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As checking method the so-called matching system has been used. For each patient, the childhood background has been examined of two healthy women of the same age, marital state, occupation and whether grown up in town or in the country. It was found that in the childhood background of the schizophrenic women there was no difference worth mentioning from that of the healthy controls.

(Author's Abstr.)

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The Effect of Ion Exchange Resins in the Paroxysmal Disorders of the Nervous System

Paroxysmal disorders of the nervous system such as epilepsy, migraine, and Ménière's disease can develop a disturbance of electrolyte and water balance of cerebral and labyrinthine tissues when the paroxysms of the attack become frequent and severe. Experimental work and tissue analysis support this assumption. The introduction of ion exchange resins into the field of therapy has offered an opportunity to influence electrolyte (particularly Na and K) and water balance in these conditions. Clinical experience and results from the use of these resins have established their usefulness in the therapy of epilepsy, migraine, and Ménière's disease.

(Author's Abstr.)

Changes in Symbolic Expression with Sodium Amytal

1. Attitudes toward and recognition of illness and hospitalization were studied before and during the intravenous administration of amobarbital sodium. Changes in language patterns and nonverbal aspects of behavior were compared in 50 patients with pre-existing brain disease and a like number of normal subjects with comparable disabilities.

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2. Prior to receiving the drug, all patients expressed awareness of illness, were completely oriented for place, and identified the examiners correctly. With the drug, explicit denial of illness, disorientation for place, and gross misidentification of the examiners occurred only in some of the patients with brain damage. In the normal group, subjects talked of illness in terms of a third person, used more "concrete" symbols, selectively misinterpreted questions about illness and misnamed the examiners in "paraphasic" fashion.

3. Amobarbital sodium did not necessarily make patients more communicative. Thirty patients in both groups showed no changes in verbal or nonverbal behavior. Some talked more, others less.

4. Euphoria was noted in 11 patients in the normal group and in 17 with brain disease. The euphoria frequently alternated with paranoid and depressed attitudes. It was not related to the dosage of the drug and in some instances came on after the interview was terminated. Ludicrous aspects of behavior were prominent.

5. The euphoria, drowsiness, dysarthria, and dystaxia produced, unlike the nystagmus, cannot be explained in terms of any particular neurophysiologic mechanism of action of barbiturates but must be considered in symbolic as well as physiological concepts.

6. Amobarbital sodium, given under the conditions described, appeared to provide a milieu of brain function in which not new motivations but new symbolic forms for their expression could be evolved and maintained. These are best interpreted not in terms of "release of repressed material" but as an adaptive, more effective defense in a situation of greater stress.

7. The productions of patients under the influence of amobarbital sodium should be interpreted not only in a factual referential context but as a symbolic representation of wishes and feelings expressed in personal, spatial, and temporal terms.

8. The observed behavior could not be explained in physiological or psychophysiological terms as "cortical depression" or "release of inhibition". It is suggested that much of the behavior ascribed to such mechanisms may be largely manifestations of a particular observer subject relationship.

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Some Prognostic Factors in 538 Transorbital Lobotomy Cases

A statistical analysis was made of the significance of 18 psychiatric and sociologic factors in improvement and unimprovement of 538 mental patients following transorbital lobotomy. The results indicated that 57 per cent. showed improvement while 43 per cent. failed to improve. Fatalities amounted to 2 per cent. Fifty-three per cent. left the hospital following transorbital lobotomy with 31 per cent. still remaining out of the hospital to date.

Thirteen factors were found to significantly discriminate between improvement and unimprovement following transorbital lobotomy: sex, color, diagnosis, duration of illness, duration of hospitalization, number of electric shock treatments, number of insulin coma hours, marital status, education, occupational class, church affiliation, venereal history, and readmission status.

The remaining 5 factors found to be insignificant in improvement and unimprovement following transorbital lobotomy were: age, onset of illness, suicidal tendencies, birth order, and number of siblings of the patient.

Profiles of the theoretical patient more likely and less likely to improve following transorbital lobotomy are presented.

(Authors' Abstr.)

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Effects of Castration on Hypersexual Behavior induced by Rhinencephalic Injury in Cat

Lesions of the rhinencephalon, largely limited to the amygdaloid nuclei, precipitate a state of chronic hypersexuality in the adult male cat. Such behavior is abolished by castration. It is maintained, therefore, by endocrine secretions of the intact testes, since after gonadectomy the daily administration of 50 mg. of testosterone propionate restored the hypersexual behavior to precastration levels.

Some neuroendocrine relationships bearing upon these findings are discussed. Ablation of rhinencephalic structures appears to release from suppression certain subcortical structures which, together with neocortical influences, contribute to the initiation and maintenance of hypersexual behavior displayed by the gonadally intact, adult male cat.

(Authors' Abstr.)

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Psychiatric and Neurological Side-effects of Isoniazid and Iproniazid

In a group of 602 tuberculous mentally ill patients treated with isoniazid with a dose of 4 mg. per kilogram per day, the toxicity in comparison with the effectiveness of the drug was considered not to be serious. Only five patients who required isoniazid because of their tuberculosis had to have interruption of the drug because of toxicity, three because of seizures, and two because of peripheral neuropathy. One patient who was moribund with advanced tuberculous meningitis and who was given a larger than normal dose, apparently died of convulsions induced by isoniazid.

Isoniazid has an aggravating effect on convulsive tendencies even in therapeutic dosage, especially in brain-damaged patients. That this effect is not so great as to contraindicate treatment of such patients was shown by administration to 25 patients who had had lobo-

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tomies. Antiepileptic drugs, especially phenobarbital, can usually, but not always, be depended on as antidotes. They were very effective in 18 of 19 patients with epilepsy who were given isoniazid.

Isoniazid even in normal dosage sometimes causes agitation, which usually can be readily managed by sedatives without discontinuation of the isoniazid. However, in excessive dosage it is capable of causing psychoses, as the toxicity is proportional to the plasma level; 16 patients with psychosis caused by isoniazid have been received at the Edgewood Division of Pilgrim State Hospital. In addition, iproniazid, which is far more toxic and which is used by few physicians, has caused the transfer to this hospital of nine psychotic patients. Twenty-five is a very small number when compared with the many thousands of patients who have been treated in New York City with these drugs from March, 1952 to March, 1954.

In excessive dosage isoniazid frequently causes peripheral neuropathy, but when normal therapeutic doses are used this effect is mild and does not contraindicate treatment in the presence of alcoholic neuropathy.

It does not appear to be dangerous to the aged, to arteriosclerotic patients, or to alcoholics. There is considerable individual variation in reactions to the drug, and some symptoms may appear early and disappear while the drug is continued, while others may appear only after prolonged administration. Hence large single doses do not give a reliable test of the long-term toxicity.

(Author's Abstr.)

Familial Occurrence of Migraine Headache

Highly significant evidence has been offered demonstrating the hereditary character of migraine and permitting one further to assume correctly that the inheritance of the migraine headache trait is through a recessive gene with a penetrance of approximately 70 per cent.

(Authors' Abstr.)

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Prefrontal Ultrasonic Irradiation—A Substitute for Lobotomy

Transcranial and direct irradiation of the animal brain with high frequency sound was studied. A technique was developed for the production of graded subcortical lesions.

