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Memory Disturbances After Electroconvulsive Therapy

Thirty patients were examined with one form of test battery a few days before the first, and with the other form one week after the last electroshock treatment in a series. The two forms of the test battery were used alternately before and after the treatments. The mean number of treatments was 3.6 over a mean period of 10.1 days.

The test battery comprised the three memory tests for evaluation of reproduction immediately after learning and three hours later, described by Cronholm and Molander (1957), called the 30 word pair test, the 20 figure test, and the story test. Another, new test, using paired associates and intended to serve the same purpose, called the 15 letter-symbol pair test, was added to the battery. A vocabulary test was also given.

After the series of treatments there was a significant decline in the measures on the operationally defined variable "delayed reproduction" (the number of items reproduced three hours after learning) in the word pair and the figure tests. In the word pair test there was also a significant decline in the score for "retention" (the quotient of the number of items reproduced after three hours over immediately) and a significant increase in the score for "forgetting" (the difference between the number of items reproduced immediately and after three hours). In the other tests no significant differences between the performances before and after treatment were found.

It is concluded that the adverse effect on memory functions mainly affecting the hypothetical variable "retention", shown to exist six hours after the second treatment by Cronholm and Molander (1957), still persists one week after the termination of a series of treatments, but to a less degree.

(Authors' Abstr.)

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The Occurrence of Paranoid Incidents and Abstinence Delirium in Abusers of Amphetamine

During a period of ten years (1947-1957) 14 patients in all were admitted to Ullevål Hospital, Psychiatric Department for Men, for treatment for amphetamine addiction. Seven of these patients were hospitalized either with an acute paranoid psychosis or they had undergone one or more such psychoses prior to admission. This psychosis was of a temporary nature and disappeared in the course of a few days. None of the patients suffered from a lengthy schizophreniform condition. In the other 7, all of whom had abused other medication, no psychotic symptoms were apparent, but they showed other psychotic reactions (sleeplessness, irritability, suspicion) which were related directly to amphetamine.

In accordance with the pharmaco-dynamics of amphetamine, all the reactions may be understood as a continuum, where the individual disposition, the amount of amphetamine, and the admixture of other substances are the deciding factors for the nature of the reaction.

The psychotic reactions are regarded as special toxic psychoses, and it is suggested that they are connected with the effect of amphetamine on the mechanism of cerebral oxidation.

Four patients developed a delirium psychosis during the abstinence. It is shown that in these 4 patients a common symptomatology is evident, different from that seen in delirium occurring in alcohol addicts and abusers of barbiturates and opium. The characteristic difference is, in the first place, the lack of anxiety and the only slight pronounced vegetative symptoms, while activity and restlessness are greatly increased. There is also a lengthy period of latency and the delirium lasts longer.

It is concluded that it is probable that there is an abstinence delirium characteristic of amphetamine abuse, and that amphetamine is a drug which is as dangerous for addiction as other medication which can lead to toximania.

(Author's Abstr.)

Depressions in Patients Treated with Reserpine for Arterial Hypertension

After a review of the literature 11 female patients are mentioned, all hospitalized, who were suffering from depressions appearing after 1-10 months' treatment with reserpine in daily doses from 0.50 to 0.75 mg.; one patient had been given a whole-root preparation of *Rauwolfia serpentina*, containing 0.3 mg. reserpine. The patients were 42-76 years old (average 58.4 years). A predisposition for depressions is known in five patients. The symptoms were a deep sensation of unhappiness, frequent crying episodes, accompanied by restlessness and anxiety. In one case suicide was attempted. Seven patients had E.C.T., 2 patients a combination of E.C.T. and chlorpromazine, and 2 patients had only chlorpromazine. The treatment had good effect in all cases. Five-8 months after leaving hospital 2 patients had once more reserpine prescribed against arterial hypertension and were later readmitted to the hospital after relapse.

As the discontinuation of treatment with reserpine does not imply cessation of the symptoms, it is not supposed that reserpine can be the only cause of symptoms, but rather that it is a question of provoked endogenous depression.

(Author's Abstr.)

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Childhood Patterns Predictive of Adult Schizophrenia: A 30-Year Follow-up Study

A 30-year follow-up study of 526 children seen in a child guidance clinic shows that of the 284 so far interviewed, 10 per cent. were diagnosed in adult life as schizophrenic and

20 per cent. were diagnosed as no disease. The childhood histories and adult adjustment of the schizophrenic and no disease groups were compared. This comparison shows the following:

1. In childhood the schizophrenic group have more symptoms of all kinds than the no disease group including a large number of anti-social symptoms.
2. More areas of function were disturbed in the pre-schizophrenic child than in the child who in adult life had no psychiatric disease.
3. As adults the schizophrenics have a higher rate of mental hospitalizations than the no disease group.
4. The schizophrenic adults have a higher arrest rate than the no disease group. The schizophrenics are consequently often treated as criminals rather than mentally ill persons.

(Authors' Abstr.)

Iproniazid Chemotherapy in Melancholia

1. Chemotherapeutic remission of melancholia can now be accomplished, in a majority of cases, without resort to E.C.T., by carefully supervised administration of Marsilid (Roche), iproniazid (1-isonicotinyl, 2-isopropylhydrazine phosphate).

2. However, until methods are discovered for accelerating Marsilid's effectiveness in the first few days of treatment, the aggressively suicidal case must still be given E.C.T., which assures most immediate remission of depression. Each case must be carefully evaluated when first seen.

3. This chemical, introduced 6 years ago for the treatment of tuberculosis, is now found to possess much wider scope in medicine including therapeutic efficacy in some apathetic and withdrawn, seclusive types.

4. A major factor in effectiveness of this chemical in accomplishing psychic energization is the prevention of inactivation of the brain-stored powerful hormone serotonin, by its amine oxidase inhibitor action, but other equally powerful chemical interactions may be simultaneously involved.

5. The powerful chemical forces released may induce serious complications unless the physician psychiatrist is constantly alert to the need for frequent alteration of dosage as indicated by his physical findings.

6. Excellent antidotes for certain complications are available.

7. A by-product of major significance is the enhancement of psychotherapy through increased spontaneity, improved sense of well-being and resulting betterment of rapport.

A Hypothesis on the Possible Causation of Hepatitis in Association with Iproniazid

Without doubt the major enigma in administering Marsilid lies in the fact that in rare cases the iproniazid becomes bound in the brain in some unknown way. When this occurs even a small dose can push the B.P. very low and keep it there. The only antidote for this is cortisone, a fact that is not well known. It is these rare cases that may well have resulted in acute hepatitis and death since the B.P. may have remained low without the doctor's knowledge with hepatic anoxic effect inducing acute yellow atrophy.

In discussing this problem, a well-known pathologist, Dr. Edwin Albano (Coroner of Essex County, N.J.) pointed out that anoxia can cause acute hepatitis. Therefore, it is possible that anoxia alone may have been a mysterious X factor we have been seeking to explain through allergy or something else. Therefore it is quite possible that the liver damage cases that have been reported (with a few deaths) may have been due entirely to *anoxia*. How?

This study, although it contains a relatively small number of cases to be sure, establishes the incontrovertible fact that iproniazid has a *hypotensive* effect in the great majority of cases. The author's experience shows that this is so frequent that it is almost a universal effect.

There could be no possible way of determining continuously what the blood pressure level is over a 24-hour period for any patient, but it is perfectly possible that in the variable gyrations of the B.P. that could occur, any patient that shows marked gyrations as a result of this drug, irrespective of the dosage, could have hypotensive effect of such degree as to cause temporary anoxic effects in the liver. This might occur not only once but intermittently while the patient was taking the drug.

It is possible that in the rare fatal case, the outcome might have been prevented if B.P. determinations had been frequent, and excessive hypotensive effect thereby prevented by reductions in Marsilid dosage in accord with the degree of hypotension observed.

(Author's Abstr.)

Trilafon (Fentazin) in the Treatment of Chronically Psychotic Hospitalized Patients

1. Experience with a new "tranquillizer", Trilafon or perphenazine, in treating 90 chronically psychotic hospitalized female patients for a limited period is described.

2. The effects were noted during the period of active administration of the drug and then for a period after termination of the drug therapy. Seventy-two per cent. of the patients showed some degree of improvement; 15 per cent. rose above minimal clinical gains.

3. Side-effects were not serious, were controllable and no deterrent to therapy. The absence of jaundice, blood-dyscrasia and photo-sensitivity are noteworthy.

4. The overall impression is that Trilafon is a useful drug with possibly distinct advantages over the older "tranquillizers" in the treatment of chronically psychotic hospitalized patients. (Authors' Abstr.)

Atropine Coma: A Somatic Therapy in Psychiatry

A somatic therapy for the treatment of selected cases of mental illness is described. Coma is produced by the administration of massive doses of atropine and terminated by physostigmine. Increased accessibility, better contact with reality, and more appropriate affective responses are found immediately after termination of coma, persisting several hours, providing the opportunity for more effective psychotherapeutic assistance.

(Authors' Abstr.)

The Treatment of Depressive States with G 22355 (Imipramine Hydrochloride, Tofranil)

Over a three-year period, more than 500 psychiatric patients of various diagnostic categories were treated with imipramine hydrochloride. It was demonstrated that the compound has potent anti-depressant action. Best responses were obtained in cases of endogenous depression showing the typical symptoms of mental and motor retardation, fatigue, feeling of heaviness, hopelessness, guilt and despair. The condition is furthermore characterized by the aggravation of symptoms in the morning with a tendency to improvement during the day. Treatment with imipramine hydrochloride resulted in full or social recovery in a high percentage of the patients. As a rule, the initial response was evident within 2 to 3 days, while in some cases 1 to 4 weeks of therapy were required. In view of the symptomatic nature of the action of imipramine hydrochloride, therapy must be maintained as long as the illness lasts. The side-effects noted were relatively slight, and with the exception of one case of severe allergic exanthema necessitating discontinuance of treatment, no serious complications were encountered. In some cases of depression, particularly those associated with organic brain damage or schizophrenic psychosis, transitory states of agitation or exacerbation of the psychotic features were noted. These observations suggest the importance of a proper selection of the patients as to type and etiology of depression. While in a number of instances, neurotic, schizophrenic or other depressions were also benefited by the drug, particularly when used in combination with chlorpromazine, electroshock or psychotherapy, it is concluded that imipramine hydrochloride is primarily indicated and effective in the treatment of endogenous depression.

(Author's Abstr.)

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Effects of Nuclear Radiation

A news release from the World Medical Association contains information that because of the great concern of the doctors of the world over the problem of the possible ill effects of radiation from the testing of nuclear weapons, as well as "the hysteria which has developed chiefly from ignorance", the W.M.A. at the request of many of its 55 member medical associations set up a plan to keep the medical profession of the world informed of the facts.

To this end the W.M.A. secured the services of Dr. Lewis M. Orr, of Orlando, Fla., consultant to the Institute of Nuclear Studies, Oak Ridge, Tenn., to address the 12th General Assembly of the W.M.A.

Dr. Orr reminded his audience that processes involving radiation were necessary in the diagnosis and treatment of disease and that "some hazards are implicit in almost all technological advances", and that the use of the X-ray for example in diagnosis, treatment and research is "for the benefit of mankind and can be controlled". It must not be discontinued.

Turning to the hazards of radiation fallout, and in particular to the genetic effects of strontium 90 as compared to the amount of radiation to which the human race has been subjected from natural sources, as well as from tests, the report is mathematically more specific: "the 30-year dose to the gonads received by the average person in the United States of America is estimated to be (a) from background radiation—about 4.3 roentgens, (b) from X-ray and fluoroscopy—about 3 roentgens, (c) from nuclear weapons testing if continued at the rate of the last five years—would give a probable dose of only 0.1 of one roentgen. If nuclear testing were continued at the rate of the two most active years the possible exposure of 30 years would be only about 0.2 of one roentgen."

Dr. Orr gave the opinion that every possible precaution should be taken in making nuclear tests, but that properly controlled testing that could contribute to knowledge and be beneficial to all people in many fields of investigation should not be discontinued.

It is gratifying to note that the report issued by the W.M.A. is in substantial agreement with that of an investigation carried out by the United Nations Scientific Committee.

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The Communication of Suicidal Intent: A Study of 134 Consecutive Cases of Successful (Completed) Suicide

1. A study of the communication of suicidal ideas by 134 consecutive suicides has been done by means of systematic interviews with family, in-laws, friends, job associates, physicians, ministers, and others a short time after the suicide.

2. Two striking findings were that over two-thirds (69 per cent.) of the suicides had communicated suicidal ideas and that 41 per cent. had specifically stated they intended to commit suicide. In the majority of instances, the suicidal communications were of recent onset (months), repeatedly verbalized, and expressed to many persons.

3. Another striking finding was that 98 per cent. of these persons were probably clinically ill prior to their suicides.

4. The frequency of expression of suicidal ideas was not significantly related to age, sex, marital state, religion, whether living alone or not, clinical diagnosis, occupational status, income, or education. Chronic alcoholics had a somewhat greater tendency than the other diagnostic groups to make the specific statement that they intended to commit suicide.

separately. In one psychiatrist's group, the 3 agents were equally effective. In the other psychiatrist's group, the 2 active drugs were equally effective, but superior to placebo.

Differences in the expectations of the two psychiatrists are discussed as a possible factor in these results, despite successful operation of the "double-blind" technique.

(Authors' Abstr.)

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Marsilid (Iproniazid) and Electroshock

Marsilid (iproniazid), so far, is the only drug with powerful anti-depressive properties. Twenty-five out of 32 patients derived benefit from the drug. It is helpful in depressive syndromes in which somatization and retardation predominate, particularly so, if strong neurotic features are present. In one severe chronic schizophrenic syndrome Marsilid had a powerful euphorizing, unblocking effect. It is ineffective in most agitated depressions. It requires considerable length of time before exerting effect. Half of the successfully treated patients relapsed and had to be kept on maintenance therapy.

Toxic features are of considerable degree and frequency. Fifteen out of 32 patients showed serious complications, among them 7 cases of liver damage. The well-known minor complications occurred in the vast majority of patients.

Indications for electroshock and Marsilid will rarely overlap since depressions with neurotic features were never a first choice indication for electroshock, and since the prevalent group of psychotic depressions, the agitated depressions, failed to respond to Marsilid. It appears that the anti-depressive effect of Marsilid is exerted over the sense of increased physical well-being and increased energy induced by the drug. A possibly important chance observation was the disappearance of the manifestations of psoriasis of 40 years uninterrupted duration and their reappearance after discontinuation of the drug.

(Author's Abstr.)

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Studies in Multiple Sclerosis. I

The investigations presented here show that a study of the blood and cerebrospinal fluid from patients with multiple sclerosis presents a clear change in the distribution of the globulins in the cerebrospinal fluid, in the lipid content of the cerebrospinal fluid in the direction of an increase in cholesterol, and an abnormal distribution of lipoproteins in the cerebrospinal fluid without corresponding change in the blood.

A reduced cholinesterase activity in the cerebrospinal fluid was found, as well as a rise in the neuraminic acid content of the cerebrospinal fluid followed by a reduced amount in the blood. There was also a slight increase in the iron content of the cerebrospinal fluid in a few individuals, as well as an abnormal distribution of copper and neuraminic acid with respect to the proteins.

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Cortical and Subcortical Electrical Effects of Psychopharmacologic and Tremor-Producing Compounds

1. The administration of chlorpromazine was invariably followed by the appearance of slow activity of increasing voltage which was very similar to that of natural sleep. This change was not seen following reserpine.

