mg. three times daily is sufficient for therapeutic effectiveness with minimal occurrence of untoward reactions. For agitated hospitalized patients and ambulant patients with the anxiety state, nialamide was not found effective with the 75 mg. dose used.

(Authors' Abstr.)

Clinical Experiences with Nialamide in Depression

What conclusions can be drawn from this series of 50 cases? First, nialamide seems to offer considerable promise in the treatment of certain depressive reactions. It seems most useful in the treatment of neurotic-depressive reactions in patients under 50, and it is of benefit in some patients with depressions of the manic-depressive type. In the older patients suffering from depression. it seems more useful in males than in females. I am unable to explain these differences clinically. Nialamide is remarkably non-toxic as side-effects are very few and minimal. Certainly nialamide seems to be a useful addition to the psychopharmacologic armamentarium.

(Author's Abstr.)

SEPTEMBER

Treatment of Depressions in Private Practice with Imipramine

There were 305 patients in 369 diagnostic entities, given imipramine in dosages varying from 25 mg. to 200 mg. daily. Patients were selected on the basis of the presence of depression or symptoms indicative of a basic depression. Other therapies were used as indicated.

Improvement varied from 36·75 per cent. in those patients who received an initial daily dosage of 25 mg. to 71·4 per cent. in those patients receiving an initial daily dosage of 100 mg. Only those patients who were able to return to their former state of relative well-being were considered improved. The majority of patients were able to discontinue medication in six months, others needed continuation of medication over a period of two years. These latter patients were usually able to continue their state of improvement on a reduced dosage.

Side-effects were generally mild and did not contradict the continuation of the medication. The more severe reactions usually responded to reduction of dosage or by the administration of a tranquillizer.

On the basis of the results obtained, imipramine has excellent properties as an antidepressant without serious side-effects.

(Authors' Abstr.)

A Clinical Study of the Anticonvulsant Properties of Meratran

A group of 40 epileptic patients who had previously received only phenobarbital as an anticonvulsant were divided into two comparable groups in regard to age, I.Q. and sex. One

group was given Meratran therapy; both groups continued phenobarbital therapy at the same dosage level they had been receiving prior to this study.

Statistical analyses indicate that clinically Meratran exhibits a significant anticonvulsant effect and simultaneously overcomes some of the soporific effects of phenobarbital.

Further indications of the anticonvulsant activity of Meratran were found clinically in a small group of patients who had received combinations of phenobarbital and one or more of the other anticonvulsants prior to and during Meratran therapy. The greatest reduction in seizures during treatment with Meratran occurred in this group.

Central stimulating effects of Meratran therapy, when present, were for the most part favourable: increased alertness, less drowsiness, increased motor activity. Undesirable side-effects occurred in two patients whose pre-Meratran psychiatric condition indicated a tendency to anxiety or hallucinations.

(Authors' Abstr.)

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MARCH-APRIL 1959

VOL. 59 J. AB. SOC. PSYCHOL. JULY, 1959

SEPTEMBER 1959

VOL. 94 J. GENET. PSYCHOL. JUNE, 1959

VOL. 61 J. GEN. PSYCHOL. JULY, 1959

The Contributions of Enzymology to Neurochemistry

It is evident as they survey the field of neurochemistry today that the enzymological approach is exercising considerable influence on the minds of those who seek a relation between mental activity and brain chemistry. It has always been the author's belief that such a relation must exist, and this belief has dominated his own investigations in the neurochemical field since he first became acquainted with mental disorder problems nearly thirty years ago. The subject of neurochemistry in relation to mental behaviour has grown rapidly since then in spite, perhaps, of a variety of psychiatric dogmas. It is now developing vigorously and fruitfully, so much so that he feels justified in claiming that in the enzymological approach to neurochemistry they have one of their finest tools for the exploration of the processes of the mind.

(Author's Abstr.)

The Effect of LSD on the Associative Processes

1. The responses of 25-LSD subject to the word association test employed by Rapaport, Gill and Schafer have been compared to those of a control group and to the responses given by groups of schizophrenic, depressive, and neurotic patients tested by Rapaport *et al.*

2. Our analysis shows that in the associative processes, at least, the LSD reaction does not closely approximate any of the principal "functional" psychiatric disorders.