Therapeutic ultrasonic damage to the prefrontal lobes was applied to human beings as a substitute for lobotomy. Eight case histories representative of a series of 20 patients are reported. The procedure is comparatively simple, carries a minimal risk, and has, among this limited number of patients, given clinical results that compare favorably with those of surgical lobotomies in similar cases.

Fifteen of the patients treated for intractable pain due to malignant tumors later succumbed to their diseases, and 14 complete necropsies were performed. The histological damage in the path of the sound beam was localized mainly to the white matter. A satisfactory lobotomy effect was obtained in most cases in spite of the fact that the tissue alterations were minimal. The ultrasonic damage can be controlled and graded, from a reversible or minimal effect to a gross necrosis in the subcortex, without opening the dura. Unintentional mutilation can be avoided.

(Author's Abstr.)

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Prognosis in Transorbital Lobotomies Relative to Body Type

In a series of 84 somatotyped patients with transorbital lobotomies, (*a*) mesomorphic males and (*b*) females with above average endomorphy gave the best response.

The percentage of females discharged was smaller than that of males.

Patients with above-average total endowment did better than those with total endowment below the average.

A more extensive study relating somatotype to response to psychosurgery would be of value in selecting candidates for this procedure.

(Authors' Abstr.)

Studies of 17-Hydroxycorticosteroids

Adrenocortical function was studied in subjects with convulsive disorder. Response tests used were the eosinophile response to corticotropin, the glucose response to corticotropin, and the plasma 17-hydroxycorticosteroid response to corticotropin.

Although the eosinophile response to corticotropin was adequate in all groups, the steroid response to corticotropin in those patients receiving diphenylhydantoin was reduced very significantly as compared with the control group.

This observation in the diphenylhydantoin-treated group is discussed. The suggestion is made that diphenylhydantoin therapy produces a relative adrenocortical unresponsiveness which may be a factor in the action of diphenylhydantoin on brain excitability.

(Authors' Abstr.)

Localization of Discharge in Temporal Lobe Automatism

In a series of 155 patients operated upon for the treatment of temporal lobe seizures, 121 (78 per cent.) had attacks characterized by behavior automatism. This would include unresponsiveness, confusion, masticatory movements, and inappropriate but often elaborate behavior, for which the patient is later amnesic.

From a detailed analysis of the seizure patterns of 50 patients with temporal lobe automatism, it is concluded that automatism may be preceded by no warning, or by one or more warning features. There is, therefore, true ictal, as well as postictal, automatism.

Among the variety of phenomena which may precede the automatism in the seizure pattern, the commonest are abdominal sensation, conscious confusion, tonic or adversive motor features, somatic sensation, cephalic sensation, and feelings of unreality.

Conscious confusion followed by tonic or adversive motor features constitutes a common epileptic "march" leading into automatism.

Stimulation of the brain in the conscious patient undergoing surgical treatment for temporal lobe seizures has produced automatism and amnesia, sometimes with widespread suppression of the electrical activity of the cortex. Twelve cases are presented to illustrate these stimulation responses.

The area responsible for the initiation of behavior automatism appears to center in the periamygdaloid region. This includes the uncus, the amygdaloid nucleus, the ventral claustrum, and the temporoinsular cortex deep in the anterior part of the Sylvian fissure. The anatomy of this complex region is reviewed.

It is pointed out that the periamygdaloid region is particularly susceptible to involvement by tentorial herniation, either by direct mechanical distortion of the tentorial edge or by interference with its blood supply by compression of the anterior choroidal artery. The present studies, therefore, are consistent with previous views that incisural sclerosis produced by tentorial herniation at birth is a cause of temporal lobe seizures coming on later in life.

Evidence is presented that the deep mesial structures of the temporal lobe are concerned in motor responses which may be additional to those derived from the Rolandic, supplementary motor, and second sensorimotor areas.

The term uncinate fits is inappropriate to describe attacks with olfactory and gustatory aura, since only about 5 per cent of patients with behavior automatism have such features. It is noted that temporal lobe seizures with behavior automatism more closely correspond, as regards both the seizure pattern and the site of the pathological lesion, to the uncinate fits as described by Hughlings Jackson.

The present observations, together with subsequent animal experiments, would support the view that the claustroamygdaloid gray matter can be considered along with the diffuse projection systems of the thalamus and brain stem as a region capable of exerting diffuse regulatory effects on other parts of the brain. Evidence, in particular from the studies in man, indicates that the periamygdaloid region is also concerned in the processes of memory recording and the maintenance of the normal conscious state, both of which are clearly essential factors in the mechanism of behavior.

(Authors' Abstr.)

Classification of the Epilepsies with Particular Reference to Psychomotor Seizures

To sum up, temporal lobe epilepsy comprises a group of epilepsies having in common a site of discharge in the region of the temporal lobe. The clinical pattern of these seizures varies with the precise situation and direction of spread of the discharge. The seizures may be of major, minor, or minimal degree. We may hope that with better correlation of clinical pattern with demonstrable lesion or EEG focus more accurate localization will be achieved. The clinical features of anterior and posterior, deep or superficial, discharging lesions may prove to

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be distinct. The pathological classification of the temporal lobe epilepsies is a separate problem. Why are focal seizures in this situation so common without any clinical evidence of coarse or progressive lesion? The concept of incisural sclerosis from birth injury (Earle and associates) may provide an answer, but there is much scope still for the neuropathologist in the elucidation of this problem.

(Author's Abstr.)

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Carbohydrate Metabolism in Brain Disease. I

Carbohydrate metabolism in patients with multiple sclerosis is abnormal. Fasting whole blood lactic and alpha-keto glutaric acid concentrations are elevated. After the oral administration of 100 gm. of glucose there is a lag in the return to fasting level of the true blood glucose, an increased accumulation of lactic and perhaps pyruvic acids, and a rise, rather than the normal fall, in plasma citric acid and whole blood alpha-keto glutaric acid concentrations.

(Authors' Abstr.)

Carbohydrate Metabolism in Brain Disease. III

Pure fructose was administered to normal subjects and psychotic patients. Fructose tolerance was normal in patients with schizophrenic, manic-depressive, and involutional psychoses. The intermediate metabolism of the fructose was only slightly abnormal in the psychotic group. The most important difference from the normal was the occurrence of a rise, rather than the normal fall, in true blood glucose concentration after fructose given orally; this rise, together with the entrance of some fructose into the common metabolic pool, perhaps explains the moderately increased accumulation of citric acid in the blood of the psychotic patients who received fructose. This increased accumulation of citric acid was also observed after the intravenous infusion of fructose.

The finding of normal fructose tolerances in patients with the psychoses discussed here rules out any commonly recognized hepatic disease as the cause of the disordered intermediary carbohydrate metabolism described previously.

(Authors' Abstr.)

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New Problems of Aphasia

The author has sought to prove that aphasia regarded as a disturbance of the actual genesis of the process of verbalization is consonant with the basic ideas of Jackson on evolution and dissolution of function. The physiological ideas of Jackson can be transferred to the psychological field. They have then to deal with the evolution and dissolution of gestalts. Aphasia is an example for the dissolution of the process of gestalt in the course of verbalization.

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This disturbance appears, not through the destruction of special foci in the cortex as presumed by the classical theory, but through the collaboration of various factors out of which only one is the factor of localization, the others being diaschisis and the quantity of the grey matter which has been damaged, which are factors unrelated to localization.

(Author's Abstr.)