2. Of the subcortical structures studied, the intralaminar nuclei of the thalamus showed the greatest response to chlorpromazine and the hippocampus the least. The globus pallidus showed less slowing under chlorpromazine than during natural sleep.

3. Within the limits of testing, chlorpromazine had little effect on the electrical response to sensory stimulation.

4. Seizure-like activity sometimes followed the administration of either chlorpromazine or reserpine, but was more frequently seen after the latter.

5. The cortical and subcortical electrical effects of four compounds (chlorpromazine, reserpine, Tremorine and pentobarbital (Nembutal)), each capable of producing tremor under various conditions, showed very little resemblance to one another.

6. Potentiation of cortical fast activity normally produced by Tremorine, when pentobarbital was added to the same preparation, correlated to a fairly high degree with the persistence and amplitude of the tremor was seen clinically. Conversely, the "competitive" effects of chlorpromazine and Tremorine in combination frequently were manifested by subsidence of the tremor.

7. Present results do not allow the conclusion that activation of the midbrain reticular formation may be evoked as the mechanisms of chlorpromazine or reserpine tremor.

(Authors' Abstr.)

Evoked Electrical Activity of the Brain During Hypothermia

The retina, optic tract, lateral geniculate body, and visual cortex of the cat were stimulated photically during hypothermia. A progressive decrease in the responsiveness of the visual system was observed. This was manifested as an increase in the latency and as a decrease in the amplitude of response. These changes were reversible with re-warming. The average rate of change in the retina was greater than the average rates of change observed in the optic tract, lateral geniculate body, and visual cortex. A high degree of correlation was shown to exist between the latency and the amplitude of response in the visual system during the cooling-rewarming cycle.

(Authors' Abstr.)

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Pallidotomy and Pallidoamygdalotomy in Certain Types of Convulsive Disorders

Pallidal lesions or combined lesions of pallidum and amygdala were produced in stages in nine epileptic patients selected because anticonvulsive medication was ineffective, and seizure discharges were demonstrable in the basal ganglia by means of depth electroencephalography.

The study of simultaneous electrograms from the scalp and from the basal ganglia showed variable time relationships; in some instances there were apparently simultaneous discharges in all these areas; in others, the scalp discharges preceded; in a third type, they followed the basal-ganglia discharges. This third type suggests the existence of subcortical foci producing secondary cortical discharges.

The post-operative observation period was four months to over two years. Unilateral pallidotomy was sufficient in two of four cases to control the seizures or to diminish their frequency. In one instance bilateral pallidotomy stopped generalized tonic-clonic seizures and drastically reduced the minor attacks. After unilateral pallidoamygdalotomy, in three cases the frequency of the seizures was significantly diminished; in a fourth, this procedure combined with a small lesion in the anterior part of the opposite pallidum was insufficient. For a proper evaluation of the possible therapeutic value of these procedures long-range observations will, of course, be necessary.

The favourable effect of pallidotomy was particularly striking in the so-called salaam convulsions of children. This observation seems to suggest that the basal ganglia play an important part in the mechanism of this poorly understood type of seizures.

The favourable effects of pallidotomy and pallidoamygdalotomy may be due to interruption of corticofugal impulses in the basal ganglia and/or to elimination of subcortical epileptogenic foci.

(Authors' Abstr.)

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Dystonia Musculorum Deformans Alleviated by Chemopallidectomy and Chemopallidothalamectomy

Dystonia musculorum deformans, which has previously been demonstrated to be a progressive incapacitating disease of childhood, characterized by involuntary movements and deformities of the entire body, has heretofore been considered to be unresponsive to medical, surgical, physical, or psychiatric therapy. This investigation demonstrates that dystonia musculorum deformans in children can be alleviated by sufficient-sized, accurately placed lesions in the globus pallidus and/or ventrolateral nucleus of the thalamus.

During the course of this investigation, 16 children with advanced dystonia musculorum deformans were subjected to chemopallidectomy and/or chemothalamectomy. In three cases operation was carried out bilaterally. Thirteen of these sixteen cases demonstrated marked alleviation and reversal of the involuntary movements and deformities of this disease. Documented case reports illustrating this alleviation are included in this report. Such relief has now persisted for more than two years in several of these cases. The disease entity of dystonia musculorum deformans can no longer be considered as a hopeless, irreversible disease. The treatment of choice of dystonia musculorum deformans is chemopallidectomy and/or chemothalamectomy.

(Author's Abstr.)

Studies on Lysergic Acid Diethylamide

Pre-treatment with the neurohumoral blocking drugs phenoxybenzamine (Dibenzylamine), scopolamine, and 1-benzyl-2-methyl-5-methoxytryptamine (BAS) did not attenuate or accentuate the lysergic acid diethylamide (LSD-25) psychosis in man.

(Authors' Abstr.)

Effect of Some Indolealkylamines on Man

Snuff prepared from seeds of *Piptadenia peregrina*, of Puerto Rico, has not been found capable of producing the intoxication attributed to it by natives or by explorers, who have described the use of these seeds under the names cohoba, parica, yopo, and niopo. Two major constituents, bufotenine and dimethyltryptamine, did not appear capable of inducing the reputed action of the snuff, or that of *Amanita muscaria*. Bufotenine, up to 20 mg. intravenously, did not produce hallucinations in schizophrenic subjects, despite profound EEG changes, loss of consciousness, and intense peripheral action of serotonin character. Dimethyltryptamine had less intense physiological action but, above 20 mg. given intravenously or intramuscularly, eruption of preconscious ideations occurred. The action of both compounds was very rapid in onset and of brief duration. The compound 3-(3-dimethylaminopropyl) indole had no physical or psychological effect when given up to 70 mg. intramuscularly.

(Authors' Abstr.)

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Acetylcholine in the Mechanism of Headaches of Migraine Type

By use of a sensitive and specific bioassay method, an acetylcholine-like substance was detected in the cerebrospinal fluid of five of nine patients during headache of the migraine type presumed to arise from dilatation of intracranial arteries.

No such substance was found in specimens from a group of 28 patients with extracranial vascular headache or headache due to nonvascular or uncertain mechanisms; none was detected in specimens from patients with miscellaneous other neurologic disorders, except for two patients with epileptic illnesses, confirming earlier reports.

The results are consistent with, but do not prove, the hypothesis that acetylcholine or a closely allied substance is an active participant in the mechanism of headaches of the migraine type.

(Author's Abstr.)

Studies With a New Hallucinogen

Dosage-response data for some effects of N-ethyl-3-piperidyl benzilate (JB 318) are described.

With doses in the range of 5 to 15 mg. given orally in humans, atropine-like peripheral autonomic effects were induced.

Following administration of the same doses, anxiety, somnolence, illusions, visual and auditory hallucinations, decreased immediate recall, and feelings of "unreality" or a "dream-like" state predictably occurred.

Tactile and olfactory hallucinations, delusions, and ideas of reference were at times noted, but were not predictable in their occurrence.

In doses of 20 mg. or greater, it is likely that a true toxic delirium is induced by this agent.

The peripheral autonomic effects and psychotomimetic effects paralleled each other in intensity.

Individual differences occurred in degree and type of hallucinations and illusions.

Experiences of the immediate past or of early childhood largely determined the subject matter of the illusions and hallucinations.

(Authors' Abstr.)

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Study of Excretion of 5-Hydroxyindoleacetic Acid in Mental Patients

Reserpine, 2 mg. twice daily, was administered to 11 schizophrenic patients and to 6 high-grade mentally defective patients. The excretion of 5-HIAA was increased on the first day of medication in both groups of patients.

The excretion of the serotonin metabolite after the first day of medication and after its cessation was reduced to premedication levels or less.

When these patients were given a second or third course of reserpine at a later date, the excretory pattern of 5-HIAA was essentially the same as during the first course.

The most consistent feature of the experiments was the marked rise in the excretion of the serotonin metabolite on the first day of reserpine medication.

(Author's Abstr.)

Studies of Sleep Deprivation—Relationship to Schizophrenia

The clinical observation that a few schizophrenic episodes are preceded by prolonged insomnia led the authors to postulate that sleep deprivation, although a consequence of the emotional turmoil, might play a critical role in the precipitation of some psychoses. Therefore, studies were made of normal subjects who were kept awake for 72 hours. The setting was a social one, where anxiety was kept minimal. Changes on psychological tests were insignificant, but behavioral and subjective alterations were considerable. Feelings of depersonalization, illusions, hallucinations, disturbances in time perception, and auditory changes were common. Despite the long period of wakefulness, adrenocortical activity remained normal.

In another study subjects were kept awake for 48 hours and then given small amounts of LSD-25. Sleep deprivation markedly enhanced the ego-disruptive effects of the drug. It is suggested that sleep deprivation, when combined with isolation and incapacitating anxiety, may have a pathogenic potential that has not been adequately appreciated.

(Authors' Abstr.)

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Cerebral Atrophy Associated with Boxing

While neuropsychiatric complications in boxers are well known and subject to increasing interest, the cerebral pathology has not been fully explored, particularly with regard to the late sequelae.

Two patients with the symptoms of dementia pugilistica were studied.

Cerebral cortical biopsy in one case revealed mild neuronal degeneration and definite plasmatic gliosis in the lower cortex.

The brain of the other patient was severely atrophic, presenting a picture which grossly and microscopically resembled Pick's disease.

As in other cases, the disease became manifest some years after cessation of professional boxing.

In the absence of focal lesions, the pathogenesis is explained best on the basis of a thixotropic process, leading to premature aging of the brain.

These cases emphasize the complexity of the pathologic processes and the desirability of careful examination of the brains of former boxers.

(Authors' Abstr.)

Studies of the Hypoglycemic Brain

1. Severe insulin hypoglycemia does not lead to any appreciable change in the total deoxyribonucleic acid or the pentonucleic acid content of the brain.

2. The "protein-side-group ionization" of cerebral protein is unaltered.

3. The pattern of the cerebral free amino acids is altered in hypoglycemia. Glutamic acid is markedly decreased; γ -amino-butyric and alanine are also reduced, but to a less extent. Aspartic acid increases during the early stages but later decreases. Aminoacetic acid (glycine) is slightly increased.

4. There is a small tendency for the total nitrogen and acid-soluble nitrogen of the brain to decrease during hypoglycemia.

5. The energy that might be made available from the changes in the cerebral protein, free amino acids, and nucleic acids could supply only a negligible fraction of the total cerebral energy requirement of the brain in the hypoglycemic cat.

(Authors' Abstr.)

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Penicillin Treatment of General Paresis (Dementia Paralytica)

1. Repository penicillin is quite as suitable as aqueous penicillin for the treatment of general paresis (dementia paralytica). Although the minimal effective dose is unknown, the present study permits the pragmatically important conclusion that 6,000,000 units is ample.

2. Penicillin prevents paresis. None of the present group of 1,086 patients had received penicillin for early syphilis. Paresis has not been observed to develop after the penicillin treatment of asymptomatic neurosyphilis.

3. The present study cannot be said to reflect the effect of penicillin alone; rather, it presents only the effect of penicillin with or without fever therapy on a mixed group of paretics, a small, but undetermined, number of whom already had a process apparently arrested by other types of therapy before penicillin was given. That this detracts from the accuracy of the absolute percentages cited cannot be denied, but that it significantly affects the order of magnitude seems unlikely.

4. The trend in recent years in the United States has been toward the treatment of general paresis with penicillin alone. The possible additive effects of fever therapy are not sufficient to justify its use in any significant number of patients. The early diagnosis and prompt penicillin treatment of incipient paresis will result in clinical remission and ability to work in

more than 80 per cent. of patients, and will prevent practically all deaths from neurosyphilis. Even the severely affected or institutionalized patient has 1 chance out of 3 for improvement and rehabilitation for work. In contrast to the dire prognosis of untreated paresis, only 9 per cent. of penicillin-treated paretics are dead of neurosyphilis 10 years after treatment. Even so, the penicillin-treated paretic has nearly four times the death rate of his or her nonsyphilitic age, race, and sex counterpart.

5. The effects of treatment upon the individual symptoms and signs of paresis are, in general, strikingly beneficent. In the majority of cases, however, impairments of speech, insight, calculation, judgment, and general information do not entirely disappear.

6. Paresis strikes most frequently during life's most productive years. It is seen approximately three times as frequently in men as in women, and over twice as frequently in white persons as in Negroes. The usual incubation period is 10 to 24 years after infection, with a spread from 2 to more than 30 years. The simple demented type of psychosis is more frequent than all other types combined. In the absence of previous treatment the spinal fluid Wassermann reaction is always positive, usually with small amounts of fluid, and the spinal fluid cell count is almost always elevated. The blood serologic test may rarely be negative.

7. In general, more than one adequate course of penicillin (6,000,000 units or more) is of no demonstrable additional value in the treatment of paresis. Absence of clinical improvement, persistently abnormal spinal fluid protein level, or persistently positive spinal fluid Wassermann reaction are not indications for re-treatment. Re-treatment with penicillin is indicated under the following circumstances: an initial course of therapy of less than 6,000,000 units, temporary clinical improvement following an initial course with subsequent clinical progression, or spinal fluid cell count of 5 or more after the first post-treatment year. The essentially identical probabilities of death in patients who received one course of treatment and in patients who received more than one is strong evidence against the value of routinely repeated courses of penicillin in the treatment of paresis.

8. Herxheimer reactions, notably exacerbation of the paretic psychosis or convulsive seizures, occur more frequently in the presence than in the absence of spinal fluid pleocytosis. Pre-treatment sedation and often the use of anticonvulsants are advisable. The Herxheimer reaction does not cause long-term damage in paresis.

9. The diagnosis of paresis will frequently be missed if formal pre-treatment examination of mental status is omitted. Indeed, it may be stated that skilled neuropsychiatric examination affords definite prognostic data as to the probability of improvement in psychosis, rehabilitation for work, and, to a certain extent, death itself.

10. Progression and death due to neurosyphilis occur almost altogether in patients with severe pre-treatment psychoses. Post-treatment psychiatric hospitalization is directly proportional to, and clinical improvement and rehabilitation for work are inversely proportional to, the severity of pre-treatment psychosis. Type of psychosis is of less importance prognostically than is severity of psychosis. The shorter the duration of paretic psychosis at time of treatment, the more frequent is clinical improvement and rehabilitation for work.

11. The presence at times of treatment of incontinence, inability to dress self and perform other simple acts of personal toilet, and, to a less extent, of convulsions, affords a particularly poor prognosis for longevity.

12. Work status at time of treatment is of great prognostic import. Of perhaps equal significance is the length of time which has elapsed since the patient has been able to work at his usual occupation.

13. Age within the limits of 30-59 years, race, and sex are relatively unimportant factors in the prognosis of paresis.

14. Pre-treatment pleocytosis indicates an active inflammatory process more susceptible of improvement by treatment, but in a minority of cases leaving behind sufficient brain damage to nullify any real clinical effect. The absence of pleocytosis indicates a relatively static process less susceptible of improvement but, at the same time, less likely to progress. Pre-treatment spinal fluid protein levels are of less prognostic import.

Persistent cell counts of 11 or more were not usually encountered after penicillin treatment. Clinical progression did, however, occur significantly more frequently with persistent cell counts of 5 to 10 than with cell counts of 4 or less. Persistent spinal fluid protein elevations were relatively frequent, but of no prognostic import.

(Authors' Abstr.)