3. Probably the most striking way in which the LSD reaction differs from all other conditions is the abolition of the differential response to traumatic and non-traumatic stimuli. We have attempted to place this phenomenon within the framework of modern ego-psychology theory.

(Authors' Abstr.)

The Value of Photic Stimulation in the Diagnosis of Epilepsy

1. A total of 1,366 patients with unquestionable or suspected epilepsy and non-paroxysmal routine EEGs were exposed to photic stimulation.

2. In 11·2 per cent. of the cases paroxysmal activity was excited. Positive responses were most frequent in the group of cryptogenic epilepsy (24·7 per cent.) and less common in that of symptomatic epilepsy (6·7 per cent.).

3. Photic stimulation was most effective in the younger age groups and in patients with abnormal routine EEGs.

4. In the group with cryptogenic epilepsy there was a higher proportion of paroxysmal reactions in females than in males.

5. Flicker frequencies of 12 and 14 f/s were most effective. ETM resulted in an increase in positive results, particularly in adult patients.

6. In 44 cases, responses occurred which must be regarded as non-specific.

(Author's Abstr.)

Studies on Human Saliva: a Tyramine-like Component and Its Response to Autonomic Stimulation

A tyramine-like compound has been detected as a component of human mixed saliva.

The secretion of this compound is apparently regulated by the autonomic nervous system, as seen by the changes in concentration following a single injection of autonomic drugs in human subjects.

Injection of urecholine gives rise to a definite response curve. Epinephrine also elicits changes in concentration, but not as uniformly as does urecholine.

There is no consistent correlation between changes in salivary flow volume and concentration of this salivary component.

The application of these preliminary findings to the study of autonomic function in man is discussed.

(Authors' Abstr.)

Psychological Studies of Korsakoff's Psychosis: I. General Intellectual Functions

1. The Wechsler-Bellevue Intelligence Scale and the Wechsler Memory Scale were administered to two groups of patients with the Wernicke-Korsakoff syndrome secondary to alcoholism. The first study included observations of 15 patients, who were tested shortly after the onset of their illness and then at periodic intervals ranging from three weeks to 12 months. The second study was restricted to a group of 22 patients who had all reached the relatively stable and chronic phase of the disease and who were tested at periods ranging from 12 months to over 12 years after the acute phase of the illness.

2. The test results disclose a characteristic pattern of cognitive deterioration in the Wernicke-Korsakoff syndrome. There is, however, no evidence that this pattern is specific to this syndrome. The relative degree of deterioration in different cognitive functions changes with the progress of the disease, more particularly as the initial symptoms of general confusion clear up. Presumably because of this differential progress no stable profile of intellectual functioning could be determined for the disease.

3. Memory functions clearly suffer more severely than other cognitive processes, and the most marked and persistent defect is the low capacity for learning new associations or the retention of newly-presented information such as short stories. This failure is particularly marked in tests or situations which require the reproduction of chronological sequences. The clinical disability of Wernicke-Korsakoff patients is largely accounted for by these defects.

4. The results of this study agree in general with previous reports of mental deterioration in Korsakoff's psychosis. However, attention is drawn to the defects in cognitive functions other than those directly dependent on retentive memory. The data also stress the gradually changing character of the mental abnormality, from the onset of the disease to the late stable stage.

5. Results obtained by the standard psychological tests used in these studies can only serve for a preliminary or tentative determination of the psychological profile of this disease. We have therefore regarded the conclusions presented here as a point of departure for a more intensive research geared specifically to an investigation of this cognitive damage in Korsakoff's psychosis. The results of this investigation as well as our observations on confabulation will be presented in future publications.

(Authors' Abstr.)

An Exploratory Investigation of the Effect of Meprobamate on Stuttering Behaviour

Ten stutterers given 600 mg. of meprobamate per day for the first week, 1,200 mg. per day for the second week, 1,600 mg. per day the third week, and 2,000 mg. per day the fourth week showed a reduction in the mean number of stuttered moments. This reduction, while not achieving statistical significance, did show a definite trend and was significant at the ·10 level of confidence for the group that received meprobamate. Non-parametric statistics revealed a statistically significant amount of progressive success with each trial for this group. Their own subjective evaluations confirmed the findings. On the basis of these results, further study is indicated.