An Unusual Type of Pre-senile Dementia

Two cases of pre-senile dementia are described. In the first case there was probably an hereditary factor present while in addition to the dementia there were also signs of a spastic paresis of one limb. Pathologically the findings were in part reminiscent of Alzheimer's disease but they also included a severe amyloid vascular change and plaque formation of unusual type and severity.

A remarkably similar clinico-pathological syndrome appears to have been described previously in three other families.

The second case of pre-senile dementia also showed the amyloid vascular change in addition to the more usual features of Alzheimer's disease.

The histological findings coincide with Divry's and with Scholz's observations on the amyloid basis of the various changes found at times both in the senile and pre-senile brain.

The relation of these cases to each other, and to Alzheimer's disease and vascular disease is discussed, with a brief reference to amyloidosis in general.

(Authors' Abstr.)

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Experimental Psychiatry. III. A Chemical Concept of Psychosis

Experimental evidence has been presented that seems to indicate that a natural error in the adrenalin cycle may be an important, although probably not the only, factor in the origination of psychosis. This brings into focus a new chemical concept of psychosis, and calls for more intensive research in experimental psychiatry in the production of artificial psychosis.

(Authors' Abstr.)

Results of Lobotomy in Chronic Psychosis

It would appear that there is little change in the psychotic ideation of these patients but adverse behavior manifestations have been altered considerably, as manifested by the high percentage of improvement shown in assaultiveness, agitation, and impulsiveness. In other words, the authors were finding that lobotomy does not eliminate the psychosis in many of their patients but enables them to live more comfortably with it and, as a result, they are easier to manage. The improvement in the 77 chronic patients, who were not helped by any other form of treatment, may be best indicated by the fact that ten are out of the hospital, either going to school or working, and three more could be considered for discharge if conditions at home were more favorable for their adjustment. The results of lobotomy on carefully selected patients, whose illness has been very chronic and who have not responded to other types of treatment, are sufficiently favorable to warrant further use of this therapeutic procedure.

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Orbital Undercutting in the Treatment of Psychoneuroses, Depressions and Senile Emotional States

1. Presentation is made of 47 cases of intractable psychoneuroses, depressions and senile emotional states undergoing undercutting of the orbital cortex of the frontal lobes.

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2. The undercutting operation permits precise sectioning under direct vision of a measured extent of cortical connections and can be exactly duplicated in successive cases.

3. When limited to the orbital cortex, there is no appreciable late blunting of personality even in the elderly.

4. Eighty-seven per cent. of the patients have shown significant improvement with a gratifying diminution of anxiety, tension and obsessive thinking, a lift in mood, and a lessening of visceral consciousness.

5. Optimum results have unexpectedly occurred in the older age group, sufficient to warrant a separate report.

6. Operation may uncover an underlying schizophrenia in pseudo-neurotic schizophrenic patients.

7. Physiologic observations are made on the functions of the extreme posterior portion of the orbital cortex.

(Author's Abstr.)

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Comparison of Electrographic Effects of Stimulation of the Amygdala and Brain Stem Reticular Formation in Cats

1. A comparison of the electrographic effects of stimulation of the amygdaloid nucleus and the brain stem reticular formation was made in 15 cats under Nembutal anaesthesia.

2. Stimulation of the amygdala can produce a diffuse electrographic effect consisting of a low voltage, fast, asynchronous activity, having all the characteristics of the "arousal" pattern as produced by stimulation of the brain stem reticular formation. During such a response the barbiturate spindles are blocked and abnormal activities such as delta waves and strychnine spikes may be eliminated. A more restricted activation confined to certain cortical areas, particularly the temporal and sensori-motor cortex, is sometimes produced and more often from the amygdala than from the brain stem reticular formation.

3. The electrical activity of the amygdala itself is activated in an identical way by stimulation of the reticular formation or of the opposite amygdala. This effect consists mainly in the production of a fast rhythmical type of activity, occurring often in spindles, which may represent the arousal pattern of the amygdala. This effect may occur with or without generalized cortical activation.

4. Although it is as yet not possible to ascribe this activation effect to a stimulation of any particular nuclear sub-division of the amygdaloid complex, it seems clear that this effect is not obtainable from the whole amygdaloid complex, nor does it necessarily involve those nuclei receiving direct olfactory connections.

5. These experimental results suggest that the amygdala, like the brain stem reticular formation and the intralaminar system of the thalamus, represents a structure capable of exerting diffuse regulatory effects on other cerebral regions.

6. The role of the amygdala in epileptic automatism is discussed in the light of these findings.

(Authors' Abstr.)

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Subcortical Electrical Activity in the Golden Hamster during Arousal from Hibernation

1. Results of a systematic electrical exploration of cerebral hemispheres and brain stem in golden hamsters (*Mesocricetus auratus*) arousing from hibernation are presented.

2. Three types of subcortical electrical activity were recorded during the process of arousal, namely (*a*) transient, regular, initially 17/sec. activity, (*b*) fairly continuous waves, and (*c*) activity in bursts.

3. The electrical activity recorded was confined to components of the limbic system and its presumed descending efferents. Olfactory bulbs, corpus striatum, thalamus, and anterior hypothalamus were conspicuously quiescent.

4. These findings appear consistent with contemporary theories of the function of the limbic system and would serve to account for the apparent agitated state of the hamster immediately upon full arousal from hibernation.

5. It is concluded that the process of arousal in the golden hamster is initiated when the limbic system is activated either directly or indirectly by afferent impulses from the periphery.

(Authors' Abstr.)

The Electrocerebellogram as Modified by Afferent Impulses

This study on the electrocerebellogram is primarily concerned with frequencies of less than 60/sec. (thus excluding the better-known 300/sec. activity) which can be recorded on the average EEG equipment and especially modifications of these slow frequencies by various afferent stimuli.

1. Slow frequencies can be observed in the cerebellum of unstimulated animals, in its nuclei, and its outflow.

2. They are not uniform in all regions, not always transmitted through to the outflow and often resemble activity appearing concurrently in the cerebral cortex.

3. Many of the slow frequencies are abolished by high decerebration.

4. Stimulation of various cerebral areas, various peripheral nerves or an afferent peduncle to the cerebellum alters the electrocerebellogram.

5. Repeated tonic-like photic and auditory stimulation alters these waves, but not always in a uniform manner since either high voltage irregular slow waves or uniform fast waves may occur during or following such stimulation.

6. Single stimuli whether electrical, single click, or single flash usually produce one or more sharp spikes followed by a slow wave recorded from the cerebellar cortex. Likewise, spikes of similar appearances (different latency) occur in a cerebellar outflow, i.e. brachium conjunctivum. The slow wave usually does not appear in the brachium conjunctivum, but when present, its form commonly varies from that recorded at the cortical surface.

(Authors' Abstr.)

The Effect of Introduction of Some Drugs into the Cerebral Ventricles on the Electrical Activity of the Brain of Cats

The electrographic changes following the injection of acetylcholine, carbachol, eserine, atropine and cholinesterase into the cerebral ventricles of cats are described.

1. The effect of several drugs in the cerebral ventricles of the cat on the electrical activity of its brain in a series of 23 animals is described. Some of the complex relations of the activities of periventricular grey and of other areas of brain stem are indicated and the incompatibility of their rhythmic activity with their transmission of information has been discussed.