The Pathology of Schizophrenia

The conclusion seems inescapable that no specific change in any tissue or system of the body has been demonstrated that can account for the clinical syndrome of schizophrenia. Even nonspecific histological changes appear to be rarely found, and, when detected, to be unrelated to the psychological derangement. The vast body of literature on the subject falls into two categories: positive pronouncements of anatomical alterations believed to be responsible for the pathogenesis of schizophrenia, and negative reports demolishing this claim. As noted in each of the four successive periods of this review, the great majority of well-controlled and critical studies fall in the latter category. As far as was possible, the reports selected to represent the two categories in any of the four periods have been allowed to speak

for themselves, often in the original author's words; this apposition of one type of work or of one sort of conclusion against another has usually made criticism self-evident, and has absolved the reviewer from the necessity of commenting on each paper separately.

At the end of the longest, most recent review of the subject, the author (Peters) lamented: "The result of this communication is unsatisfactory. The basic pathology in schizophrenia, as in idiopathic epilepsy is not clear." It is pertinent that Peters does not restrict his remark to histopathology; in the term "basic pathology" he probably includes physiological pathology and metabolism as well, implying that the pathogenesis of schizophrenia is not clear. Whether agreeing or disagreeing with this generalization, and without attempting to review all aspects of the currently popular and already extensive subject of biochemistry and metabolism in schizophrenia, the research worker of today might profitably take stock of his specific field of interest and make sure that thought and theories are not passing for facts and things.

At the risk of sounding pessimistic, it appears to the author that it is the lesson of the past that history repeats itself. One need not be shocked, therefore, if the current notion of there being a distorted molecule behind a distorted thought is as difficult to demonstrate as the older belief of a defective neuron behind a defective thought.

(Author's Abstr.)

Effects of Imipramine (Tofranil) on Depressive States

Imipramine, an iminodibenzyl derivative, was given to 145 patients, consisting of 126 with depressive states and 19 with other mental syndromes, with an average oral daily dose of 100 mg. and an average duration of three months.

The depressive states consisted of 98 "typical" and 28 atypical cases. In the former group 82.6 per cent. showed marked to moderate improvement and in the latter group 67.0 per cent.

There was a therapeutic lag of three days to three weeks before the clinical response would become manifest. The optimum period of therapeutic trial was about three months. Side-effects were minimal.

The specific changes concomitant with imipramine administration were investigated in 10 closely observed patients. These were the disappearance of feelings of guilt; a change from feelings of helplessness to those of hopefulness; a change from relatively excessive pre-occupation with internal object relations to a relatively optimal pre-occupation with external object relations; appearance of elation in eight patients, hypomanic state in one patient, and manic state in another; an increased ability to express aggression; the disappearance of the need for alcohol intake in four alcoholics; the lack of alteration in basic, predepression personality structure, which reappeared after the relief of depression. Based upon these observations, a dynamic hypothesis was forwarded that concomitantly with imipramine administration a change in the direction of aggressive drives and aggressive cathecting energies seemed to occur in relation to the internal object system of control (superego elements).

(Authors' Abstr.)

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Corticobulbar Connexions to the Pons and Lower Brain-stem in Man. An Anatomical Study

The distribution of degenerating fibres was studied in the medulla oblongata and the pons of four human brains, in which either an encephalomalacia was present, due to occlusion of the middle cerebral artery, or a haemorrhage in the internal capsule. This was done with the aid of the Nauta-Gygax silver impregnation technique.

In these brain-stems, many degenerating fibres were distributed to the trigeminal motor, facial, hypoglossal and supraspinal nuclei, whereas the spinal accessory nuclei received only

a few degenerating fibres and none were present in the abducens nuclei. In view of its clinical importance, the distribution of degenerating elements throughout the ipsilateral facial nucleus was studied in more detail.

Moreover, the accumulation of degenerating fibres and end-ramifications present in the dorsal grey substance of the spinal cord, was found to continue rostralwards throughout the entire lower brain-stem. Degenerating elements were observed in the region ventral to and in the "hilus" of the nuclei cuneatus and gracilis, as well as in the spinal trigeminal complex and the lateral tegmentum up to the level of the isthmus. In addition, degenerating fibres were found to be distributed to the ipsilateral pontine tegmentum, the medial part of the tegmentum of the medulla oblongata as well as to the lateral reticular nucleus of the medulla, predominantly contralateral to the lesion.

A similar distribution of degenerating elements was found earlier (Kuypers, 1956, 1958) in the cat, after either lesions of the motor cortex or hemispherectomy. However, in this animal, the degenerating fibres to the motor nuclei were almost completely lacking. In view of these and more recent findings in the monkey, it would appear that specifically the fibres to the lateral tegmentum represent the corticofugal link in a phylogenetically older indirect corticonuclear pathway interrupted by one or more synapses in this region, and which in man is paralleled by a more recent direct corticonuclear system.

(Author's Abstr.)

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Neuropathic Observations in Phenylketonuria

Neuropathologic examination of the brain of an 18-year-old patient with phenylketonuria reveals multiple areas of altered myelination associated with variable degrees of fibrillary gliosis. The pertinent literature has been reviewed, and on the basis of this as well as previously published case reports it is concluded that the underlying pathogenetic defect in phenylketonuria may be a metabolically determined disturbance of the glial cell-myelin sheath relationship.

Neuropathologic observations indicate that this disease should be classified with the leucodystrophies and the cerebral lipidoses in the general group of dysmyelinating diseases.

(Authors' Abstr.)

Sudden Bodily Jerks on Falling Asleep

Many normal people occasionally, when falling asleep, experience a sudden jerk of the whole or a part of the body, sometimes accompanied by a vivid sensory experience.

Recordings of electroencephalogram, electrocardiogram, respiration and limb movements have been made during a number of these jerks. The jerks have only occurred during light sleep, often of very brief duration. They have sometimes appeared as part of an arousal response to a faint but significant external stimulus. They sometimes have occurred during

apparent small K-complexes in the EEG. A sudden, sharp, expiratory movement has sometimes immediately followed the jerk; alternatively a more delayed deep inspiration.

The jerks seem to occur, with widely varying frequencies, in nearly every normal person. The view that, when frequent, they should be classed as epilepsy, is critically considered.

(Author's Abstr.)

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Inequality of Palpebral Fissures Before and After Onset in Multiple Sclerosis (A Preliminary Report)

A gross inequality of palpebral fissures was observed in approximately 92 per cent. of 51 patients with multiple sclerosis. The inequality was usually due to ptosis, most often combined with a homolaterally small pupil. The high incidence of this inequality in multiple sclerosis has escaped previous observation, although true Horner's syndrome is generally known as an occasional occurrence.

The question arose whether this finding was or was not a consequence of the disease. Patients were therefore asked for full-face photographs taken prior to the onset of the disease, starting as early in life as possible. Satisfactory prior photographs were studied in 65 cases. Marked inequality was found in approximately 80 per cent. of the group. Usually it was due to ptosis. Pupils could rarely be carefully observed in these pictures.

Study of the photographs was made as follows: enlarged copies (not too much enlarged to obscure clarity of detail) were made of the ocular portions of photographs. These enlargements were studied in two ways: (1) for gross differences in palpebral fissures and for gross evidence of ptosis and of lower lid elevation; where possible, pupils were observed. (2) Careful drawings of lid-edges and irides were made by projecting the enlargements from an epidiascope; these drawings were then used for measurement of maximum interpalpebral differences.

A control study was made from approximately 360 photographs in college and other yearbooks. These photographs were comparable in quality to those of the patients. The control study was deemed necessary because of the commonness of fissure inequality in the general population. Definite inequality of a magnitude comparable to that characteristic of the multiple sclerosis series, was limited to slightly less than 30 per cent. of the controls. Minute narrowing was also more abundant in the multiple sclerosis than the control series. The difference between controls and patients was not only striking, but had a high degree of statistical significance.

The narrowing of the fissure in pre-onset pictures of patients, often may be seen as far back as infancy.

(Author's Abstr.)

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Evaluation of Therapeutic Results of Electric Stimulation of the Diencephalon

The aim of this study was to evaluate selective electric stimulation of different brain areas. Choice of cortical or diencephalic areas had been made possible by the use of special electrodes (naso-pharyngeal electrodes) which can be brought close to the centre of the base of the skull. This method (diencephalic stimulation) with currents of varying intensities, has been practised on several hundred cases of various diagnostic categories and the results tabulated.

It was found that the effects of diencephalic stimulation differ in a characteristic and repeatable manner from the effects of E.C.T. (cortical stimulation).

It was noted that in cases where anxiety and excitement were predominant symptoms, the diencephalic approach produced better results. Neurotic anxiety states as well as manic psychoses usually respond in one to five treatments with minimal currents (one to 3 ma.) with the Reiter machine.

Paranoid conditions with delusions and hallucinations seemed to respond better to a longer series (8 to 15 treatments) with higher currents (up to 15 milliamperes). The diencephalic approach never produced confusion nor memory loss and the EEG remained normal.

Depressive states clear up better with conventional electrode placement on the outside of the skull and higher currents (cortical approach).

Some schizophrenic reactions, particularly chronic conditions previously unimproved, have shown remarkable improvement or complete remission with a combination of cortical and diencephalic approach.

A tabulation of treatment results on 280 patients in Arizona State Hospital was given.

It is concluded that therapeutic results of conventional E.C.T. can be improved by the selection of treatment techniques which vary in local electrode placement, as well as in intensity and quality of current used.

(Author's Abstr.)

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The Mode of Action of Taraxein and LSD

Cerletti summing up the pharmacodynamic properties of LSD suggests that the psychotomimetic part of the LSD effect might involve a "trigger function". Heath, *et al.*, after a series of experiments in monkeys with taraxein followed by Kabi 888 and adrenolutin according to the authors' technique discuss various possibilities of the mode of action of taraxein, e.g. interference with amine metabolism or permeability changes of the blood-brain-barrier. Our experiments discussed above suggest that taraxein and LSD both have the property of enabling certain intravenously injected drugs to act on selected brain centres, not normally accessible to them. Endogenous compounds present in the blood might also produce behavioural changes through the same mechanism.

(Authors' Abstr.)

The Use of Glucagon in Terminating Insulin Coma

The absence of untoward reactions indicated a high degree of safety. Glucagon produces a slow, gradual, and smooth termination of coma in contrast to the sudden awakening with intravenous glucose. No prolonged coma occurred. Tube feeding was not necessary. The outstanding advantage of Glucagon over intravenous glucose was the increased ease of injection, 5 c.c. intramuscularly vs. 50 c.c. of 33 per cent. glucose given intravenously. With Glucagon there was no local reaction when given intravenously or better still, intramuscularly.

(Authors' Abstr.)

A Clinical Study of Marsilid in Psychotic Depressed Patients

The administration of iproniazid to eleven female psychotic patients with depressive features resulted in a lessening of the depression in nine patients. Only one patient went home, while three were transferred to open wards. Analysis of the rating scales showed that the depressive features disappeared, to reveal underlying schizoid thought processes.

(Authors' Abstr.)

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Effect of a Cholesterol Lowering Agent on the Aged Mentally Ill

An emulsion containing pyridoxine and linoleic acid glyceride was administered post-prandially in an oral dosage to ten mentally ill patients on a normal institutional diet. This medication resulted in a substantial decrease in serum cholesterol concentration in nine of the ten patients. A confirmatory study resulted in a decrease of serum cholesterol levels in four out of five of these patients. It appears that the administration of this emulsion to patients on such a diet is an effective therapy for hypercholesteremia.

(Authors' Abstr.)

Toxicology of Marsilid and Other Amine Oxidase Inhibitors*

1. RO 5-0700 (1-picolinyl-2-benzyl hydrazine) and RO 5-0831 (1-benzyl-2-(5-methyl-3-isoxazolylcarbonyl) hydrazine) are more potent inhibitors of amine oxidase than is Marsilid.

2. RO 5-0700 and RO 5-0831 can potentiate the central stimulation produced by 5-hydroxytyptophan and dihydroxyphenyl-alanine and this potentiating activity is stronger than that exerted by Marsilid.

3. Toxicity measurements in various species indicate that the higher potency of RO 5-0700 and RO 5-0831 over Marsilid as inhibitors of amine oxidase does not greatly increase the toxicity. Therefore, smaller dosages of the new drugs may achieve a desirable therapeutic response with less side-effects when compared with Marsilid.

(Authors' Abstr.)

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Migraine and Seizure States in Children

A series of 55 cases of migraine in children seen in the Seizure Control Clinic has been presented. The frequency of this condition in children and its occurrence at an early age have been emphasized. The theoretical consideration of the relationship of seizure states to migraine has been discussed with the general conclusion that severe migraine attacks may be mistaken for seizures in some cases, but that in many cases the convulsive phenomena is actually simply secondary to vascular changes related to migraine.

Excellent results from treatment combining regular medications with either the barbiturates or hydantoin drug and elimination of psychological stress is reported, improvement or control being obtained in slightly more than 80 per cent. of the cases. Prognosis is therefore thought to be good in most such cases despite a severe picture of migraine, seizures and EEG abnormality when the child is first seen.

(Authors' Abstr.)

Evaluation of Two Ataractic Agents

Two drugs—prochlorperazine and benactyzine—were evaluated in separate but similar groups of patients.

Of 188 psychoneurotics and 19 schizophrenics treated with prochlorperazine, 80 per cent. showed marked or moderate improvement in their clinical syndromes. The psychoneurotic reactions, especially anxiety, responded very well to prochlorperazine, as did paranoid delusions in the schizophrenics. The patients were free of disturbing negative psychological effects while on the medication, and their ability to sleep was significantly improved. Prochlorperazine provided no serious or prolonged side-effects during one year of administration.

Of 60 psychoneurotics treated with benactyzine, 25 per cent. showed slight to moderate improvement in their clinical syndromes; the syndromes of remaining patients either remained unchanged or became worse. Severe absent-mindedness disrupted therapy in 40 patients, causing 20 of them to stop the medication voluntarily.

(Author's Abstr.)

Treatment of Depressed and Regressed Patients with Iproniazid and Reserpine

1. Additional evidence of the value of iproniazid in the treatment of depressed, hypoactive patients is presented.

2. The drug increases psychic energy and this may result in clinical worsening as well as improvement in certain types of mental disease. It does not seem to be an ataraxic but can be used in combination with one.

3. The combination of iproniazid followed a week later by reserpine seems to increase the degree of activity.

4. The addition of d-amphetamine to iproniazid accelerates the action remarkably and makes the treatment much more valuable for office use.

5. A variety of other possible applications are suggested.

(Authors' Abstr.)

The Electroencephalogram of Multiple Sclerosis

The EEG findings are reported in 192 cases of multiple sclerosis who had no prior history of epilepsy. Some of these were treated by INH. INH does not influence the EEG in multiple sclerosis. EEG abnormality does not seem to relate to severity of symptoms, nor to the predominant system involved, nor to mental symptoms in multiple sclerosis. The usual abnormality is a random, irregular slowing 5 to 8 per second, diffuse and shifting, but particularly in frontal areas. One hundred and six, or 55 per cent. of the cases at some time or another showed an abnormal tracing. This is a much higher figure of abnormality than is usually reported and would seem to demonstrate the obvious—namely, that when serial electroencephalograms are made, more abnormality is found. Because of this the differential diagnostic value of one electroencephalogram in a case of multiple sclerosis seems small unless it is correlated with the clinical neurological findings.

(Authors' Abstr.)

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Trifluoperazine in Emotionally Disturbed Office Patients

This report summarizes one year's experience with trifluoperazine, a new compound to relieve anxiety, which was evaluated in 155 office patients suffering from anxiety reactions, menopausal syndrome, or functional disorders. Of those treated 71 per cent. showed marked symptomatic relief. The percentage improved was similar even in the 59 patient control group, two had not responded well to previous tranquilizers. Side-effects of drowsiness and lethargy were negligible. In fact, on trifluoperazine, patients reported that their powers of concentration and attention increased and that they experienced no diminution of drive or initiative. Response to trifluoperazine usually occurred within the first week of administration, frequently within the first 24 to 48 hours. Used in low dosages, it does not cause daytime drowsiness or inhibit normal interest and initiative. For this reason, it appears to be particularly useful in treating office patients.