(Authors' Abstr.)

VOL. 129 JULY, 1959

A New Drug Causing Symptoms of Sensory Deprivation

Neurological, electroencephalographic and pharmacological data have been presented on over 100 individuals who have been treated with Sernyl, a drug that appears to exert a blocking action on the thalamus and midbrain. This drug eventually produces a blocking of all forms of sensation with pain sensation disappearing first. Motor movement is not impaired, except for ataxia, until the patient becomes unconscious. Blood pressure and reflexes are increased and vertical nystagmus appear in high dosage of the drug. Early and sometimes prolonged symptoms appear that are similar to those reported in sensory deprivation studies; namely, anxiety, illusional, delusional and hallucinatory phenomena with a feeling of displacement. Interference with thinking processes is an early complaint. It is concluded that Sernyl produces a "centrally medicated" sensory-deprivation syndrome.

(Authors' Abstr.)

Blood and Urinary Serotonin and 5-Hydroxyindole Acetic Acid Levels in Schizophrenic Patients and Normal Subjects

The mean concentration of blood serotonin in normal non-psychotic male subjects was found to be 0·19 μg./ml., in chronic schizophrenic male patients 0·17 μg./ml., and in acute psychotic male patients 0·12 μg./ml. The mean urinary excretion rate of 5-HIAA in normal male subjects was found to be 203 μg./hour, in chronic schizophrenic male patients 225 μg./hour, and in acute psychotic male patients 332 μg./hour. The results do not indicate a metabolic defect in serotonin metabolism and therefore do not support the hypothesis of a causal relationship between serotonin metabolism and acute or chronic schizophrenia.

(Authors' Abstr.)

AUGUST

The Influence of Chlorpromazine on Pathologic Emotions and Sexual Unrest

The effective use of drugs in psychiatric treatment requires specific knowledge of the influence of pharmacologic agents on emotions and related psychodynamic factors which may markedly influence the clinical state of any patient. When attention is paid to these features, it is possible to develop a useful scheme, which not only deepens the understanding of the nature of clinical changes induced with drugs, but also allows for the selection of the correct method of treatment for an individual patient in a particular phase of an illness.

This study reports the effects of chlorpromazine in a series of 142 patients who received the drug as an adjunct to intensive psychotherapy in a hospital setting. Good therapeutic results were obtained in patients demonstrating fear, hostility, or related paranoid features. Contrary to general opinion, chlorpromazine appeared to be singularly ineffective in many conditions where anxiety was a leading feature. The marked ability of chlorpromazine to reduce sexual unrest has received very little recognition, yet this influence may contribute substantially to its broad clinical usefulness in the treatment of psychiatric disorders.

(Authors' Abstr.)

The Metabolism of Mescaline with a Note on Correlations Between Metabolism and Psychological Effects

Eleven volunteer subjects were given mescaline intravenously in twenty experiments. For the period of intoxication blood levels and rates of urinary excretion of mescaline and trimethoxyphenylacetic acid were measured and observations made of the subjects' behavioural responses.

The behavioural responses of the subjects varied widely in severity of symptoms and in the pattern of disturbance of mental function.

An average of 31 per cent. of the drug administered was recovered in the urine within the first six hours after the administration of the drug. An additional 7·4 per cent. (average) of the administered drug was recovered as trimethoxyphenylacetic acid.

The blood levels and rates of excretion of mescaline did not fall off asymptotically, but formed a flattening curve and often one with some elevation between the third and sixth hour after administration of the drug. The blood levels and rates of excretion of trimethoxyphenyl acetic acid showed such secondary peaks to an even greater extent.

The period of maximal behavioural changes followed the period of maximal blood level and excretion by one to two hours.

No correlations were observed between degree or type of behavioural responses and blood levels or rates of excretion of mescaline.