2. Acetylcholine, carbachol and eserine produce rhythmic, fast activity in the periventricular areas and spindles resembling the "recruitment" response in the larger nuclear masses, the white matter and the cortex.

3. This action can be reversed with cholinesterase and is depressed by atropine.

4. Cats with a lesion between the mammillary bodies and the nuclei rubri do not show this response, but will show spindles, under the influence of intraventricular atropine.

(Authors' Abstr.)

The Role of Frequency Selective Reverberatory Nets in Cerebral Function

A possible neurological basis for visual discriminator mechanisms was described on the basis of prior work utilizing rhythmic photic stimulation. It was suggested, as a working hypothesis, that discriminator mechanisms employ frequency selective reverberatory nets of neurons which when activated produce specific behavior patterns. An experimental evocation of a GSR, which had been conditioned to color was accomplished by means of photic stimuli flickering at appropriate rates. Clusters of responses appeared at frequencies within which color illusions had been reported by the subjects and at approximate multiples and submultiples of these frequencies. The response patterns obtained supported the hypothesis that there is, in fact, a frequency selective mechanism associated with visual discrimination. Some further hypotheses with regard to the electroneural correlates of visual learning were suggested.

(Author's Abstr.)

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An Unusual Structure in the Floor of the Fourth Ventricle of the Golden Hamster (Mesocricetus auratus)

The floor of the 4th ventricle of the golden hamster (*Mesocricetus auratus*) discloses an ependymal invagination over which lies a mass of neural tissue which we have designated the locus incertus. This tissue, which appears to be an exaggeration of the central grey, contains a large celled nucleus and sends fibers to, or receives fibers from, the mesencephalic tegmentum and the interpeduncular nucleus. The area receives collaterals of the lemniscus systems, and presumably descending fibers of the dorsal longitudinal fasciculus.

The locus has not been described in other hibernators, but is present in the muskrat (*Ondatra zibethica*) which belongs to the same family as the hamster (*Cricetidae*). It is postulated that the locus is a center concerned with central autonomic mechanisms.

(Authors' Abstr.)

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The Treatment of Manic Psychoses by the Administration of Lithium Salts

The effect of lithium salts on manic psychoses has been tested in a controlled experiment. During treatment the patients were under close clinical observation, and the effects of suggestibility were minimized by an alternation between periods of lithium and placebo administration; neither the patients nor the observers were told whether the tablets given contained lithium or were placebos. The effect of the treatment was evaluated with due consideration of the spontaneous course of the disease in each case.

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Thirty-eight manic patients were treated. The response of 14 patients was classified as "+effect"; in these cases it was highly improbable that the changes occurring during the treatment were due to spontaneous variations. Eighteen patients were grouped under the heading "possible effect"; the condition was improved during lithium administration but a spontaneous cessation of the mania could not be excluded. In six patients lithium treatment did not influence the mania beneficially; these were classified as "−effect".

The therapeutic doses of lithium varied usually between 24 and 48 mEq. per day. On the higher dosage symptoms of slight intoxication were seen in some cases, the most frequent toxic symptoms being nausea and vomiting, diarrhoea, tremor of the hands, a feeling of general fatigue, and slight drowsiness. The symptoms of intoxication disappeared in three to four days when lithium administration was stopped.

Serum lithium levels were usually between 0·5 and 2·0 mEq./1 during treatment; the lithium content of the spinal fluid was considerably lower. In some patients lithium treatment gave rise to slight, reversible changes in the E.E.G.; in a single patient transient inversions of the T waves in the electrocardiogram were observed during the treatment.

It is concluded that lithium administration may be of considerable therapeutic value in a number of manic cases, but the danger of lithium intoxication necessitates a careful clinical and biochemical control.

Finally it is pointed out that the beneficial effect of lithium in cases of mania appears to offer new possibilities for a study of the pathophysiology of the manic-depressive psychoses.

(Authors' Abstr.)

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Patterns of Vascular Failure in the Central Nervous System

Three patterns of vascular failure are recognized and discussed. They are: (1) failure in the area of anatomic distribution, (2) failure in areas which lie between territories of primary vascular distribution, and (3) failure in part of the terminal area of anatomic distribution. The first type of failure can only be encountered in the primary area of distribution of vessels in which either because of absence or disease little or no overlap or anastomosis exists. The second type of failure is encountered along the entire capillary edge of the primary distribution of a vessel which is usually located at a zone of transition where the arterial supply is shifted from one principal source of supply to another. In both of the preceding cases the nature of the ischemic defect can be accurately forecast from a knowledge of the anatomical distribution of the vessel in question. The third type of failure, which occurs in the area of distribution of a vessel which has some degree of overlap or anastomosis with another vessel cannot be accurately foretold by knowing only the anatomic distribution of the vessel. It is also necessary to know what anastomotic possibilities exist, and especially what shunts are available and operative. Post mortem material casts some light on the nature of the areas which fail but, since post mortem examinations are usually conducted in accordance with definite preconceived frames of reference, failures due to uncomplicated occlusions of vessels may be missed and only those instances picked up in which contributory pathologic changes have resulted in unusually large lesions which produce prominent clinical neurologic signs.

Surgical occlusion of the anterior chorioidal artery produces a smaller area of ischemia than one would expect from the pathologic literature. The focal area of necrosis is along the internal medullary lamina of the lentiform nucleus. In larger lesions the enlargement occurs caudally into the internal segment of the pallidum and next into the adjacent portion of the internal capsule and dorsolateral part of the internal segment of the pallidum. The escape from ischemia of a large portion of the internal capsule and internal segment of the pallidum (which usually are colored by injection masses) appears to be due to anastomoses between branches of the posterior communicating and anterior chorioidal arteries as these lie on the cerebral peduncle and optic tract. Similar anastomoses exist between the anterior chorioidal and posterior cerebral arteries and are evidently responsible for some of the sparing of the internal capsule and for the sparing of the visual system. Where, because of pre-existing vascular disease, such anastomic channels are affected, much more extensive effects will, of course, follow ligation of the vessel. Most clinical cases diagnosed as "syndrome of the anterior chorioidal artery" have probably occurred in patients who have also suffered from generalized cerebral vascular disease. Probably many cases which have thromboses of the anterior chorioidal artery fail to show what have been considered typical signs. Consequently, such cases may not be diagnosed and attention may not be directed to this vessel if death should occur from other causes.

(Authors' Abstr.)

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Histopathology of Catatonic States

The patho-physiologic conditions under which astroglia is transformed into ameboid forms can be determined in human neurosurgical material under conditions approximating those of an experiment: 72 hours after surgical trauma (trephine), the wound is surrounded by 3 histologically well defined areas of activated cells: (*a*) the zone closely adjacent to the wound contains only remnants of proliferated and completely destroyed cells; (*b*) in the second zone adjacent to the first, the astroglia is in a state of ameboid and pre-ameboid degeneration; and (*c*) in the third zone, some distance from the wound, the astrocytes are hypertrophic, proliferated and well preserved. The subsequent organization is carried out by the elements of this outer zone. The interpretation of these findings is not difficult: the irritation caused by the acute focal destruction of the tissue is most severe in the areas adjacent to the wound where the acutely irritated astrocytes disintegrate within a few hours; in the second, less traumatized zone, the astroglia is able to produce hypertrophic forms but the effect of the trauma is still very strong and the cells suffer clasmatodendrosis within a short time; in the third zone the astroglia is sufficiently stimulated to respond in an organized manner. The observations in neurosurgical material, in which the time factor is exactly known, prove that the ameboid degeneration can develop within a few hours, that it occurs only in previously irritated glia, and that the histologic character of the reaction is determined by the acuteness of the trauma. The latter is, obviously, very strong in acute fatal catatonia and is much milder in its chronic forms; this may account for the clinical course.