(Author's Abstr.)

Parenteral Methylphenidate Hydrochloride (Ritalin) in Chronic Underactive Schizophrenics

1. The literature on methylphenidate hydrochloride (Ritalin) and its employment as a psychoanalytic drug is briefly surveyed.
2. An investigation into the use of parenteral methylphenidate hydrochloride in chronic withdrawn underactive patients using an Activity-Withdrawal Rating Scale is described.
3. The results of this investigation show that only slight overall improvement resulted except in individual cases where the improvement was more marked but transient and not reproducible.
4. Methylphenidate hydrochloride in the dosage used seems a non-toxic drug, its chief side-effect being anorexia.
5. The results are discussed and some speculations made upon the mode of action of methylphenidate hydrochloride.
6. It is suggested that this drug is worthy of further trials.

(Author's Abstr.)

Iproniazid Used in Attempted Suicide

It was concluded that:

1. There was no evidence of any liver damage as far as could be ascertained.
2. The amount of Marsilid the patient swallowed, 1,500 mg., is apparently the largest amount recorded for any one time.
3. Instead of destroying herself with the Marsilid, the drug temporarily lifted her depression.

(Author's Abstr.)

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Effects of Iproniazid on Chronic and Regressed Schizophrenics

Iproniazid was given for 8 weeks in doses of 150 mg. daily to 32 chronically ill, withdrawn, apathetic and depressed mental patients of both sexes, mostly schizophrenics. An equal number of controls received a placebo. Strict randomization and double-blind procedures were followed. Results obtained by a rating sheet showed that 20 per cent. of the

32 patients treated had shown improvement as to apathy and/or depression. Additional information was obtained from close clinical observation of the group of 14 female patients and their controls included in this study. These results can be summarized as follows:

1. The drug improved alertness, contact, and spontaneity in more than 50 per cent. of patients, and at the same time caused undue agitation in a considerable number, rendering them more aggressive, tense and irritable, and increasing their psychomotor activity.

2. Marked individual weight changes were noticed ranging from a gain of 25 pounds to a loss of 13 pounds. Weight loss occurred in those who displayed tension and agitation under the influence of the drug.

3. Reactivation of psychotic patterns was observed in a small but significant number of patients. No side reactions in the somatic area were observed.

Iproniazid in doses of 150 mg. daily has a marked effect on a considerable number of chronically ill mental patients. The nature of this effect is complex, but therapeutically promising and requires further investigation.

(Authors' Abstr.)

Use of Hydroxyzine in Psychosis

Hydroxyzine was used in 17 cases which were studied closely over a period of six months. Generally, all patients became more interested in their surroundings and became more alert. The drug is considered safe since no side-effects, blood dyscrasias or dysfunction of the liver were encountered. Certain symptom complexes were noted and described in the paper. Hydroxyzine was exceptionally beneficial in alleviating the symptom complexes consisting of overwhelming fear, anxiety or tension and the symptoms of bizarre, autistic or delusional thinking.

In this study, one patient was discharged, one was placed on trial visit and three patients showed continued improvement. One of the improved patients had his medication discontinued and within one week had a return of symptoms. When hydroxyzine was re-prescribed, the symptoms disappeared.

Hydroxyzine has been shown to have a definite place in the treatment of psychotic patients since all these patients had been tried on other tranquilizers and other forms of treatment.

The improvement noted and the results reported have continued to date.

(Author's Abstr.)

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Basic Studies in Mongolism

Investigations on 89 mongoloid and 60 controls have indicated an elevated serum gamma globulin. This finding is statistically significant. Serum glycoprotein and serum free amino acids comparative studies showed no significant differences in the groups studied.

(Authors' Abstr.)

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Cumulative Index of Antidepressant Medications

A preliminary screening procedure was conducted over a period of 15 months in order to evaluate the effectiveness of a number of antidepressant medications. Eleven individual preparations and two drug combinations were studied. Two groups of nine patients were used as controls—the first group received no treatment and the second group was treated with electroconvulsive therapy. As a result of this investigation, β -Phenylethyldihydrazine (Nardil) was selected as the most promising chemotherapeutic agent in depression.

A total of 180 patients with depressions of both endogenous and exogenous origin was treated with this drug for varying periods ranging from 30 to 60 days. This study was conducted over a period of 10 months and comprised twenty series of nine patients.

In the treatment of depression, the response to this antidepressant therapy approached the response generally obtained from electroshock therapy; 80 per cent. of patients were discharged from the hospital as recovered within 60 to 90 days following commencement of treatment with Nardil. The remaining 20 per cent. improved with supplementary medications to the extent that electroshock treatment was never required. No significant side-effects on laboratory abnormalities were encountered.

(Author's Abstr.)

Administration of Taraxein in Humans

We have described the clinical effects noted in humans when administered taraxein, a large protein molecule isolated from the blood of schizophrenics. We feel the symptoms which are produced by rapid intravenous injection of this substance to be characteristic of schizophrenia and not similar to the effects obtained from injection of positive control substances such as bulbocapnine or D-LSD-25.

(Authors' Abstr.)

Evaluation of Deprol in Psychiatric Out-Patients

1. Deprol (meprobamate 400 mg. and benactyzine 1 mg) is not particularly effective in the treatment of out-patient schizophrenics at a dosage of four tablets daily for two weeks.

2. Meprobamate alone produces more overall improvement in such patients. In the author's opinion, it is superior to Deprol or benactyzine and may be used in doses of 400 to 1,600 mg. one to four times daily depending upon the acuteness and severity of the anxiety.

3. Deprol seems to have more antidepressant effect than benactyzine or meprobamate alone.

4. Deprol has no specific effect on delusions or hallucinations.

5. In dosages of one tablet four times a day, Deprol has no consistent side-effects but does produce occasional drowsiness.

6. Drug studies such as this are replete with pitfalls. Patients with a good prognosis may easily be selected. Double-blind techniques are not a guaranteed safeguard against bias. Statistics based upon numbers which have no basis in any unit of measurement are of questionable validity.

(Author's Abstr.)

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Clarification of the Action of Successful Treatment in the Depressions

Taking into consideration only such types of depression as called by the author affective and endogenous, a research design was established to determine if organic drastic therapy beneficially influenced such conditions by their symbolic apperception or through biological action. "Mock" E.C.T. and transorbital leucotomies were compared in results to real surgery and electrocoma applications, under strictly controlled conditions, and the results showed no effect from the "mock" treatments and excellent results from the actual ones.

The action of E.C.T., psychosurgery and the phrenopraxic drugs was studied and it was concluded that they act by lowering to normal exacerbated psychocerebral centres whose overactivity inhibits associative and conative, in addition to affective, areas, thus inducing depression.

An analysis of the results obtained with all the above methods of treatment, their mutual comparison, and their further comparison with the results obtained with analeptic and special central stimulants of the coca type, brought out the fact that three elements are involved in depressions of the types described; effective and conative inhibition, motivational inhibition and psychomotor inhibition. All the successful antidepressant treatments studied act on one or two of the inhibited areas, but not all three except indirectly. The complete antidepressant has not yet been produced.

(Author's Abstr.)

CO₂ Therapy in Broad Spectrum Psychiatric Treatment

Carbon dioxide therapy (CDT) has an important place in office psychiatric treatment of mild psychoneurotics, but it must be used with discrimination or adverse reactions and wasted efforts result. CDT should not be used unless the physician also has facilities for giving E.C.T. because CDT can bring out a latent endogenous depression which may lead to suicide if the warnings are overlooked and appropriate supervision and E.C.T. treatment are not instituted. Non-coma carbon dioxide treatments (CDTnc) are useful in clearing repressed material from the upper layers of the unconscious mind so that coma treatments result in less violent reactions. CDT is an abreactive therapy which is mainly useful as an adjunct to intensive psychotherapy of a type which the author calls psychopcnetration. CDT is dangerous in endogenous depressions, may cause the patient to interrupt prematurely therapy if over-reactions are permitted, and is futile in the treatment of established schizophrenics and psychopaths. It sometimes is useful in the final reconstruction phase of the successful treatment of schizophrenics and of severe schizoid neurotics. Theories regarding dissociation were discussed.

(Author's Abstr.)

Effect of Phenothiazine Derivatives on Liver Function

In 60 psychiatric patients with weekly controls and another 55 patients less carefully studied during therapy with different phenothiazine derivatives (chlorpromazine; KS 75-, KS 33-, TP 21-Sandoz) transient and slight liver cell dysfunction was observed in about one-fifth of the patients receiving chlorpromazine and KS 75. In addition in both of these drugs the cholestatic reaction was observed. A possible relation of the two mechanisms of liver dysfunction is discussed and the literature is reviewed. More consideration should be given to the potential liver toxicity of phenothiazine derivatives when new derivatives are used in therapy.

(Author's Abstr.)

Histopathologic Findings in the Liver and C.N.S. Following Administration of Tranquilizing Drugs

On the basis of the review of the literature as well as on the basis of the authors' own material it appears that:

1. The liver dysfunctions are frequently associated with structural changes caused by biliary stasis of an obstructive variety. The clinical and pathologic findings are generally mild, transitory and reversible in character, thus indicating a possible relationship to idiosyncrasy or constitutional predisposition. The severity of the dysfunction and the pathologic findings

appear frequently to be related to pre-existing abnormalities of the hepato-biliary tract or to the existence of other disease processes which might have an effect on the liver.

2. The adverse neurological reactions are represented predominantly by extrapyramidal symptoms followed in order of decreasing frequency by epileptiform seizures and dystonic-like symptoms. The frequency and intensity of epileptiform attacks appears to be related also to predisposing factors (questionable history of previous epileptiform manifestations, post-lobotomy, and associated with E.C.T. treatment).

3. Definite conclusions concerning characteristic structural alterations as the basis for the observed neurological complications cannot be drawn from the neuropathologically studied cases reported in the literature (3 cases) or from the authors' own personally studied 10 cases because their number is too small when compared to the number of discussed complications and because these cases appear to be associated with other pathological processes which could have conceivably masked or intensified whatever changes were present. However, the structural alterations of the basal ganglia, some hypothalamic and mesencephalic structures observed in some of the human cases may possibly be the result of a neurotropic activity of the studied tranquilizing drugs.

4. The liver dysfunction, agranulocytosis, and neurological complications appear in general not to be related to dosage, duration of treatment or age. Generally they were mild, transitory and reversible in character. In the majority of cases clinical recovery followed upon decrease or interruption of drug therapy.

5. The increased severity of the above discussed complications, in certain predisposed individuals strongly militates against indiscriminate use of these drugs.

(Authors' Abstr.)

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Treatment of Depressive States in Office Practice

Deprol was used in the treatment of 77 ambulatory depressed patients in private office practice. Two psychiatrists and two internists participated. Maximum dosage used was one tablet four times daily and average duration of treatment was five weeks.

The drug was effective in the treatment of depression. Best results were obtained in neurotic depressions in which 85 per cent. of the patients were improved to some extent by the medication, and 64 per cent. almost completely recovered. In psychotic depressions 53 per cent. showed some improvement, 21 per cent. improved to a measurable degree.

When compared with stimulant drugs or other antidepressant medications used for the same patients, Deprol was found to produce greater improvement in 61 per cent., comparable improvement in 27 per cent., and less improvement in 12 per cent.

The cardinal symptoms of depression—psychomotor retardation, self-reproach, insomnia and anorexia—were all favourably influenced by Deprol. In neurotic patients, suicidal thoughts were strikingly counteracted. Doctor-patient rapport was better and psychotherapy was facilitated by the use of Deprol when this was part of the treatment.

Important benefits of treatment noted were: (1) prompt action; (2) unimportant side-effects: (3) lessened insomnia; (4) no loss of appetite; (5) no liver dysfunction; (6) or other toxic symptoms requiring constant surveillance and laboratory tests.

(Authors' Abstr.)

Deanol: A Clinical Trial

The results indicate that about one-fourth of psychiatric outpatients with depression show improvement of this symptom after one month of treatment with deanol. This improvement was more marked in the psychotic patients who were depressed than in the depressed neurotics. A control group would be necessary in order to compare this with a spontaneous remission rate in similar depressed patients. These results can be compared to the remission rate of 23 per cent. in depressions found by Gottlieb using amobarbital and amphetamine, and to the 40 per cent. remission rate with iproniazid therapy of depression reported by Cook. This clinical evaluation indicates that deanol may be worth a trial of at least four weeks, particularly for depression with insomnia in psychotic patients.

(Authors' Abstr.)

Preliminary Study of Isocarboxazid, an Iproniazid Analog

1. Ro 5-0831/1 was given in a mean dosage of 30 mg. daily to a group of depressed hospitalized patients; 11 showed maximal improvement, seven moderate, and three minimal; five were unimproved and four worse.

2. It was given in mean dosage of 60 mg. daily to 21 extremely regressed patients. Two of these patients obtained maximal psychiatric improvement and seven others showed varying degrees of "psychic energization".

3. Seven schizophrenics, chronic but not extremely regressed, were given Ro 5-0831/1. Two improved maximally, one moderately, and one minimally. One was unchanged and two became worse.

4. Hypotension plus vertigo occurred in five patients of the 58. Three patients were taken off the medication due to this difficulty. Other patients were able to tolerate the drug despite side-effects. Four patients had extrapyramidal-like symptoms. Two cases had edema temporarily. Side-effects were less frequent among the vegetative patients on 60 mg. daily than among the depressed patients on a mean dose of 30 mg. daily.

(Authors' Abstr.)

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An Assessment of the Value of Sleep-Electroencephalography for the Diagnosis of Temporal Lobe Epilepsy

1. The diagnostic importance of sleep electroencephalography for the EEG diagnosis of temporal lobe epilepsy was studied in two groups of patients. Group I consisted of 228 temporal lobe epileptics who underwent temporal lobectomy for their seizures. Group II represents a sample of 100 patients who gave a typical history of temporal lobe attacks, but were not subjected to surgical therapy.

2. In Group I the EEG diagnosis of temporal lobe epilepsy was made without sleep in 94.3 per cent. of the cases. In Group II the EEG diagnosis of temporal lobe epilepsy was made in 72 out of the total number of 100 patients. In Group II sleep was only necessary for the diagnosis in 6.9 per cent. of the 72 patients in whom a positive EEG diagnosis of temporal

lobe epilepsy could be made. Out of 25 cases in whom no clear EEG diagnosis was made 10 had sleep records taken with negative results.

3. Among the 77 patients of Groups I and II in whom sleep records were obtained 44 showed more active epileptic discharge during sleep, whereas 23 showed no such activating effect or even some reduction of epileptiform abnormality during sleep.

4. Patients with a history of nocturnal attacks are more likely than others to require sleep activation to bring out the epileptiform abnormality, although even in this group the number of cases in which the diagnosis can be made from the waking record is still high. The higher incidence of cases in which sleep is necessary for the EEG-diagnosis among patients giving a history of nocturnal attacks is statistically significant.

5. No statistically significant difference was found between natural and drug-induced sleep with regard to their propensity to activate temporal lobe abnormalities.

6. It seems that electrocorticograms taken in temporal lobe epileptics during general anesthesia tend to show less clear diagnostic signs than those taken under local anesthesia.

7. The pathological lesions found in patients whose temporal lobe EEG abnormalities were activated by sleep and those found in patients where no such activation occurred show the same relative incidence of atrophic versus space-occupying lesions.