The curves of blood levels and rates of excretion of mescaline and trimethoxyphenylacetic acid and the delay in occurrence of maximal behavioural change suggest that mescaline may be converted into some other substance which is directly responsible for the effects on the central nervous system.

(Authors' Abstr.)

An Evaluation of the Therapeutic Use of Triflupromazine in Mental Disease

Examination of the results of this investigation leaves no doubt that triflupromazine is an effective and useful phrenotropic agent. This seems a particularly valid conclusion when the nature of the patient group is considered. All patients treated were classified as chronically ill and were considered to have relatively poor prognosis. Side by side comparison with chlorpromazine in this series of 124 patients showed triflupromazine at least to equal the effectiveness of the older drug. It is likely that if chlorpromazine had been administered by other than a blind technique larger doses would have been prescribed. With regard to potency, our impression is that for equal therapeutic effect, the dosage of triflupromazine should be approximately one-quarter or one-fifth that of chlorpromazine. Few patients required a dosage in excess of 100 mg. of triflupromazine daily and some were adequately maintained on 50 mg. daily. Toxic central nervous system reactions, in our experience, seldom occurred unless the daily dosage exceeded 200 mg.

The battery of psychological tests employed in this investigation confirmed the clinical finding that triflupromazine produced significant improvement in this series of hospitalized patients. The techniques adopted were such as to preclude the possibility that the changes observed were the result of chance. The inclusion of a placebo group provided an objective estimate of changes due both to the increased attention received by patients involved in this study and to the psychological effects of the ritual of taking medicine.

(Authors' Abstr.)

VOL. 22 J. NEUR. NEUROSURG. PSYCHIAT. AUGUST, 1959

Slowness in Schizophrenia

The influence of various factors on the mental speed of a group of schizophrenic patients was investigated by means of the Nufferno speed test. Longer duration of illness was associated with slower performance on the unstressed portion of the test, this being more definite in the case of those patients who also showed inappropriate affect. Patients who had had physical treatment tended to be slower on the unstressed portion of the test and those whose illness had a favourable outcome tended to be faster than the others. A significant relationship appeared between low stress-gain score and favourable social outcome. No satisfactory formula for predicting outcome on the basis of this test could be devised. An effort to correlate speed with disease and recovery failed because of the difficulty of finding patients who had gone through their illness without receiving physical treatment, since this latter formed a complicating factor which could not be allowed for.

(Authors' Abstr.)

The Use of an Object Sorting Test in Elucidating the Hereditary Factor in Schizophrenia

A significant number of parents of schizophrenics with "thought disorder" were found to obtain scores on the sorting test of Rapaport (1945) different from those of control normals but similar to those found in schizophrenic patients.

It is suggested that this test may provide an objective means of estimating the presence of "schizoid" features in the relatives of schizophrenics, and thus aid in the elucidation of the hereditary factors in schizophrenia.

(Author's Abstr.)

A Clinical and Biochemical Study of a Trial of Iproniazid in the Treatment of Depression

A controlled trial of iproniazid on 50 patients with depression showed that 26 of them improved and that the improvement in at least 12 of these was due to the drug. The danger of liver damage was stressed.

An attempt was made to differentiate these groups and to determine the mode of action of iproniazid in those patients who responded. Methods used included parenteral administration of 5-hydroxytryptophan and 3,4-dihydroxyphenylalanine and assessment of urinary 5-hydroxyindole excretion.

(Authors' Abstr.)

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VOL. 18 J. NEUROPATH. EX. NEUR. JULY, 1959

OCTOBER 1959

VOL. 50 J. SOC. PSYCHOL. AUGUST, 1959

Tryptophan Metabolism in Porphyria, Schizophrenia, and a Variety of Neurologic and Psychiatric Diseases

The urinary excretion of 9 metabolites of the essential amino acid L-tryptophan has been determined in 18 patients with acute, chronic, or mixed hepatic porphyria, 19 patients with schizophrenia, 8 patients with a variety of psychoses, and 10 patients with a variety of neurologic diseases. Of 18 patients with porphyria, 13 showed evidence of abnormal tryptophan metabolism characterized by increased urinary excretion of kynurenine, acetylkynurenine, kynurenic acid, hydroxykynurenine, and occasionally, xanthurenic acid or other metabolites. A similar metabolic response was found in 6 of the patients with a variety of types of psychoses. Each of the patients with neurologic conditions metabolized tryptophan in an essentially normal manner.