The etiology remains obscure, but certain considerations should be mentioned. The ameboid degeneration appears frequently in severe disorders of metabolism, such as uremia, diabetes mellitus, in chronic toxic conditions (ulcerative colitis), in infectious diseases, and many others. This seems to suggest a profound disturbance of metabolism in catatonic states. (Authors' Abstr.)

Enzymatic Action of Fluids from Cystic Brain Tumors

Enzymatic action against nucleic acids and most of their pyrimidine and purine derivatives has been demonstrated spectrophotometrically and against tigroid bodies histologically in the fluids of various cystic brain tumors. The enzymatic activities are heat labile and inactivated by Mg salts. A group of tumors (craniopharyngioma, and gliomas) could be differentiated in which cyst formation was associated with definite enzymatic activity against nucleic acids and tigroid bodies, while such an activity was absent in a cystic acoustic neurinoma. This seems to suggest that various mechanisms may be responsible for cyst formation in tumors, one of which is destruction of cells by enzymatic products originating in the tumor metabolism. (Authors' Abstr.)

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Autonomic Hypothalamic Outbursts elicited by Cerebellar Stimulation

1. Somatic and autonomic outbursts of sham rage were observed in the thalamic cat (i) during cerebellar stimulation or (ii) immediately thereafter as a rebound effect. The struggling movements sometimes concealed the classic postural responses. The postural reactions persisted unmodified when the thalamic cat deteriorated, although sham rage outbursts were no longer elicited by cerebellar stimulation and only localized autonomic responses were observed.

2. Histological controls showed that the rostral and central parts of the fastigial nuclei yielded sham rage outbursts during stimulation, whereas the rebound effects were elicited from midline fibers between the posterior parts of the roof nuclei and from the buried folia of tuber, pyramis and uvula.

3. The cerebellar origin of these effects is shown by their abolition following histologically controlled destruction of the stimulated structures.

4. Diencephalic centers are essential since the responses were abolished by rostral midbrain electrocoagulation. Anatomical and physiological evidence suggests that the cerebellar influence on diencephalic structures might be mediated over the ascending reticular formation.

(Authors' Abstr.)

Cerebellar Projection of Paramedian Reticular Nucleus of Medulla Oblongata in Cat

In a previous publication (7) part of the median reticular formation of the medulla oblongata was outlined as a particular nucleus which was called the paramedian reticular nucleus. It consists of three small cell groups and is found in the space between the hypoglossal root fibers, the raphe and the inferior olive, at the level of the middle third of the olive. Following decerebellations practically all cells of this nucleus (large, medium-sized and small ones) disappear, showing that it projects on to the cerebellum. More than half of its cerebellar connections are uncrossed.

In the present paper the occurrence of retrograde cellular changes in this nucleus has been studied following lesions of restricted parts of the cerebellum. Only cells presenting fully developed alterations have been considered positive.

By this method all three groups of the paramedian reticular nucleus are found to send fibers to the anterior lobe, the pyramis and uvula; probably some fibers pass also to the lobulus c_2 of Bolk. No evidence is found of connections with the cortex of the anso-paramedian lobule, the flocculus and paraflocculus or the dentate nucleus. It is likely, but has not been conclusively demonstrated, that the nucleus fastigii receives fibers from it.

The paramedian reticular nucleus is situated close to the areas of the reticular formation outlined by physiological methods as the inhibitory center for motor activities, but the nucleus does not appear to belong to this center proper (7). The cerebellar projection determined in the present study lends support to the assumption that the paramedian reticular nucleus, although not part of this center, is functionally closely related to it.

(Authors' Abstr.)

Consequences of Cortical Convulsive Activity in the Rabbit

Faradic stimuli of sufficient strength to produce after-discharges were applied to the exposed cortices of rabbits. As the strength of stimulation was increased the following phenomena were observed: (*a*) the weakest stimuli elicit no after-discharge, although a spreading depression may develop; (*b*) an after-discharge, observed near the stimulating electrodes, may be accompanied by a small, non-propagated, slow potential change (s.p.c.); (*c*) an after-discharge develops, accompanied by a larger (s.p.c.) which is propagated to more distant electrodes as the concomitant of a spreading depression; (*d*) after-discharges accompanied by large (s.p.c.), are recorded in electrodes at considerable distance from the stimulating electrodes. Support was found for the thesis that the (s.p.c.) concomitant with the spreading depression, the large (s.p.c.) accompanying an after-discharge, and the small non-propagated (s.p.c.) are all based on identical processes. The observation that an incision through the cortex between stimulating and recording electrodes prevents the spread of the after-discharge and accompanying (s.p.c.) supports the concept that the after-discharge acts as the stimulus for the (s.p.c.).

When preparations are in conditions favorable for eliciting spreading depressions the after-discharge was found to be followed by a depression of cortical activity, the post-convulsive depression. This post-convulsive depression may be transformed into convulsive activity by the same means which had been found to transform spreading depression into spreading convulsive activity, namely by several antecedent spreading depressions (elicited by d.c. stimulation), or by topical application of compounds with vasodilator action, such as pilocarpine and acetylcholine.

A convulsion produced by a Metrazol injection may also be followed by a post-convulsive depression accompanied by a slow potential change. When injection of this drug had been preceded by several spreading depressions a prolonged convulsion was observed.

In the rabbit the post-convulsive depression may be considered as a protective device—it is initiated by electrically or chemically produced convulsive activity, and limits the convulsions to relatively short periods.

(Authors' Abstr.)

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Hippocampal Electrical Activity in Arousal

The electrical activity of the hippocampus has been studied in unanesthetized rabbits, cats and monkeys, immobilized either by tubocurarine or by transection through the midbrain. Observations have also been made in rabbits and monkeys with electrodes chronically implanted in the brain.

Arousal or desychronization of the neocortical record, whether induced by any one of a variety of afferent stimuli or by direct excitation of the activating mechanism in the brain stem, is invariably associated with the concomitant appearance of an undulating series of large slow waves in the hippocampal record. This hippocampal response is induced by connections from the septum, in the dorsal fornix, and is conducted to the hypothalamus and thalamus through the fornix proper. It may be elicited in the absence of the neocortex, but is prevented by septal lesions, section of the dorsal fornix, or by anesthesia. It is possible to interpret this evoked wave sequence in the hippocampus as a specialized paleocortical arousal reaction, whose unusual pattern is somehow correlated with distinctive morphological or functional properties of this part of the brain.

Similarly inverse patterns of discharge in neocortex and hippocampus are frequently observed in records of spontaneous activity in wakefulness and sleep, however, the hippocampal record being synchronous when that of the neocortex is desynchronized and vice versa.

(Authors' Abstr.)

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Ascending Pathways Activating Thalamus of Cat

1. This paper presents a study of the activating pathways afferent to the thalamus.

2. Thalamic activity is produced by ipsilateral afferent paths as well as contralateral.

3. The pathway for the earliest and largest activity in the thalamus derives from the medial lemniscus, which from the data presented here appears to have both crossed and uncrossed components.