8. The main conclusion drawn from these findings is that although sleep tends to activate the temporal lobe epileptiform abnormality in a majority of cases, sleep electroencephalography need not be carried out as a routine procedure in patients giving a history of temporal lobe seizures, since in more than 90 per cent. of the cases in which a positive EEG diagnosis can be made this diagnosis can be established in the waking record.

(Authors' Abstr.)

Electroencephalographic Changes in Man During Use and Withdrawal of Barbiturates in Moderate Dosage

1. In contrast to doses of over 0.6 g. per day, the withdrawal of 0.4 g. daily of secobarbital or pentobarbital after three months was not followed by psychotic or convulsive manifestations in any of 18 non-epileptic subjects.

2. Seven of 13 individuals demonstrated some evidence of EEG tolerance to 0.4 g. daily of secobarbital or pentobarbital during 90 days.

3. During withdrawal from this same barbiturate regimen, 5 of 18 subjects developed paroxysmal EEG discharges which later disappeared and were not associated with observable clinical abnormalities.

(Authors' Abstr.)

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The Relationship of Epilepsy to Breech Delivery

In a group of 92 patients with epilepsy whose EEG's revealed diffusely distributed, bilaterally synchronous, spike and slow wave discharges the proportion of breech born individuals (19.6 per cent.) was found to be significantly greater than the proportion of breech birth (3.4 per cent.) in the general population. In contrast, the proportion of breech born individuals (2.8 per cent.) in a group of epileptic patients with localized EEG disturbances did not differ significantly from that in the general population. The proportion of breech born in a group of 20 patients who had petit mal seizures and also in a group of 20 patients with "classical spike and wave" was significantly greater than that in the general population. The high incidence of breech birth in patients who have epilepsy of the type associated with bilaterally synchronous spike and wave EEG disturbances strongly suggests that breech delivery is an important factor in the pathogenesis of this disorder. Breech delivery does not appear to be an important factor in the origin of focal cerebral seizures.

(Author's Abstr.)

Effects of Lesions of the Rostral Thalamus on Brain Waves and Behaviour in Cats

The EEG and behavioural effects following rostral thalamic lesions were studied in 14 cats; 3 with complete transection, 5 with complete electrolytic lesions, and 6 with partial destruction.

Behavioural effects following either complete transection or complete destruction of the rostral thalamus were similar in quality, but different in the degree of severity. The signs and symptoms were: spasticity, difficulty in walking and swallowing, reduced motility and reactivity, catatonic reaction, tendency to stick the head in a corner, and so on. These changes could last from 2 to 8 weeks. The only residual effects were some spasticity of the legs and a slight increase of docility. Cats with rostral thalamic destruction could learn a visual discrimination.

EEG effects following either complete transection or complete destruction of the rostral thalamus were again similar in quality but different in the degree of severity. (a) The arousal pattern could be elicited within from 3 to 25 days after surgery. As shown by 3 cats with massive lesions, EEG arousal could be absent during behavioural arousal. (b) The sleep spindles were either absent throughout the post-operative survival period or might have recovered to some slight extent within 3 (transection lesion) or 5 (electrolytic lesion) months. (c) Both barbiturate bursts and recruiting responses were seen to be affected at the terminal experiment, i.e. restricted to localized cortical areas and poorly organized in form.

Partial damage to the rostral thalamus caused only transient and slight behavioural and EEG changes in the immediate post-operative period.

The results are discussed in relation to the thalamic role in behaviour and the functional significance of the final common path from the thalamic diffuse projection system to the cortex.

(Authors' Abstr.)

Electrocortical Manifestations of Epilepsy in Monkey

1. Studies were made on the local cortical potentials evoked in different areas of the monkey brain. These potentials appeared as predominantly surface-negative waves, and consistent patterns in the appearance and amplitude of the responses were exhibited by each area studied. Maximal voltages characterized the "motor area", while minimal deflections were found in the prefrontal and occipital cortex, intermediate values were present in other areas.

2. Correlation was found to exist between the excitability of cortical loci to single-shock stimuli as manifested by local cortical responses and to high-frequency stimulation as indicated by seizure after discharges.

3. When enhanced epileptogenesis was induced in a locus of the motor region by chronically circumsecting an area of cortex in a mirror site on the opposite hemisphere, increased responsiveness to single shocks was observed in the remote cortical locus. This epileptogenic effect was not due to tonic influences from the circumsected area since its excision or procainization or callosal section did not alter the augmented response.

4. The concept of dendritic depolarization as an index of neuronal excitability was discussed in relation to observed variations in the local cortical response. It was proposed that this concept could conceivably be extended to account for differences in seizure susceptibility exhibited by various cortical regions.

(Authors' Abstr.)

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A Behavioral Study of the Functions of the Rolandic Cortex in the Monkey

The experiments reported were designed to study the functional role of the precentral and postcentral gyri with special reference to somatic sensation. Six monkeys were studied neurologically and while they performed visual and somesthetic discrimination tasks. The somesthetic tasks were performed in darkness and the animals were observed with an infra-red television device.

Ablation of somatic receiving areas I and II resulted in a severe tactile defect in the limbs contralateral to the lesion, but a simple somesthetic form discrimination task was relearned after unilateral and bilateral ablation. The ability of the animals to perform this task together with the presence of a "grasp reflex" and a form of cutaneous placing reaction suggests that some form of cutaneous sensation remains after ablation.

Ablations of the precentral agranular cortex result in a temporary sensory defect detected by the initial loss of the "instinctive grasp" and tactile placing reactions, but the somesthetic form discrimination was performed without deficit.

Unilateral ablations of the combined precentral and postcentral arm area resulted in a severe sensory loss in the contralateral arm and the two animals studied were unable to perform the somesthetic discrimination task with the affected limb although a visual discrimination task was readily performed.

These findings suggest that the precentral gyrus subserves somesthesia in the absence of the postcentral gyrus. The relation of these findings to the character of the precentral afferent projection and to the functional differences between the precentral and postcentral gyri are discussed.

Analysis of the retrograde thalamic degeneration in the brains of the animals reported here, suggests that the granular tactile receiving area is the essential projection field of the ventro-basal (tactile) complex of the thalamus. Observations on the effect of Rolandic lesions on motor function are also presented.

(Authors' Abstr.)

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Projection of the Gracile and Cuneate Nuclei in Macaca mulatta: An Experimental Degeneration Study

1. Following lesions to the gracile and cuneate nuclei in three monkeys, axon degeneration was traced by the method of Nauta.

2. The efferent fibres from these nuclei were found to decussate completely, and to terminate almost exclusively in the nucleus ventralis posterolateralis thalami.

3. A small amount of terminal degeneration was seen in the n. paralemniscalis, embedded in the medial lemniscus in the mesencephalon.

4. No terminal degeneration was found in the brain stem reticular formation, or in nuclei of the extrapyramidal motor system.

5. The significance of these findings is discussed with particular reference to:

1. The extrapyramidal motor system.

2. Lateralization of sensory representation.

3. The nature of afferent impulses to the brain stem reticular formation.

(Author's Abstr.)

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Some Projections from the Peri-central Cortex to the Pons and Lower Brain Stem in Monkey and Chimpanzee

In monkeys, using the Nauta-Gygax silver technique, cortico-bulbar fibres were found to distribute to the motor nuclei, the spinal trigeminal complex, and adjacent lateral tegmentum. The origin of these projections appeared to be the following:

The fibres to the motor nuclei originate primarily in the posterior parts of the pre-central gyrus (face area), while the fibres to the lateral tegmentum exhibit a more diffuse pre-central origin. In the chimpanzee, in contrast to the monkey, the posterior parts of the pre-central gyrus (face area; approximately area 4) project almost exclusively to the motor nuclei, while the fibres to the lateral tegmentum originate from rostrally adjacent cortical areas, together with additional fibres to the motor nuclei. It was inferred that the fibres to the lateral tegmentum represent an "indirect" cortico-nuclear projection.

The cortical fibres to the spinal trigeminal complex originate primarily in the post-central gyrus. This gyrus also distributes fibres to the posterior horn of the spinal cord (nucleus proprius) as well as to the region of the nuclei cuneatus and gracilis. The latter projection has an additional origin in the pre-central gyrus.

(Author's Abstr.)

Responses to Electrical Stimulation of the Cerebellum of Unanesthetized Birds

1. Selected loci in the cerebellum have been stimulated in a series of 40 chickens and three pigeons.

2. The responses observed can be divided into three phases—stimulus, rebound and long after-effect.

3. Every bird stimulated responded by swaying or rotating and squatting (flexion of antigravity muscles).

4. Appendicular responses associated with balancing were noted and compared with like responses observed in a normal animal.

5. Head turning was observed in all cases except when the stimulating electrode was on the midline. Simple ipsilateral turning only followed stimulation of all areas except the region of centralis and culmen. Stimulation of points in these regions but not on the midline gave mixed head turning responses.

6. Neck movements were elicited from all areas stimulated, but the pattern of responses varied from folium to folium. Extension of the neck musculature was obtained from centralis, folium IV of culmen, declive, and uvula. Retraction was obtained from folium Vb of culmen and tuber; mixed responses were obtained from folium Va of the culmen and from the pyramis.

7. Movements of the beak, tongue or nictitating membranes were recorded from centralis, declive, tuber and pyramis.

8. The pyramis was the most consistent source of discrete wing movements. Other areas, Va of culmen, VIa+b of declive, and pyramis also gave wing movements that were not associated with balancing.

9. Centralis, IV of culmen, and uvula gave precise stimulatory and rebound movements of the tail.

10. Birds stimulated in areas posterior to the fissura secunda had a hyperactive long after-effect; those stimulated in other regions of the cerebellum showed a period of quiescence which in some instances was interrupted by a period of activity.

11. Three pigeons stimulated while flying required a greater intensity of current to produce a response than was needed while they were standing or walking.

12. Under comparable conditions to those of the chicken, stimulation of the pigeon's cerebellum gave similar responses, i.e. homolateral head turning, tilting, and flexion of leg muscles. The rebound phase of head turning, while the animal was walking or standing, was observed in every case.

(Author's Abstr.)

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A Life-table for Mongols With the Causes of Death

A life-table has been prepared for nearly 700 mongol children attending The Hospital for Sick Children between 1944 and 1955. This indicates that of live-born mongols thirty per cent. are dead by the age of one month, fifty-three per cent. by one year and sixty per cent. by the age of ten years. The findings are in good agreement with a series from Birmingham born between 1942 and 1952. It is confirmed that the sex-ratio for mongolism increases with age and is probably already high at birth. A comparison of the mortality for those attending from 1944 to 1948 and from 1949 to 1955 suggests that the mortality has decreased by forty per cent. in the later period.

An increase in the survival rate of mongols is confirmed by estimates of the incidence of mongolism in the population at age ten. Figures supplied by the Medical Officers of Health for London and the Home Counties indicate that this incidence in 1958 is a little over one in 1,000. Compared with earlier estimates this indicates that the incidence of mongolism at age ten has doubled since 1949 and doubled again since 1929. The fall in mortality for mongols is of the same order as, though a little less than, that for children in general.

Comparing the life-tables with the estimates of survival for incidence of mongolism among live-births and at age ten shows fair agreement for earlier years, but the most recent population figures suggest that the mortality between birth and ten years is only about 340 per thousand. This indicates either that the true incidence of mongolism among live-births is more than the estimated figure of 1.6 per thousand, or that the life-tables are over-estimating the mortality in recent years.

The causes of the 136 deaths in the series are analysed. The major causes are broncho-pneumonia and congenital heart disease. The association of mongolism and leukaemia in childhood is confirmed and attention drawn to an association between mongolism and Hirschsprung's disease.

(Author's Abstr.)

The Polymorphonuclear Lobe Count in Mongolism and Its Relation to the Total Leucocyte Count

The number of lobes per nucleus of the polymorphonuclear neutrophil leucocytes have been counted in fifty children with mongolism and fifty non-mongol mentally defective children of the same age group. By relating the polymorphonuclear cell lobe count to the total leucocyte count and to the neutrophil count, it was found that for any constant total leucocyte or neutrophil count the polymorphonuclear count of the mongols was lower than that of the controls.

The lobe count was unaffected by age.

It is concluded that infections are unlikely to account for the lowered lobe count of mongols.

(Author's Abstr.)

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Psychological Studies of Korsakoff's Psychosis: II. Perceptual Functions

A battery of psychological experiments exploring various perceptual processes, shows that the cognitive disturbance in Korsakoff's psychosis is neither exclusively, nor primarily in memorizing or learning. Patients suffering from this disease, even when capable of rational

behaviour and immune from confusional and confabulatory symptoms, are markedly defective in their perceptual functioning. Comparing them with controls drawn from psychiatric patients in an alcoholic clinic and from hospitalized neurological patients not diagnosed as brain-damaged or as alcoholic, the Korsakoff patients show a deficit on most perceptual tests. A notable exception to this observation are tasks which depend on the immediate apprehension of spatially and temporally unitary patterns or situations. The several discrete findings of this study can be subsumed most satisfactorily under a common principle by thinking of the Korsakoff patient as limited in his capacity to sustain more than a single perceptual set or attitude at a time, or to alter his orientation while the sensory input continues to confirm an expectancy he has adopted. This dependence on one aspect of the stimulus situation prevents him from integrating experiences, which may be the cause of his inability to learn or recall them; it also deprives him of those constant checking operations the absence of which has been proposed as an explanation of confabulatory behaviour. The perceptual disorder appears to be a primary factor in the mental syndrome characteristic of Korsakoff's psychosis; though indeed it may jointly with other cognitive defects manifest a common underlying attitudinal impairment.

(Author's Abstr.)

Investigations of the Urinary Excretion Pattern in Psychotic Patients

Chromatographic analysis of urines of 21 psychotic patients for urinary indoles revealed the presence in the majority of schizophrenics of an unknown compound, which was absent from the majority of urines of non-schizophrenic mental patients.

The urines of psychotics showed on chromatographic analysis for amino acids and in the "Fluorindal reaction" no significant abnormalities.

A modification of the standard glyoxylic acid test is described. The results of the test with urines of 128 psychotic patients are evaluated. It is concluded that the modified test confirmed results previously obtained in the positive range, increased the number of negative tests with schizophrenics and added to the sensitivity of the test. It also improved the clarity of the test colours.

The effect of treatment of urines with hydrogen peroxide on the glyoxylic acid test was studied and it was found that the oxidizer eliminates the interference of non-indolic substances with the test. The effect of some organic non-psychotic disorders on the test results is noted and the implication discussed.

(Author's Abstr.)

Clinical and Pharmacological Studies of Marsilid and Theoretical Considerations Concerning Its Antidepressant Action

1. Marsilid is an antidepressant agent and is active in psychogenic depressions, in depressions caused by chronic physical illness, and in so-called psychosomatic disorders. This drug action suggests the possibility of a common pathological denominator in all these conditions.

2. The following three stages are typical of Marsilid therapy: (a) Lessening of tension, depression and accompanying symptoms; (b) well-being, increase of interests and energy; (c) elation, overactivity and shallow affect. This pharmacodynamic process may occur in the treatment or post-treatment period.

3. An attempt was made to offer a comprehensive interpretation of Marsilid action. It was hypothesized: (a) that certain autonomic and affective reactions are the result of a specific action on subcortical centres; (b) that behavioural and affective changes are related to an increased input of sensations.

4. The use of the drug is limited by its toxicity, its widespread action on the brain and by the difficulty of achieving a satisfactory psychophysiological homeostasis.

5. It was hypothesized that the drug's value lies in its ability to correct neurohumoral imbalance. Due to this action the effect of Marsilid on depressions and allied conditions is corrective and not symptomatic.