Although the type of abnormality of the tryptophan metabolism of these patients suggests a functional pyridoxine deficiency, neither biochemical nor clinical improvement resulted following pyridoxine supplementation. Both clinical and biochemical improvement were often observed following treatment with chelating agents.

The possibility that the clinical and biochemical manifestations of porphyria might be related to a disturbance in polyvalent cation balance was discussed.

(Authors' Abstr.)

The Effects of Lysergic Acid After Cerebral Ablation

The observations reported above are typical of 70 experiments conducted over a two-year period. In these tests, all animals were used in various combinations. According to these observations, the young chimpanzee reacts to lysergic acid with a panorama of abnormal behaviour which is consistent and characteristic. If such an animal is subjected to bifrontal lobectomy, his reactions in ordinary situations are radically changed; yet his reactions to the drug are not. Paradoxically, he reacts to lysergic acid in the same way as before operation,

although this massive ablation has obviously affected all other reactions in social, test, and training situations. Indeed, among his various post-operative responses, only the drug reaction remains comparable to those observed before bifrontal lobectomy. Apparently, intact frontal lobes are not essential for the characteristic drug reaction.

On the other hand, if such an animal is subjected to bilateral temporal lobectomy, his responses to ordinary situations are remarkably unchanged, except for a four-week period after surgery. Yet, his response to the drug is obviously changed. Some autonomic reactions remain thereafter, but panic or perceptual aberration does not increase in the post-operative drug reaction. However, unilateral temporal lobectomy does not change the animal's reaction to lysergic acid. Nor does lobectomy alter social or training responses. Apparently, one or the other temporal lobe is essential for this drug reaction in young chimpanzees.

When the temporal ablation includes only the mesial structures, the reaction to lysergic acid is unchanged. Yet, after selective ablation of both lateral temporal cortices, the reaction changes or disappears. Perhaps the lateral temporal cortex and its tapetal connections form essential links in the neurologic chain which constitutes the background of this panoramic reaction.

The reaction itself is a compound of perceptual aberration and panic. As the animal reacts, he may look at his hand and scream. Then his pupils dilate, and his hair stands on end. Or he will react abnormally to the usual forms, colours, and sounds of his habitual surroundings.

According to recent reports, the lateral temporal cortex is concerned with perception. The human reaction and the reaction of the chimpanzee to administration of lysergic acid are certainly characterized by gross perceptual aberration in the chimpanzee. Perhaps the drug disturbs perceptual mechanisms represented in the grey mantle of the temporal lobe.

(Authors' Abstr.)

Effect of Drugs on Discharge Characteristics of Chronic Epileptogenic Lesions

Chronic epileptogenic lesions were produced in the visual cortex of rabbits. The effect of anticonvulsant agents was measured against the discharge frequency of the spike focus, the threshold to photic activation, and the characteristic patterns of spread. A standard Metrazol challenge was used as a means of comparing our results with those obtained in the more usual pharmacologic assays. Dilantin did not produce suppression of the primary focus nor did it appear to limit spread to the basal diencephalon or to protect against Metrazol challenge. However, transcortical propagation was effectively limited.

Spirodone demonstrated effective suppression of the primary focus as well as limitation of spread both to basal nuclei and transcortically. Some protection also existed against Metrazol challenge. Tridione also appeared to suppress the primary focus as well as to limit spread to the basal diencephalon. However, transcortical spread was not effectively limited until the primary focus itself was suppressed. Metrazol protection was the highest of any of the drugs tested. Phenobarbital produced only slight suppression of the primary focus and transcortical spread, good limitation of spread to the basal diencephalon, and good Metrazol protection.

(Authors' Abstr.)