4. While the latency between medullary and thalamic responses is longer for activation afferent from the brachial plexus than for activation afferent from the hind-limb nerves, the difference does not imply additional synaptic complexity in the pathway from the fore-limb to the thalamus. This difference is explicable on the basis that Group 1 fibers, which do not activate the thalamus, produce early activity at the nucleus cuneatus.

5. The existence in the thalamus of ipsilaterally and contralaterally evoked activity caused by different afferent pathways further supports the earlier findings that somatotopic localization in the ventral posterior nucleus of the thalamus is relatively poor.

(Author's Abstr.)

Interaction Between Afferent and Cortically Induced Reticular Responses

Interaction between afferent and cortically evoked reticular potentials was studied by employing single and repetitive trains of conditioning volleys. Unitary analysis of the interaction gave additional information concerning the degree of sharing of reticular neurones and the characteristics of their activation by incoming impulses.

1. The results indicate an extensive but not complete overlapping of reticulopetal pathways. Unit analysis showed partial sharing of reticular neurones for different incoming volleys and recruiting of reticular neurones by repetitive stimulation.

2. Both blocking and facilitatory interaction was demonstrated between two reticular responses. Evidence is presented that the blocking effect is due to occlusion and refractoriness of reticular neurones while the facilitation is due to a summation phenomenon in the subliminal fringe.

3. A long-lasting depression of afferent responses in the reticular formation occurs following cortical, subcortical or peripheral repetitive stimulation. This is mainly ascribed to occlusion or refractoriness, no conclusive evidence being found of active inhibition of reticular neurones.

4. Repetitive cortical and reticular stimulation was shown to cause a depression of an afferent test volley in the sensory trigeminal nucleus. It cannot be excluded that such a central influence upon specific sensory relays is partly responsible for the cortically induced depression of afferent reticular responses.

(Authors' Abstr.)

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Projections from Cortex to Cephalic Brain Stem (Reticular Formation) in Monkey

1. Studies were made on 31 monkeys in which corticifugal pathways to the central cephalic brain stem were revealed by evoked potential and physiological neuronography techniques.

2. These corticifugal pathways were found to arise in the frontal oculo-motor area, cingulate gyrus, orbital surface of the frontal lobe, sensorimotor cortex, posterior parietal or para-occipital regions, and the superior temporal gyrus. Other regions of the cortical mantle were negative with respect to evoked potentials and strychnine spikes in the central cephalic brain stem.

3. The subcortical region to which these cortical loci were found to project corresponded to that previously identified as the reticular activating system and known to be implicated in the arousal response as elicited by peripheral sensory stimulation.

4. The evidence presented indicates that the same system of neurons which mediates this ascending arousal mechanism is itself under the influences of impulses descending in the corticifugal pathways described.

5. The physiological implications of these pathways between specific cortical zones and the reticular activating system are discussed.

(Authors' Abstr.)

Respiratory Responses from Fornix and Wall of Third Ventricle in Man

In a series of patients in which these structures were exposed at craniotomy, stimulation was applied to the columns of the fornix or the lateral wall of the third ventricle. Excitation of the fornix induced expiratory apnea and occasionally a clouding of consciousness. Stimulation of the wall of the third ventricle caused polypnea. The findings are discussed in the light of similar observations by others in man.

(Author's Abstr.)

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Rorschach Scores in the Manic State

The Rorschach scores of 42 manics were compared with those of 42 schizophrenics, matched on the basis of age, sex, and total number of responses. The manics' scores were higher than the schizophrenics' for Sum C, Z, H, and M; they were lower for lambda, TIR, and TR. Comparison of the manics with Beck's normals showed the manics to be higher on Sum C, Z, W, Pure C, FC, and Y; they were lower on F+%, A%, lambda, P, V, and TIR. A number of hypotheses advanced by various writers were evaluated in the light of these empirical findings. Three of 12 hypotheses advanced by Rorschach were confirmed, and a consistent trend was noted in two others. Also confirmed were six of Beck's 12, four of Klopfer and Kelley's seven, and three of Phillips and Smith's five.

(Authors' Abstr.)

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Intolerance of the Primate Brainstem and Hypothalamus to Conventional and High Energy Radiations

1. From experimental and clinical studies, the brainstem and hypothalamus of man and monkey appear to be intolerant to large doses of X-rays from conventional X-ray equipment and to biologically equivalent doses of radiations (X-rays and electrons) from the betatron.

2. The intolerance of the primate brainstem and hypothalamus to large doses of radiation is due to two factors: (1) these areas subserve many functions essential for survival, and (2) these areas are much more radio-responsive than cortical areas.

3. The primate brainstem and hypothalamus will also respond to moderate dosages of radiations.

4. The significance of these observations was then considered with respect to: (1) the brainstem in brain tumor therapy, (2) the possible potential damage to the brainstem in atomic radiations, when restricted to the head, and (3) the effects of X-irradiation of the pituitary-hypothalamic region on clinical disorders related to pituitary dysfunction.

(Authors' Abstr.)

Investigation of the Primate Amygdala

From these preliminary observations the authors' conclude that movements of face and jaw follow electrical stimulation of the mesial amygdala in the Macaca mulatta. The movements which they have observed follow a particular pattern. This begins with eversion of the upper lip on the same side as the stimulus. The movements of face become bilateral following repetitive stimulation of the amygdala on one side. Then an after-discharge may be recorded in the region of the opposite amygdala. This suggests a functional connection between the amygdaloid nuclei, and it may be that they have interrupted the structural basis of this connection by cutting the anterior commissure in one animal. These relationships await further study.

The movements of face and jaw which follow electrical stimulation of the inferior mesial temporal region in patients seem analogous to those they have described as the results of stimulation in the amygdala of Macaca mulatta.

On the basis of this physiologic evidence they suggest that epileptiform discharge in one amygdaloid nucleus may spread rapidly across the midline to the other amygdaloid nucleus. Thus clinical and electrographic evidence of this discharge may appear on either side soon after its origin deep within one temporal lobe. Such discharge need not originate in the amygdaloid nucleus itself. It may arise in the temporal cortex and spread to the amygdala beneath. Pribram, Lennox, and Dunsmore have demonstrated that epileptiform discharge arising in the temporal cortex may affect the ipsilateral amygdaloid nucleus.

(Authors' Abstr.)

Stimulation of "Second" Motor Areas in the Macaque Temporal Lobe

There is a "second" or "additional" motor area in the temporal lobe of the monkey which, upon stimulation, will evoke ipsilateral facial movements. This area is located at the tip of the temporal lobe, in the superior and middle temporal gyri, and particularly in the lateral and basal portions of the inferior temporal gyrus.

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These face movements are combined frequently with shoulder and arm movements when the middle and inferior temporal gyri are stimulated and particularly with leg movements when the inferior temporal gyrus is the site of stimulation. Farther back in the temporal lobe there is some indication that arm and leg movements may be obtained independently of motor responses of the face.

(Authors' Abstr.)

SEPTEMBER

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Effects of Serpasil on Behavior and Autonomic Regulating Mechanisms

1. Reserpine (Serpasil) was given to a group of Macaca mulatta monkeys in varying doses and by different routes of administration. The effect on behavior, electroencephalograms, body temperature, systolic blood pressure, heart rate, respiratory rate, and pupillary diameter were studied.