(Author's Abstr.)

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Pharmacological Reduction of Abnormality in Multiple Sclerosis Within Minutes: A Statistical Study

1. A statistical study is reported of the phenomenon of pharmacological reduction of abnormality within minutes (PRA) in multiple sclerosis (this was previously termed "relief by flush"). This phenomenon is the reduction within an hour or (usually) less, of neural deficits in multiple sclerosis, after the administration of certain drugs.
2. It is the phenomenon itself which is of major interest, and not its therapeutic application. In studying a patient, the essential thing is to learn whether the phenomenon can or cannot be demonstrated in relation to one or more specific symptoms, regardless of whether it is transient or permanent in duration, and regardless of any possible therapeutic utility.
3. Neural deficits of every type are equally affected.
4. The drugs chiefly employed have been histamine diphosphate, carbon dioxide and amyl nitrite, which have in common the production of intracranial vasodilatation, and Hydergine (Sandoz).
5. The study is of 4,458 separate observations, on 311 symptoms in 116 patients.
6. The producibility of PRA and the length of time it lasts are largely dependent on the prior duration of the symptoms involved. With symptoms of brief prior duration, PRA is much more likely to occur with predictable regularity, to be marked and to be enduring, than with symptoms of long prior duration. Extensive neural damage residual from earlier attacks reduces the chances of occurrence of the phenomenon.
7. The incidence of PRA is far greater than that of spontaneous remissions, according to a comparison with the data of Kurtzke concerning spontaneous remissions.
8. The phenomenon is not dependent on spontaneous remissions, psychological factors, nor rest, as attested by control data.
9. The phenomenon often lends itself to therapeutic uses. The same control methods used for the phenomenon itself in excluding psychological, rest and spontaneous remission factors, are employable here.
10. In many cases a lasting effect follows a single drug administration. This is regarded as a demonstration of the phenomenon, and of its therapeutic applicability in "pure form". It means that the indicated symptoms ran an unchanged course from their onset until a few minutes after the first or other early drug administration, at which time a lasting change occurred.

(Author's Abstr.)

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Tumors of the Septum Pellucidum and Adjacent Structures with Abnormal Affective Behavior: An Anterior Midline Structure Syndrome

The hypothesis correlating neoplasia affecting the septum pellucidum and the adjacent structures with abnormal affective behaviour has been strengthened by further clinical observations. In addition, the modern concepts of the mechanism of emotion both from an anatomical and a physiological point of view seem to support this hypothesis. In the authors' own study they attempted to explore the problem of the degree to which a neoplasm will produce behavioural changes similar to those which follow electrolytic lesions. Although the technique was only partially successful, it was found that tumor and experimental lesions produced strikingly similar behavioural results. In addition, the notion that mechanisms associated with expansion of the tumor are sufficient to interfere with normal functioning of the structures involved was given support. It appears reasonable to conclude that a clinical syndrome of hyperemotionality may be associated with tumors of the anterior midline structures, more specifically of the septum pellucidum and fornix.

(Authors' Abstr.)

The Application of Triiodothyronine in the Treatment of Mental Disorders

It sometimes happens in a psychiatric service that patients with hypometabolism are treated symptomatically for depression, while their thyroidal metabolic state is overlooked. It is understandable that this should occur since the general lassitude, irritability, somnolence and decreased mental alertness which often accompany hypometabolism may be the major complaints of the patient and the reason he is brought to the attention of the psychiatrist. In the ten patients here described, for example, these psychic symptoms predominated. An empirical trial with Lio-thyronine quickly brought about an improvement in their condition. The good responses may have resulted from a correction of a hypometabolic state showing symptoms common to both the depressive and the hypometabolic condition. Of the ten patients, only two remained in the hospital. Of the 24 patients treated with Cytomel during the period from September, 1956 to September, 1957, 17 were discharged and the majority of the remainder are improved. Of the 17 discharged patients, 15 remained out of the hospital one year or more after discharge. Since Lio-thyronine acts more quickly than Thyroxine, is absorbed and eliminated more quickly and its activity is much more potent than Thyroxine's (6), it is superior to desiccated thyroid or L-thyroxine for empirical trial in psychiatry. In the doses used no untoward effects were encountered during and after the trial.

(Author's Abstr.)

Some Effects of a New Psychotogen in Depressive States

A new anticholinergic psychotomimetic agent, N-ethyl-3-piperidyl cyclopentylphenyl glycolate (JB-329), has been used in the treatment of a small number of depressed patients. The drug induces a drive of activity accompanied by some mood elevation. This seemingly desirable effect from a therapist's viewpoint occurs after a period in which there are psychopathological effects of a definitely psychotic nature. The post-psychotic effects which seem desirable are of a prolonged duration (days to weeks possibly). There is at least slight evidence in two cases of a continuing state of improved integration of the mental functioning and behaviour.

(Authors' Abstr.)

The Use of Doxylamine in Schizophrenia: Pitfalls in the Evaluation of a New Drug

Doxylamine, used previously as an antihistamine, was given to a small number of chronic psychotic patients at a state hospital. The experimental study was of three months duration and doses up to 900 mg. per day were administered. A double blind technique was used, one-half the patients receiving a placebo. Seventy per cent. of the Doxylamine patients and fifty-three per cent. of the placebo patients remained unimproved. Side-effects were virtually non-existent; one patient on the drug had an acute hypotensive reaction.

A plea is made for the adoption of double blind placebo techniques in the evaluation of drugs used in treating the mentally ill.

(Authors' Abstr.)

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The Adrenochrome Model and Schizophrenia

Model psychoses and schizophrenia have been compared using four different experimental methods which assume that there is a major biochemical abnormality in this illness.

First, it is now possible to discriminate between schizophrenic groups and others on the basis of several biological and biochemical assays which indicate the presence of unusual biochemical substances in schizophrenic blood and urine. The adrenochrome hypothesis predicts that these differences ought to be present and may lead to the discovery of specific schizophrenic metabolites arising from adrenochrome.

Second, adrenochrome and adrenolutin produce psychological changes in normals which reproduce some of the findings in schizophrenia. Third, phosphate excretion is altered by both adrenolutin and LSD-25 in a way which resembles the excretion in schizophrenics and not that in anxiety. Substances which antagonize psychotomimetics tend to be therapeutic for schizophrenia whereas substances which potentiate are not. Finally, treatments based on the adrenochrome hypothesis have shown some therapeutic success for early schizophrenic patients.

The evidence presented shows that schizophrenia and the model psychosis have many more similarities than differences and that the adrenochrome hypothesis is a useful model for schizophrenia which may be useful in developing better models.

(Authors' Abstr.)

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Psychological Studies of Korsakoff's Psychosis: III. Concept Formation

The performance of 24 Korsakoff patients, studied in the chronic phase of the illness by means of a series of experiments, and tested against controls drawn from non-hospitalized alcoholic and hospitalized neurological patients, has demonstrated three major sources of their deficiency in concept formation. Categories the Korsakoff patients use for classification are looser than those applied by the controls. Korsakoff patients are virtually incapable of discovering the appropriate criteria of categorization if these happen to be different from attributes familiar and therefore first resorted to; they are subject to particularly severe limitations in forming sequential concepts. In addition, they often fail to apply effectively concepts which they have either discovered for themselves or been told, and have grasped and retained in memory. These defects in concept formation are neither explained by the well-known memory impairment in Korsakoff's psychosis, nor entirely by perceptual deficiencies, but appear to be additional to the latter. The defects in perception and concept formation which characterize the Korsakoff syndrome show many parallel characteristics, and suggest dysfunctioning in common basic processes, such as set rigidity, i.e. inability to adopt new attitudes of orientation to a situation. The resultant failure to order and integrate experiences could itself be a cause of the more familiar symptoms of memory disturbance.

(Author's Abstr.)

Studies on Serum Oxidase (Ceruloplasmin) Inhibition by Tryptophan Metabolites

Of the thirteen tryptophan metabolites studied to date, serotonin, 5-hydroxytryptophan, 5-hydroxyindole-3-acetic acid, bufotenine and 3-hydroxyanthranilic acid were capable of inhibiting the oxidation of N,N-dimethyl-p-phenylendiamine by purified ceruloplasmin and serum oxidase. Two types of inhibition were noted and discussed.

(Authors' Abstr.)

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Endocrine and Metabolic Conditions Related to Pathology in the Hypothalamus: A Review

The clinical case material of 100 patients, with hypothalamic pathology selected from the literature, has been surveyed. In the great majority of these cases autopsy or at least surgical evidence of hypothalamic invasion by neoplasm or other pathology was available. The effect of such hypothalamic pathology in water metabolism, electrolyte balance and release of trophic hormones from the adenohypophysis has been discussed. Experimental evidence and clinical findings in these cases have been compared in regard to each of these individual phases of hypothalamic control. As far as the effect of disturbed hypothalamic functions on the target organs is concerned the gonads appeared to be most strongly impaired, the thyroid slightly and the adrenal cortices least. Disturbances, of water metabolism, mainly diabetes insipidus, occurred in direct proportion to the destruction of the commonly accepted control centres. However, in a group of 30 patients with severe traumatic brain lesions and marked hyper-tonicity of the blood the question of impairment of other centres regulating electrolyte balance, as suggested in animal experimentation, was raised. Another group of seven patients with hypothalamic pathology and disturbed blood-protein levels has also been discussed.

(Author's Abstr.)

Serum Magnesium in Delirium Tremens and Alcoholic Hallucinoses

Serum magnesium was studied in 30 patients with delirium tremens, 20 patients with alcoholic hallucinosis, and 18 controls. Group values were significantly low in alcoholic hallucinosis and still lower in delirium tremens. Individual values had a narrow distribution in the controls and a significantly wider distribution in alcoholic hallucinosis and delirium tremens. Seven of the delirium tremens patients were studied during convalescence; the value of serum magnesium increased in each without the use of magnesium in the therapy.

These findings are discussed in relationship to the literature on magnesium in alcoholic withdrawal states and to the role of magnesium in physiological processes.

(Authors' Abstr.)

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The Effect of Age on the Non-Haemin Iron in the Human Brain

1. The content of non-haemin iron in different parts of the human brain has been determined from birth to old age. The highest iron values were found in the structures of the extrapyramidal system.

2. The distribution of the non-haemin iron in the cerebral cortex shows a characteristic pattern. The highest concentrations were found in the motor cortex, followed by occipital, sensory and parietal cortex. The lowest figures were found for the prefrontal and temporal cortex.

3. An increase in non-haemin iron occurs with advancing age in all regions of the brain examined except in the medulla oblongata. The rise in iron values is rapid during the first two decades of life, then more gradual. There are some differences in the slopes of the curves for the structures investigated.

4. The quantity of non-haemin iron in the brain is to a large extent independent of the iron stores in the body.

5. A parallel is found between iron content and phylogenetic age of the structures investigated.

6. The histological estimations of the amount of iron in the extrapyramidal centres agree fairly well with the chemical determinations. In the cerebral cortex histologically demonstrable iron could not be found in young and middle-aged individuals. After the age of about 65 minimal iron deposits were detected in the motor and occipital cortex. No microscopically visible iron was found in the white matter.

7. About one-third of the non-haemin iron of the brain can be extracted by buffer solutions. This iron is bound to a protein which seems to be similar to ferritin. It is assumed that this iron-rich protein is a store of iron reserved for the needs of the brain.

8. A high concentration of non-haemin iron is found in microsomes and mitochondria of dog brain.

(Authors' Abstr.)

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Comparative Histochemistry of Lipids in Relation to Myelination in Rabbit Brain

1. Histochemical techniques for phospho- and glycolipids were applied to the problem of myelination in the developing rabbit brain.

2. Myelinated fibres were first demonstrable, as early as 24 hours after birth, in the medulla oblongata. The process of myelination was histochemically completed between the second and fifth months.

3. The earlier development of myelin in the phylogenetically older parts of the brain was clearly shown.

4. Diffuse staining of the neuropil occurred in brains from 24 hours to 28 days old. This was considered to indicate temporary storage of sphingolipid prior to its incorporation in the myelin sheaths.

5. Diffuse intracellular phospholipid was especially apparent in all parts of the brain from the fifth to the seventh day. The adult pattern emerged at the twenty-eighth day. The nature and function of this lipid remain obscure.

6. The histochemical results, in general, agreed well with the findings of reported biochemical studies on similar material. In particular, the striking increase in cerebroside content of the myelin sheaths, observed biochemically at and after the ninth day, was reflected in the histochemical tests.

(Authors' Abstr.)

Changes in the Composition of the Developing Mouse Brain During Early Myelination

The developing mouse brain has been studied from 1 day to the adult stage (10 weeks) with respect to changes taking place in total lipid, total lipid-free residue, total water, total lipid phosphorus, total nucleic acids (RNA and DNA), cerebrosides and water-soluble glycolipids (gangliosides and polycerebrosides), in an effort to delineate the role played by water-soluble glycolipids in the early phases of myelination. An attempt was made to correlate these changes with the changing histological picture and the development of myelin. The data obtained have led to the following conclusions:

1. The onset of histologically evident myelination is preceded by a sharp drop in water and nucleic acid content of the brain, presumably due in part to a decrease in glial cellular elements.

2. Although the increase in cerebrosides parallels the increase in myelination, this increase is not accompanied by a proportional net increase in other lipids, so that the bulk of myelin-lipids appears to be formed from lipids already present in brain when myelin makes its appearance and continues to increase.

3. Water-soluble glycolipids show a steady increase until the twelfth day, and from then on maintain a relatively constant absolute level in spite of the continued growth and maturation of brain. This suggests a high rate of turnover for this group of substances.

4. In the 1-12 day period the water-soluble glycolipid fraction is poor in neuraminic acid (polycerebrosides predominate) while from then on a relatively constant proportion of gangliosides and polycerebrosides is in evidence.

The results are discussed in relation to the manner in which myelin may be formed, and with respect to the possible role of water-soluble glycolipids as precursors of cerebrosides.

(Authors' Abstr.)

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Amino Acid and Protein Metabolism of the Brain: IV. The Metabolism of Glutamic Acid

The metabolism of ¹⁴C-labelled glutamic acid was studied in intact rats and mice. It appears that the bulk of the administered amino acid enters brain, liver, kidney and muscle as such and not with prior conversion to the amide. The entry of ¹⁴C glutamic acid into the various organs was very rapid and within minutes the glutamic acid, glutamine, GSH fraction of the brain, liver and kidney, and the γ -aminobutyric acid fraction of brain were significantly labelled. Within 2 minutes after the administration of ¹⁴C glutamic acid the specific activity of the organ glutamine approached that of the dicarboxylic acid, a fact which indicates the rapidity of intraconversion of the glutamic acid-glutamine system.

In experiments of longer duration the specific activities of glutamic acid, glutamine, GSH, and γ -aminobutyric acid decreased as would be expected from their rapid metabolism. In a number of short time experiments the specific activity of plasma glutamine was higher than that of liver glutamic acid and glutamine. This finding is interpreted as suggesting that the amide is synthesized in a compartment of the organ (endoplasmic reticulum?) from labelled glutamic acid not diluted extensively by organ glutamic acid.

The flux of glutamic acid from the circulating blood into brain and liver is estimated. A method is presented for the efficient separation in isotope experiments of glutamic acid and its metabolic derivatives.

(Authors' Abstr.)

Selective Depletion of Noradrenaline and 5-Hydroxytryptamine from Rat Brain and Intestine by Rauwolfia Alkaloids

Raunescine, reserpine and yohimbine were injected intraperitoneally into rats and the animals were killed 4 hours after the drug administration. Both 5-hydroxytryptamine (5-HT) and noradrenaline from brain and intestinal tissue were analysed by bioassay.