AUGUST

SEPTEMBER

The Psychiatric Application of Vesprin

Vesprin is an effective phrenopraxic drug of the broad spectrum type comparable to chlorpromazine in its general applications. It is more effective and less toxic than chlorpromazine and should be considered the first choice for the treatment of schizophrenic conditions and the obsessive-compulsive neurosis. It is of value in the treatment of senile psychosis and valueless in the treatment of depressions and of manic psychosis—except, in the latter case, as an antikinetic. The drug is almost free from severe side-effects and complications. It interferes less than chlorpromazine with the blood-pressure-regulating mechanisms of the body, but produces a substantial amount of extrapyramidal reactions. Of these last, akathisia is the most bothersome, and this limits the usefulness of the medication in ambulatory neurotics.

(Authors' Abstr.)

JULY

VOL. 1 **PSYCHOPHARMACOL.** 1959

Relationships of Psychotomimetic to Anti-Serotonin Potencies of Congeners of Lysergic Acid Diethylamide

1. The psychotomimetic potency of 13 congeners of LSD-25 has been approximately determined in man.

2. With the exception of acetylation of the indole nitrogen, all the changes made in the LSD molecule reduced psychotomimetic potency. Bromination at carbon 2 caused the greatest inactivation.

3. High potency as a serotonin antagonist in isolated smooth muscle preparations was not correlated with high potency as a psychotomimetic.

4. The data do not support but do not disprove the "serotonin deficiency" hypothesis of the LSD psychosis.

(Authors' Abstr.)

Comparison of the Reactions Induced by Psilocybin and LSD-25 in Man

1. The reaction induced by oral administration of 57 to 114 mcgm./kg. of O-Phosphoryl-4-hydroxy-N-dimethyltryptamine (psilocybin) has been compared with that induced by a placebo and LSD-25 (1·0 to 1·5 mcgm./kg.) in 9 subjects.

2. Both LSD and psilocybin caused elevations in body temperature, pulse and respiratory rates, and systolic blood pressure. Threshold for elicitation of the knee-jerk was decreased by both drugs.

3. After both drugs, abnormal mental states characterized by feelings of strangeness, difficulty in thinking, anxiety, altered sensory perception (particularly visual), elementary and true visual hallucinations, and alterations of body image were reported by the subjects.

4. The effects of psilocybin did not persist as long as those of LSD.

5. LSD is 100 to 150 times as potent as psilocybin.

(Author's Abstr.)

Lithium in Psychiatric Therapy. Stock-taking After Ten Years

Lithium therapy is effective against manic phases of the manic-depressive psychosis; in protracted or frequently recurring mania it seems to offer advantages over other available therapies. Lithium salts are administered orally; they may be given alone or as a maintenance treatment after electric convulsive therapy.

Lithium is potentially toxic, and overdosage may lead to injury of the kidney tubules. A high sodium intake accelerates renal elimination of lithium and serves to protect the organism against intoxication.

Patients suffering from renal or cardiac disease should not be given lithium. In patients receiving lithium the dosage must be regulated according to individual tolerance, and one must make sure that the sodium intake is sufficient and remains sufficient. The patients should be supervised clinically and biochemically.

(Author's Abstr.)

Obesity and the Denial of Hunger

The relationship of gastric motility to the experience of hunger has been investigated. In accord with traditional views a group of non-obese women usually reported hunger during contractions of the empty stomach, and no hunger in the absence of such contractions. A group of obese women, on the other hand, usually failed to report hunger during the presence of stomach contractions. This denial of hunger extended to a denial of sensations of epigastric emptiness and of the desire to eat—fundamental characteristics of the hunger experience among non-obese women. That the denial of hunger was due to a specific difficulty in discrimination in the presence of gastric motility is suggested by the observation that there was no difference between obese and non-obese women in the distribution of hunger reports in the absence of gastric motility.

Obese subjects manifesting the "night-eating syndrome" showed a significantly higher incidence of denials of hunger than did obese persons not manifesting this syndrome.

The suggestion is made that denial of hunger occurs in persons with a conflict over eating who are simultaneously subjected to strong social pressures in this regard. Its function, according to this hypothesis, would be to exclude from awareness any stimuli that signal an approaching caloric deficit with its concomitant conflict over eating.

(Author's Abstr.)