2. Single intravenous doses of 0·5 to 1 mg./kg. and single oral doses of 50 mg./kg. produce a state of quietude and unresponsiveness to extraneous stimuli, characterized by an essentially normal electroencephalogram, which clearly distinguishes it from sleep induced by barbiturates.

3. Parallel to the changes in behavior a drop in body temperature, an equivocal drop of blood pressure and a reduction of heart rate and respiratory rate were observed, whereas miosis and diarrhea, commonly seen in other species after Serpasil, were not present.

4. The threshold dose for chronic daily oral administration in the monkeys was 2 to 3 mg./kg.

5. Increasing the dose by all routes of administration did not enhance the effects observed but tended to prolong them. Toxic manifestations were not encountered after Serpasil in doses up to 4 mg./kg. intravenously and 400 mg./kg. orally.

6. The results of this study are in agreement with the experimental findings in other species and in man and further support the theory that the main point of attack of this drug is probably in the brainstem.

(Authors' Abstr.)

Studies on Experimental Concussion: Relation of Physiologic Effect to Time Duration of Intracranial Pressure Increase at Impact

1. An experimental study of head injury has been carried out, in which the time duration of the increased intracranial pressure at the time of impact is controlled.

2. The experiments show that the shorter the time duration the higher the pressure necessary to result in a concussive effect. The longer the time duration the lower can the pressure be in order to effect a concussion.

3. Concussion resulting from acceleration, deceleration, or compression is caused by an increase in intracranial pressure at the time of impact. With compression an increase in intracranial pressure is more uniform throughout. Acceleration or deceleration injuries result in increased intracranial pressure with pressure gradients in the cranial cavity.

(Authors' Abstr.)

Treatment of Parkinsonism with Pagitane Hydrochloride

A new synthetic drug, Pagitane hydrochloride, has already been reported in the literature. The present report is a clinical survey of its action in a series of 142 patients with parkinsonism who had done poorly on other remedies. Of this number, 94 (66 per cent.) manifested improvement of varying degree, 40 (28 per cent.) were unimproved, and eight (6 per cent.) appeared to be worse. The study covered a period of 15 months. Methods of administration and procedure are described.

Pagitane hydrochloride was found to be considerably more potent than Artane and less disturbing in its side reactions, especially dryness of the mouth and mental clouding. It is possible that within several years, as in the case of Artane, its effects may wear off in a larger percentage of patients than is evident now, or patients may tire of it and turn to some new preparation. Nevertheless, the fact that so many of them have chosen to remain on Pagitane for long periods of time and have continued to derive benefits from it establishes the drug as a valuable addition to the armamentarium for the treatment of parkinsonism.

Pagitane can be administered to all types of cases. Other than the usual side reactions of belladonna products and their congeners, it showed no toxic effects among any of the patients in this study. It is safe for both young and old patients, and may be employed as the drug of choice in starting treatment with new cases. It exerts a favorable action against rigidity,

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oculogyria, and mild forms of tremor. It is a powerful cerebral stimulant and serves to counteract akinesia, sluggishness, tiredness, and weakness. It readily combines with other drugs for more effective action against advanced stages of rigidity and tremor, such as hyoscine, Benadryl, atropine, MK-02 and so on. It is especially beneficial as a substitute for Artane among patients in whom the latter drug no longer controls symptoms.

(Authors' Abstr.)

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Migraine and Tension Headaches

Two thousand patients suffering from migraine and tension headache were studied during the past seven years. Migraine represents a definite clinical entity and may be defined as that form of headache which is characteristically paroxysmal, periodic, unilateral, and throbbing. It is preceded by an aura and is usually associated with vomiting. There is frequently a positive family history. It is our impression that the treatment of migraine is a complex, individualized procedure. Symptomatic treatment is essentially one of pharmacotherapy, and the best results have been obtained with the use of ergotamine derivatives, notably a compound of ergotamine and caffeine (Cafergot). Prevention of an attack is best accomplished by psychotherapy.

Tension headache is that type of headache occurring in relation to constant or periodic emotional conflicts. Tension headaches are usually bilateral and may be accompanied by a variety of associated signs, including anxiety, nausea, and vomiting. Frequency and duration are variable. The best symptomatic relief is obtained with analgesics and sedatives. The best prophylactic results are obtained by psychotherapy.

(Authors' Abstr.)

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Use of Milontin in the Control of Petit Mal Epilepsy

1. Milontin has been demonstrated to be an effective drug for the control of petit mal epilepsy.
2. In certain instances of mixed epilepsy, the number of grand mal attacks may be increased with a concomitant decrease in petit mal attacks.
3. No significant changes in the blood or urine were observed following a ten month period of therapy.
4. Because of freedom from toxicity and effectiveness, Milontin is worthy of trial in the treatment of petit mal, either of pure or mixed type.
5. In a very small group of psychomotor epileptics the response to this drug was very good.

(Author's Abstr.)

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A Study of the Rationale of the Treatment of Delirium Tremens with Adrenocorticotropic Hormone

Data were collected on the course of delirium tremens in 27 patients whose adrenal cortex reserve status was determined by means of the eosinophil response to a test injection of adrenocorticotropic hormone. Adrenal cortex insufficiency was found to be related to prolonged alcoholism rather than to any of the phenomena of delirium tremens.

The high incidence of adrenal cortex insufficiency in delirium tremens may be secondary to a postulated pituitary-hypothalamic disorder which, if it existed, could account for many of the phenomena of death in delirium tremens.

Possible ways of unravelling the psychological and biological factors in alcoholism and delirium tremens are suggested.

(Author's Abstr.)

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Organization and Function of a Clinic for the Alcoholic Patient with Liver Disease. *Leevy, C. M., et al.* 537
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1. Biochemistry, Physiology, Pathology, etc.

Decreased Protein in Cerebrospinal Fluid. Hohmann, Hans. [*Nervenarzt.*, **25**, 55 (1954).]

The protein concentration of cerebrospinal fluid was abnormally low in 3 per cent. of 2,068 patients. Nearly 50 per cent. of the low values were in epileptics, the rest being distributed among 16 diseases of the central nervous system.

WARREN M. SPERRY (Chem. Abstr.)

Primary Tumors of the Brain and Meninges in Rats Fed 2-acetylaminofluorine. Hoch-Ligeti, C., and Russell, D. S. [*Acta Unio Intern. contra Cancrum*, **7**, 126 (1950).]

Two cerebral gliomas and a meningioma resulted from feeding 0·07 per cent. 2-acetylaminofluorine in the diet of 50 rats. Liver tumors were common.

RICHARD F. RILEY (Chem. Abstr.)

The Relation of Urinary Copper Excretion to the Amino-aciduria in Wilson's Disease (Hepatolenticular Degeneration). Uzman, L. Lahut. [*Am. J. Med. Sci.*, **226**, 645 (1953).]

In a 14 year old boy with hepatolenticular degeneration with persistent massive amino-aciduria and increased Cu excretion, the urinary Cu was isolated in the form of a complex with oligopeptides. The daily Cu output was unrelated to the amino-aciduria. The oligopeptides-Cu chelate complex may represent the form in which Cu passes from plasma into the glomerular filtrate, and the urinary excretion of Cu may result from the competition for tubular resorption, between the oligopeptide complex and the amino acids present in high concentration in the tubular fluid.

MARION HORN PESKIN (Chem. Abstr.)