In suitable doses raunescine (5 mg./kg.) and reserpine (2.5 mg./kg.) are able to deplete about 80 per cent. of the noradrenaline content as compared with a 40-55 per cent. loss of 5-HT in the brain. In the intestine this difference is very clear. Doses of 0.1 mg./kg. of reserpine and 0.5 mg./kg. of raunescine deplete most of the noradrenaline, but doses from ten to a hundred times higher do not lower the 5-HT content in this tissue by more than about 35 per cent.

Yohimbine (20-30 mg./kg.) leaves 5-HT intact in both tissues. In these doses it lowers brain noradrenaline by no more than 50 per cent. It does not reduce the noradrenaline content of intestine. Experiments carried out at elevated environmental temperatures indicate that the effect on brain noradrenaline is not due to the hypothermia that yohimbine is likely to produce at room temperature.

(Authors' Abstr.)

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The Metabolism of Cholesterol and Fatty Acids in the Central Nervous System

The incorporation of ^{14}C -methyl-labelled sodium acetate into young and adult rat brain cholesterol and fatty acids was accomplished by injecting the acetate directly into the brain, thus by-passing the blood-brain barrier. Only small or negligible amounts of ^{14}C were incorporated into these substances when the acetate was injected intraperitoneally into adult rats. On intracerebral injection non-saponifiable material not precipitated by digitonin became labelled also. ^{14}C activity in these various lipide fractions was detected as much as a year after injection.

(Authors' Abstr.)

The Liberation of Active Enzymes from Brain Tissue by Lysolecithin

1. A study has been made of the activity of various hydrolytic enzymes in brain homogenates "cleared" with lysolecithin.

2. It has been found that true and pseudo-cholinesterase, alkaline phosphatase, glycerylphosphorylcholine diesterase, proteinase and transaminase are all as active in the cleared as in control homogenates. Tributyrinase and acid phosphatase are also present, but are less active in the cleared preparations. Mono-amine oxidase is also less active.

3. Lysolecithin has also been shown to cause a rapid release of both true and pseudo-cholinesterase from brain slices.

(Authors' Abstr.)

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A Method for Studying Metabolic Pathways in the Brain of the Intact Animal. The Conversion of Proline to Other Amino Acids

Evidence that the living rat brain can convert L-proline to glutamic acid, aspartic acid, alanine, arginine, γ -aminobutyric acid and ornithine is presented. The implications of these findings with respect to: (1) previous tissue-slice experiments on amino acid oxidation in brain and (2) ammonia detoxication in brain are discussed.

(Authors' Abstr.)

The Penetration of Proline and Proline Derivatives into Brain

The penetration of blood-brain barrier by proline and N-acetylproline was found to be low, as compared to high penetration rates for proline ethyl ester and N-acetylproline ethyl ester. Intravenous injection of proline ethyl ester was also found to be effective in elevating the level of free proline within the brain. The significance of these findings with respect to the design of studies on cerebral metabolism of proline is discussed.

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Action of D-Lysergic Acid Diethylamide on Lateral Geniculate Synapses

1. The effect of LSD on the potentials associated with synaptic transmission in the lateral geniculate body in the cat have been studied by means of extracellular microelectrodes. The drug was delivered either by injection into the carotid bloodstream via the lingual artery or by intravenous injection. The potentials studied were mainly those evoked by electrical stimulation of the contralateral optic nerve.

2. LSD has no effect on the latency or amplitude of the presynaptic spike.

3. LSD depresses and, in larger doses, blocks transmission through the lateral geniculate. The effect is completely reversible and no excitatory action has been observed. The parameters of this blocking effect are described in detail.

4. The electrical records display evidence of two postsynaptic components, a local synaptic potential and a propagated action potential. LSD leads to a reduction in amplitude of the synaptic potential below the threshold for initiation of the propagated spike.

5. The repetitive discharge of the geniculate neurons caused by a large-fibre optic tract volley is depressed or completely inhibited by LSD. The amplitudes of the postsynaptic spikes are all equally depressed and recover together.

6. Small- and large-fibre synaptic activities in the lateral geniculate are equally affected by LSD.

7. Intravenous LSD in the cat under Dial anaesthesia requires about 15 times the total dose for a similar effect compared to relatively close intra-arterial injection. The onset of depression is slower and recovery more prolonged.

8. An intravenous dose of about 1 mg./kg. in the conscious cat probably causes blindness or at least marked impairment of vision with very much less effect on general bodily activities. The effect is reversible.

9. It is concluded that LSD blocks transmission through the lateral geniculate either by inhibiting the release of the transmitter substance or by competing for the receptor sites on the postsynaptic membrane.

(Authors' Abstr.)

Mechanism of Gamma Aminobutyric Acid (GABA) Action and Its Relation to Synaptic Inhibition

Mechanisms of the blocking action of gamma aminobutyric acid (GABA) were analyzed in isolated stretch receptor cells of crayfish and lobster. A striking parallelism between the effects of GABA and of neural inhibition has been found.

1. GABA in concentrations near 10^{-5} M/l. blocks afferent discharges caused by stretch deformation in slowly adapting receptor cells in the crayfish. Lobster cells as a rule require higher concentrations. It is proposed that the following general mechanisms bring about the blocking action of GABA and of the inhibitory neural transmitter. When the dendrites and cell body are depolarized by stretch, an impulse is set up in the axon near the cell body. GABA and the neural transmitter increase the conductance within the cell, thereby reducing the stretch depolarization reaching the site of impulse origin. Thus the excitatory "drive" (or "generator potential") which leads to the setting up of conducted impulses is effectively reduced or removed, although the excitatory stimulus persists. If the cell is at rest, application of GABA or inhibitory impulses need not change the membrane potential, although the inhibitory process is fully active.

2. In increasing concentrations GABA reduces and eventually abolishes the inhibitory synaptic potentials. This effect is brought about by the progressively increasing hyperpolarizing action of GABA which drives the cell membrane to an equilibrium level which is usually similar to that of the neural inhibitory transmitter process. At concentrations beyond 10-15 times threshold for block, GABA has a dual action; it first hyperpolarizes and then depolarizes the receptor cell.

3. At near threshold concentrations GABA not only reduces the inhibitory synaptic potential peak but also accelerates its falling phase. GABA has the same effect on the after-positivities of antidromic impulses. Their hyperpolarization peaks are reduced and the recovery phases are shortened. The acceleration of the time course of these potentials is interpreted as an increased conductance to specific ions in the dendrites and cell body. Concentrations even 1,000 times threshold for block do not affect axon conduction or change appreciably the axon time constants.

4. If K^+ in the extracellular solution is reduced or absent, the hyperpolarizing action of GABA and of the neural inhibitory transmitter is increased. This parallel effect suggests a common mechanism.

5. Depending on concentration, the blocking effects decrease or disappear while GABA solution still surrounds the cells. Such a recovery is prevented if the fluid around the cell is kept stirred or is periodically replaced by a fresh solution of the same concentration. These results indicate that GABA is inactivated by the tissue. The inactivation process can be followed by registering the sensory discharge frequencies in a slowly adapting cell or by following the recovery toward normal of the after-positivities of antidromic impulses. Gamma guanidobutyric acid which also blocks discharges by a similar mechanism as GABA is not inactivated in a similar manner.

6. The site of GABA action cannot be located exactly within the cells. GABA blocks in the lobster the 7th median thoracic receptor which histologically has no inhibitory synapses. Its action, therefore, is not confined to subsynaptic inhibitory areas. It is suggested that part at least of the GABA action takes place in the large portion of dendrites and in the cell body.

7. Although GABA is found in the nervous system, the role of an inhibitory transmitter cannot be assigned to it on the basis of available evidence.

(Authors' Abstr.)

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Blood Pressure Alterations Secondary to Amygdaloid and Periamygdaloid After-Discharges

1. Amygdaloid and periamygdaloid seizures were electrically induced in a series of 46 awake and unanesthetized and three anesthetized cats.
2. Simultaneous blood pressure, electroencephalographic and behavioural changes were recorded during the electrical stimulations and after-discharges.
3. Blood pressure depression invariably occurred during the after-discharges.
4. After-discharges of short duration (20 seconds or less) were associated with greater blood pressure depressions than those of longer duration (greater than 20 seconds).
5. Amygdaloid after-discharges in the unanesthetized cat appeared to have a greater influence on depressor rather than pressor mechanisms.
6. A rise in pressure was seen only when the amygdaloid discharges propagated to closely associated structural systems such as the hippocampus and fornix.
7. The greatest degree of blood pressure depression appears to occur more frequently following stimulation in the anterior and central-medial regions of the amygdala.
8. Various behavioural changes such as altered respiration, mastication, ipsilateral facial movements, etc., did not greatly influence the blood pressure response.
9. In all but two experiments pulse rate and rhythm were unaltered by the discharge.
10. The systolic component appeared to vary more than the diastolic component during the after-discharges which displayed pulse pressure changes.
11. Pressor and depressor reactions are discussed in relation to the frequency and duration of an after-discharge.

(Authors' Abstr.)

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Afferent Projections Through Ventrolateral Funiculi to Thalamus of Cat

1. Electrical stimuli delivered to the proximal end of cut hindlimb cutaneous nerves from both limbs evoked low-amplitude responses in the lateral white matter of the spinal cord. This evoked activity persisted after section of the remainder of the spinal cord at a level between the dorsal roots of entrance of the nerve and the active locus. Electrical stimulation of the responsive spinal loci evoked potentials in the somatosensory areas of the cerebral cortex even though both dorsal funiculi had been severed several segments rostral to the stimulating electrode.
2. Cutaneous nerve stimulation evoked responses in two regions of the rostral brainstem by way of pathways traversing the ventral and lateral funiculi of the spinal cord. One of these brainstem centres comprised the well-known primary relay nuclei of the cutaneous systems, the ventrobasal complex. The other responsive zone was situated caudal and medial to the ventrobasal nuclei and corresponded largely to the posterior nuclear group of the pulvinar-posterior system, including the magno-cellular division of the medial geniculate body.
3. The evoked activity recorded from the ventrobasal nuclei was initiated predominantly if not exclusively by stimulation of the contralateral cutaneous nerves employed in this study. The responsive regions within these nuclei were few in number and displayed a topographic organization similar to that reported previously for these cell groups. The latency of the evoked potentials recorded from the ventrobasal complex in cats in which chronic or subacute spinal cord sections were employed approximated that observed by others in intact animals for comparable cutaneous inputs.

4. Stimulation of cutaneous nerves in each of the four limbs evoked complex potentials in the posterior nuclear group. No clear evidence for a topographic organization of the input to this region was found. While the latencies of the evoked potentials recorded from this region generally were somewhat longer and more variable than those observed for the ventrobasal complex, some responses occurred after time delays similar to those recorded from the ventrobasal complex. Ipsilateral cutaneous nerve inputs evoked discharges in this posterior region after longer latencies than did the corresponding contralateral nerve.

5. Possible relationships of these ventrolateral pathways to the rostral brainstem and the cerebral cortex are discussed.

(Authors' Abstr.)

Differential Effects of Resections of Somatic Areas I and II in Monkeys

The performance of eight rhesus monkeys on six somesthetic discriminations (multiple cue, size plus form, and three degrees of roughness) were studied pre- and post-operatively. The results indicated that:

1. Animals with post-central lesions (SI) fail to retain and have marked difficulty relearning most of the tasks. This somatic disturbance was duplicated and not exacerbated by combined removals of somatic areas I and II, and Brodmann's areas 5 and 7.

2. Lesions restricted to somatic area II seemed to be without effect on these tests, and the integrity of somatic area II could not compensate for a loss of somatic area I.

These results are discussed in relation to the adequacy of lesions and tests.

(Authors' Abstr.)

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Histopathology of the Mammillary Bodies in Alcoholic Psychosis

Silver carbonate techniques were used to examine degenerative changes in the brains of 4 alcoholic patients, 2 with Korsakoff's psychosis. The different types of histopathologic findings and their specificity are discussed.

Examination with silver carbonate suggests that the mammillary bodies are the site of peculiar forms of degeneration not encountered in other areas of the brain or in other pathologic conditions.

These changes can be summarized as (1) peculiar skein formations with the degenerated cell body in the centre and concentrically arranged fragmented processes, (2) fine fibrillary degeneration of the neurons, and (3) enlarged, rounded degenerated ganglion cells.

(Author's Abstr.)

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Influence of Mesencephalic and Diencephalic Stimulation on Limbic System Seizures

The effects of brain stem stimulation on electrically induced limbic system seizures were studied in 44 cats.

Brain stem stimulation was correlated with behavioural and electroencephalographic changes, and its influence on seizure production, propagation, duration, and variability was evaluated.

Seizures which were repeatedly and regularly produced had a tendency to maintain fixed characteristics. Furthermore, brain stem stimulation did not appear to alter the character of the discharge—except for its duration and variability.

Mesencephalic and hypothalamic stimulation seemed to reduce seizure duration and variability; the thalamus was inclined in the opposite direction. It must be emphasized that these structures displayed an almost equal ability to exert opposite effects from those assigned to them.

The effects of brain stem stimulation on seizures were interpreted as being both short and long lasting: short effects caused by direct neuronal stimulation, and long effects caused by induced humoral changes.

Seizure duration and variability appeared to be independent of the behavioural and electroencephalographic changes commonly described as activation.

Duration and variability changes from thalamic stimulation appeared to be independent of the thalamic recruiting responses.

Sleep spindles appeared more frequently during discharges from the cingulate gyrus than from other limbic structures and were not associated with increased seizure duration or propagation.

(Authors' Abstr.)

Studies on Abnormal Movement: Cerebellar Ataxia

1. Only 2 forms of ataxia, spinal and cerebellar, can be distinguished, but it is necessary to differentiate between these two entities and, further, between them and disequilibrium. Disequilibrium and cerebellar ataxia often occur together.

Disequilibrium affects the bodily musculature as a whole and is usually accompanied by deviation of the head and nystagmus. Disturbance at rest is evidenced by the assumption of tense postures and a strong disinclination to move. The head is involved in the kinetic and static disturbances which result. Wide, deviated, and lunging forms of locomotion with rolling, swaying, and twisting all may be seen in disequilibrium.

Cerebellar ataxia is characterized by forceful, springy, alternating activity which, if of cortical origin, interferes with the active attempt to arrange the limbs and body more particularly than with the effort to hold truncal postures, although so-called postural and intention, or, as we prefer to call them, ataxis, tremors are true manifestations of ataxia as are a great variety of special abnormal tests such as dysdiadochokinesis, abasia, and so on. It can be produced only by damage of the cerebellum itself or of its principal efferent pathway, the brachium conjunctivum, before division of the latter after its mesencephalic decussation.

Disequilibrium is evokable not only by injury to the vestibular system proper but also by interference with the flocculonodular lobe and its associated deep nuclei and connections. Spinal ataxia is due to destruction of afferent mechanisms at spinal levels. It is a loose, non-repetitive, throwing type of disarrangement, which occurs primarily in the lower extremities. (Authors' Abstr.)

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The Diagnostic Problem: Epilepsy of Late Onset

1. A follow-up study is presented of 141 patients with epilepsy of onset after the age of 20 who were seen at the National Hospital for Nervous Diseases, London.

2. Only 16 have been shown to have cerebral tumors. Of the others, 56 are believed not to have tumors on the basis of anatomic investigations by air encephalography or arteriography or both, plus a follow-up period of not less than three years; 20 other patients are believed not to have tumor on the basis of a fifteen-year follow-up alone. Additional tumors may yet be found among the remaining 49, but reasons are presented why these should not be numerous nor invalidate statistical comparison of the 2 groups.

3. The following circumstances significantly increase the likelihood of tumor to 28 to 50 per cent. and warrant contrast roentgenogram study:

Abnormal physical neurologic signs, the best single criterion;

Focal motor seizures or seizures with focal sensory aura;

Focal abnormality in the electroencephalogram (rare in this study unless the seizures were also focal);

Initial onset of fits in a patient over 50 years old.

4. Anatomic investigation is ordinarily not warranted in epileptic patients of adult onset who do not satisfy at least one of the above criteria—provided a satisfactory future follow-up can be made.

5. Even epilepsy of more than ten years' duration may be based on cerebral tumor—without the tumor killing the patient or being obvious. Failure to find abnormal physical neurologic signs in a patient who has been having fits for as long as three years, however, is a strong argument against the presence of a tumor, unless the seizures or the electroencephalograms are focal or the patient is more than 50 years old.

6. Even a normal air encephalogram at initial investigation does not rule out the possibility of tumor, and this diagnosis was made subsequently in 2 patients who were reinvestigated after a year's time because signs and symptoms had progressed. The need for follow-up is thus not obviated by any initial study.

(Authors' Abstr.)

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Physiologic Consequences of Total Hemispherectomy in the Monkey

An entire cerebral hemisphere, including the thalamus, can be successfully extirpated from the brain of rhesus monkeys at a single operation without interference with consciousness and with only moderate reduction in motor and sensory function. The operative procedure and resulting physiologic implications are discussed.

(Authors' Abstr.)

Ethoxzolamide—A New Anticonvulsant

The anticonvulsant effect of a new carbonic anhydrase inhibitor, ethoxzolamide, was studied. In a group of 25 epileptic patients who had been under poor control in spite of trials on virtually all commercially available anticonvulsant agents, 19 were found suitable for prolonged study over a seventeen-month period of time.

Most patients with grand mal and petit mal seizures were brought under excellent control; the improvement of patients with psychomotor seizures was significant but less striking. Side-effects necessitated termination of treatment in 2 of 25 patients, but toxic effects in the remainder were minimal. Because of its high potency as a carbonic anhydrase inhibitor, ethoxzolamide appears to be a significant addition to the growing number of anticonvulsant agents.

(Authors' Abstr.)

Treatment of Narcolepsy with Ritalin

Narcolepsy in 60 patients was treated by methyl phenidate hydrochloride (Ritalin hydrochloride) for eight to twenty-seven months. Good to excellent relief of abnormal sleepiness was reported by 49. Concurrent improvement of the cataplectic attacks occurred in 15 of 27 patients who had this symptom. Of the patients in the authors' original report whose condition could be followed, 68 per cent. reported good to excellent results after prolonged use; the comparable figure in their earlier study was 84 per cent. Side-effects were common but were usually minor.

The authors still believe that Ritalin is the drug of choice in the treatment of narcolepsy. In their experience, an initially satisfactory result can be maintained after prolonged use of this agent.

(Authors' Abstr.)

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Drugs for Treatment of Depression

The use of Marsilid produces remarkable improvement in the depressive syndromes because of the drug's antidepressive and psychic energizing properties. Marsilid can energize

the patient and yet does not overstimulate him. The authors have observed improvement in depressed patients regardless of diagnostic category, but, they repeat, Marsilid has little effect on many of the psychotic symptoms that may be present and sometimes increases psychopathologic processes. The tranquilizers are still superior in treating overt psychotic behaviour; however, in patients on long-term therapy—twelve to twenty months—discontinuance of Marsilid caused a return of delusions and hallucinations. Apparently, some psychopathology may be alleviated by long-term therapy with a psychic energizer.

The authors believe their studies during a twenty-month period leave no doubt that Marsilid is a unique antidepressive or psychic energizer. The Pavlovian theory that depression is a form of inhibition due to excessive stimulation must be seriously questioned.

Considerable doubt remains as to whether Marsilid's inhibition of amine oxidase in the brain is the drug's only essential function. At this time, they are evaluating the energizing action of other amine oxidase inhibitors and psychopharmaceutical agents.

The possible hepatotoxic effects of Marsilid are at present restricting the rational use of this drug by those clinicians who do not look at facts. Marsilid is unique, and no replacement is available. Since Marsilid is used as therapy and as an investigational tool, its loss cannot be evaluated.

Cause of possible toxic action must be determined, whether due to previous liver disease and existing pathology, augmentation of pathologic processes associated with infectious hepatitis, competition with vitamin B₆, chelation and removal of copper from essential oxidative enzyme systems, complex formation with adrenochrome, or unsuspected factors.

The history of science is not simply the history of discoveries and new ideas that tend to approach closer to reality. It is also the history of the defense of these findings against errors due to propaganda, politics, and bureaucracy.

(Authors' Abstr.)

Modification of Metrazol-Induced Convulsions by Ablations of the Brain

1. After ablation of the telencephalon, the salamander has co-ordinated walking, righting, and swimming; corneal and abdominal reflexes; and positive responses to tactile and visual stimulation. Intra-abdominal injection of Metrazol induces seizures with tonic and clonic components, hypersensitivity, gasping, and writhing.

2. After ablation of the prosencephalon, Metrazol induces a seizure with an extreme, tonic phase but hypersensitivity and the clonic phase are lost.

3. When both the prosencephalon and mesencephalon are removed, the salamander still walks, rights itself, and swims but Metrazol fails to evoke seizures with tonic and clonic components.

4. The salamander still has an abdominal reflex and withdraws the limbs when touched after the entire brain is excised, but injection of Metrazol is followed mainly by writhing and erratic placement of limbs.

5. The relationship of these observations to some aspects of phylogenetic development and to walking, localization of some seizure phenomena, and the mode of action of Metrazol is discussed.

(Authors' Abstr.)

Hallucinatory Effect in Man of Acetylcholine Inhibitors

1. In cats, 5,000 r. of 250-kv. X-ray were given to the exposed lumbar spinal cords. Some of the animals were observed for clinical effect, and some were studied for electrophysiologic changes in spinal cord reflexes.

2. Some early weakness was observed but completely disappeared in twenty-four hours. Complete paraplegia developed on the sixth or seventh day.

3. Anterior root responses to posterior root stimulation before and immediately after irradiation were investigated. By the fifth hour after irradiation, response time became significantly delayed. This delay meant conduction rates were slower. The total length of time of the response was not significantly changed until nine to ten hours after irradiation. The polysynaptic response gradually diminished in amplitude, and eleven hours after irradiation, was almost absent. At this time, the monosynaptic spike showed marked reduction in amplitude but was never more than a single spike. This later suggested cellular or synaptic alterations.

4. The effect of pentobarbital on the cat electroencephalogram was investigated; 6 fairly distinct electroencephalographic patterns were found associated with increasing depth of anesthesia. As the cat goes into lower levels of anesthesia, the anterior root response with posterior root stimulation is significantly altered; pentobarbital should not be used when this response is being studied.

(Authors' Abstr.)

Disseminated Sclerosis

1. An attempt was made to contact and study all persons in whom the onset of disseminated sclerosis occurred while they were living within a given district.

2. No evidence was found within the district studied that areas of high prevalence occurred, except for the Kingston area.

3. This high prevalence in Kingston was further examined and thought to be due to errors in sampling.

4. The suggestion is made that similar errors may have occurred in other cases where variations in incidence or prevalence have been reported.

(Authors' Abstr.)

Re-evaluation of Lumbar Puncture

Lumbar puncture was performed in 70 patients with papilledema and 59 patients with increased cerebrospinal fluid pressure without papilledema. The incidence of *possible* complications—any unfavourable changes within forty-eight hours—was significantly higher in the group without papilledema. Complications that did occur were probably not caused by lumbar puncture. From this study and a review of similar studies from the literature, one can say that the actual complications of careful diagnostic lumbar puncture in the presence of papilledema are much less than 1·2 per cent.

Use of careful lumbar puncture in the diagnosis and management of patients with papilledema is of definite value and may prevent unnecessary ventriculography or surgery. Therefore, the authors conclude that papilledema and increased intracranial pressure are not absolute contra-indications to careful, diagnostic lumbar puncture. Lumbar puncture should be performed to aid in diagnosis or management of the patients with papilledema or increased intracranial pressure.

(Authors' Abstr.)

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Neurologic Aspects of Porphyria

A report is presented of 2 patients with acute intermittent porphyria and involvement of the nervous system. The clinical picture was that of progressive, peripheral polyneuropathy, predominantly motor in its manifestations. In 1 patient, diffuse cerebral involvement occurred. Both patients died of respiratory paralysis. The pathologic changes were those of a non-specific parenchymatous neuropathy with associated spinal root involvement of a lesser degree. In the central nervous system, axonal chromatolysis of cells occurred in the anterior horn and vagal nuclei. Nonspecific changes took place which were consistent with respiratory death.

The pathophysiology is considered to be an abnormality in the metabolism of porphyrin and purine compounds. Resulting disturbance of intracellular enzymes is reflected in widespread functional nervous system changes.

(Authors' Abstr.)

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Combined Degeneration of Globus Pallidus and Dentate Nucleus and Their Projections. <i>Neumann, M. A.</i>	430

Study of Lipids in Cerebrospinal Fluid. VI. The Normal Lipid Profile

1. An analytic scheme is presented for the duplicate determination of cephalins, cephalins plus lecithin, sphingomyelin, total phospholipid, total sphingolipid, total cholesterol, free cholesterol, and total lipid in 10 c.c. of cerebrospinal fluid. From these determinations, the

lecithin, cerebroside, cholesterol ester, total phospholipid, and neutral fat concentration can be calculated. The tests of the method were briefly reviewed.

2. The average, the s.e.m., and the range were given for these lipids in 27 healthy men and women 20 to 34 years old. Sphingomyelin, total phospholipid, and total lipid were significantly higher in men than in women; free cholesterol was lower in men. The rest of the lipid fractions were similar in both groups.

3. These data confirm certain reports in the literature that lumbar cerebrospinal fluid from normal individuals contains such lipids as cholesterol and phospholipids. In addition, the data indicate for the first time that cephalins, lecithin, sphingomyelin, cerebroside, and neutral fat are also present in normal spinal fluid.

4. The lipids in the normal spinal fluid were compared to those in normal fasting serum. On the average, the lipids in the serum were 514 times more concentrated. Furthermore, a similarity was apparent in the per cent. distribution of the lipids in normal spinal fluid and serum. However, if the data were expressed in terms of micrograms of lipids per milligram of protein, the differences between the various lipids in serum and spinal fluid were approximately 2.

(Author's Abstr.)

Function of Astroglia in the Water-Ion Metabolism of the Central Nervous System

In the present work, no change in the water content of the rat brain was found in a series of experiments leading to the increase of the general extracellular space such as bilateral nephrectomy followed by injection of large doses of isotonic solution or a similar treatment after craniectomy. Hydric intoxication with water and Pitressin in normal and craniectomized rats also did not change the water content of the brain. In all these cases, electron microscope study showed no alteration in the structure of the central nervous system.

Electron microscope study of the zone of "traumatic edema" in stab wounds of the brain of rats and rabbits showed that this type of lesion is not a true edema and that swelling is mainly located in the astrocytes.

Considerable increase in water content of brain slices was obtained after incubation in an isotonic solution for thirty to sixty minutes. The electron microscope study showed that the swelling is not due to the increase or to the formation of an extracellular space but to a considerable swelling of astroglia. Incubation in a hypotonic solution produced more marked swelling, and even a hypertonic solution might cause mild swelling of astrocytes. In all cases, neurons were not swollen and even showed compression of the perikaryon and dendrites by the swollen astrocytes.

On the basis of these morphologic and experimental evidences, it is concluded that there is no extracellular space or intercellular ground substance in the central nervous system. The conclusion is also reached that astroglia functions as a water-ion compartment in the central nervous system, which is involved in the selective transports of fluids and metabolites between the vascular system and the neurons.

(Authors' Abstr.)

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Physical Activity, Emotions, and Human Obesity

Caloric expenditure due to physical activity is a potentially important and largely neglected factor in human obesity. The present study indicates that decreased physical activity may play a role in the production and maintenance of the obesity of at least some persons.

Obese women appear to be far less active than non-obese women, and this difference in activity is paralleled by differences in attitudes toward activity. An investigation of the reasons for this decreased activity indicates that physical activity in man is determined by a variety of influences: biological, social, and emotional.

One of the most important and most common of these influences is the series of events associated with a depressive reaction pattern. Depression, thus, may not be a purely incidental occurrence in obese persons. It may be one of the main reasons why they are obese.

(Author's Abstr.)

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The Etiologic Significance of Emotional Factors in Onset and Exacerbations of Multiple Sclerosis: A Preliminary Report

On comparison of a series of MS patients with a control series certain features have been observed which seem to be typical of MS patients.

More often than can be due to chance, an unhappy childhood, rejection by both parents and especially by the mother, disturbed mother-child relationships, and erection of psychological defences against the feeling of being rejected have been outstanding features in the history of the MS patients studied.

Acute or chronic emotional disturbances frequently precede and apparently precipitate the onset of the disease, its relapses and exacerbations. Regardless of the specific nature of the disturbing events that precede the disease, they have in common the fact that they constitute a loss or a threat of losing a key figure in the patient's environment. MS is a disease that occurs frequently in chronically anxious individuals.

Deviation of sex behaviour and genital dysfunctions in the early stages of the disease seem to be related to the process of regression rather than to be due to organic lesions in the spinal cord.

The following preliminary observations have been made and conclusions have been drawn during the present study.

1. No uniformity of personality type prior to the onset of the disease could be detected. A broad range of personality structure was observed. Langworthy's view (1948, 1950) that patients suffering from MS are hysterical in make-up could not be confirmed.

2. Emotional and psychosexual immaturity due to early frustrations and deprivations leading to an infantilization of character formation which thus becomes vulnerable to psychosomatic disintegration in individuals with a "delicately poised security system" may be suggested as a specific dynamic constellation related to the onset, exacerbations, and relapses of MS.

3. A common feature in almost all the MS patients studied is the presence of morbid anxiety often antedating the onset of the disease by a considerable length of time and frequently reaching its peak prior to some attacks.

4. Emotional disturbances alone or in combination with such factors as physical stress and over-exertion, accidents, injuries, and other miscellaneous causes were most commonly thought of by the patients in the series as "causing" their disease.

5. MS is multicausal in origin. No claim for its psychogenesis has been made. But it has been demonstrated that more often than is generally known emotional factors play a part and may precipitate not only exacerbations and relapses of an established MS but even its onset.

(Authors' Abstr.)

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Metabolic Characteristics of Alcoholics. I. Response of Glucose Stress

1. Total leucocytes, urinary sodium, and an unidentified diazonium-coupling compound were found to occur at significantly higher concentrations in a group of 22 male alcoholics than in a group of 22 nonalcoholic controls.

2. No significant differences between the two groups in response to glucose stress were observed; both exhibited similar decreases in numbers of leucocytes, lymphocytes and eosinophils.

3. The relationship of these findings to those reported earlier for psychotic individuals are discussed.

(Authors' Abstr.)

Metabolic Characteristics of Alcoholics. II. Serum Copper Concentrations in Alcoholics

Serum copper concentrations determined in patients admitted to a state mental hospital for the treatment of alcoholism averaged 174y (range 105-273), per 100 ml. in a group of 30 who were treated with chlorpromazine, and 176y (range 115-332) per 100 ml. in a group of 19 who received no drug therapy. In 20 normal controls the average was 123y (range 102-148) per 100 ml. The difference between the alcoholics and the controls was statistically significant ($t=5.7$, $p<.001$).

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