The Changes in the Proteins of the Blood and Spinal Fluid in Syphilis of the Central Nervous System. Kutzim, H., et al. [*Die Medizinische*, **609**, (1954).]

Spinal fluid was concentrated by ultrafiltration and its paper electrophoresis diagram compared with that of the blood serum of the same patient. Normal spinal fluid had a composition of: peralbumin (I) 4–5, albumin (II) 52, α_1-globulin 4·5, α_2-globulin 8, β-globulin 16, γ-fraction (III) 6, and γ-globulin (IV) 8·9 per cent. (I) was found in the spinal fluid of all cases of syphilis and (III) in some cases. The (II) of the spinal fluid was low (20·2–39·5 per cent.) and the (IV) high (31·8–55·7 per cent.) in the syphilitic cases, but they did not reflect the composition of the blood serum. The changes in the spinal fluid paralleled the clinical picture.

A. DIETZ (Chem. Abstr.)

Metabolism of Acetylcholine. 1. Nakata, Fujio. [*Nisshin Igaku*, **39**, 493 (1952).]

With the method of Feldberg the production of acetylcholine by acetone-powder preparations of various organs of rat was examined with the help of adenosinetriphosphate. One g. of powder of brain, heart, intestine, and gluteal muscle synthesized 147, 64, 47, and 30γ of acetylcholine, respectively in three hours.

TETSURA KONO (Chem. Abstr.)

Lipides in the Chemical Structure of the Nerve System. Klenk, E. [*Naturwissenschaften*, **40**, 449 (1953).]

A review with references.

B. J. C. VAN DER HOEVEN (Chem. Abstr.)

Xenon Concentration Changes in Brain and Other Body Tissues of the Dog During Inhalation of the Gas. Pittinger, C. B., et al. [*J. Pharmacol. Exptl. Therap.*, **110**, 458 (1954).]

The rates of absorption of Xe by various tissues during inhalation of an 80:20 Xe:O_2 mixture were determined. Most parts of the brain were saturated within about 6 minutes, but the cerebral parietal cortex was not always saturated even after 20 minutes of inhalation. The Xe concentration in the adrenals rises rapidly and exceeds that of the brain after 10 minutes of inhalation. Kidney, liver, and striated muscle absorb Xe slowly.

L. E. GILSON (Chem. Abstr.)

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Disturbances in Acid Metabolism and Blood Alcohol Test After Brain Traumas. Seifert, P., et al. [*Deut. med. Wochschr.*, **79**, 193 (1954).]

In 90 per cent. of the cases the reserve alkali showed an increase and in 10 per cent. a decrease which disappeared within 3 days. During diminution of the alkali reserve the blood alcoholic values were normal. In experimental acidosis in the rabbit and man the blood alcohol showed no increase.

ERICH HEFTMANN (Chem. Abstr.)

The Precursors of Sphingosine in Brain Tissue. Sprinson, David B., and Coulon, Andrée. [*J. Biol. Chem.*, **207**, 585 (1954).]

The synthesis of sphingosine in nervous tissue was investigated with the aid of glycine-1-C^{14}, glycine-2-C^{14}, N^{15}, ethanolamine-2-C^{14}, and L-serine 3-C^{14}-2,3-D,N^{15}. C atoms 3 and 2 and the N of serine are utilized for C atoms 1 and 2 and the N of sphingosine, respectively, while the carboxyl group is lost. Ethanolamine is not used for this portion of the molecule, while the α-C and N of glycine are incorporated, probably by way of serine. The incorporation of label into C atoms 3-18 of sphingosine was compared with that of the fatty acid and D-galactose moieties of cerebrosides, and with brain cholesterol. Ethanolamine is effectively utilized for C-3 to C-18 of sphingosine, and fatty acids and cholesterol via conversion to acetate. The galactose had only low activity, although several of the compounds administered are effective glycogen formers in liver.

FELIX SAUNDERS (Chem. Abstr.)

Concentration of Sympathin in Different Parts of the Central Nervous System Under Normal Conditions and After the Administration of Drugs. Vogt, Marthe. [*J. Physiol.*, **123**, 451 (1954).]

A method is described which permits the estimation of adrenaline and noradrenaline (I) in small pieces of brain tissue. Highest concentrations of sympathin (II), an admixture of (I) and adrenaline, are in the regions containing the diencephalic, mesencephalic, and bulbar representations of sympathetic functions in dog and cat brains. Hypothalamic (I) in the cat brain was significantly lowered by apomorphine-HCl, ether, insulin, nicotine bitartrate, morphine-HCl, morphine-HCl with choline p-tolyl ether bromide, tetrahydro-2-naphthylamine carbonate, and picrotoxin; such a fall was correlated with the property of stimulation of sympathetic centers controlling adrenomedullary secretion. Asphyxia sufficiently severe to enhance medullary secretion also markedly lowered hypothalamic (I). However, adrenal denervation preventing medullary secretion did not interfere with the depleting action of drugs on (II) in the hypothalamus. Ether reduced the concentration of (I) in hypothalamus and midbrain. The amount of cat hypothalamic (II) was not affected by superior cervical ganglionectomy. The role of (II) in the central nervous system is discussed in terms of a transmittor function directly or through alteration of the transmission by other substances like acetylcholine.

MORRIS ROCKSTEIN (Chem. Abstr.)

Ascorbic Acid in the Brain Under Different Functional States of the Central Nervous System. Serdyuk, E. E. [*Ukrain. Biokhim. Zhur.*, **25**, 271 (1953).]

The ascorbic acid (I) content of the large hemispheres of the brain increased under all conditions of excitation: subcutaneous injection of camphor, interrupted electric shocks, bright lights. Animals with conditioned reflexes had, generally, a higher concentration of (I), which increased further on excitation. (I) Dropped in narcosis.

B. G. (Chem. Abstr.)

Estimation of Sphingomyelin in Nervous Tissue. Dawson, R. M. [*Biochem. J.*, **56**, 621 (1954).]

The fact that the molar choline/P ratio of alkali stable fraction of brain lipides is less than 1 suggests that other phospholipides besides sphingomyelins are involved. The estimation of sphingomyelin P in nervous tissue by alkaline hydrolysis gives only an approximate result. Preliminary treatment of tissue lipides with CCl_3CO_2H increases the accuracy somewhat because part of the interfering nonsphingomyelin lipide P is thus removed (without affecting the recovery of sphingomyelin). However, for more precise determination the estimation of the choline in the alkali-stable fraction is advised.

S. MORGULIS (Chem. Abstr.)

Parkinson's Disease. Durel, P. [*J. med. Lyon*, **30**, 431 (1949).]

In 250 cases of parkinsonism, Diparcol was effective (moderate to very good action) in all but 6·1 per cent. of the cases (which showed side effects which are discussed). The action is greatest on the hypertony and bradykinesia, and least on the tremor. Salivation is not affected. The action is discussed in relation to the effects of parpanit, phenergan, and benadryl.

A. C. TOBIE (Chem. Abstr.)

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The Inhibition of Cholinesterases by Antagonists of Acetylcholine and Histamine. Todrick, A. [*Brit. J. Pharmacol.*, **9**, 76 (1954).]

The ratio for 50 per cent. inhibition (I_{50}) of brain cholinesterase/I_{50} for cholinesterase of intestinal mucosa had a value less than 0·2 for most neuromuscular blocking agents. For antimuscarinic agents the ratio was between 5 and 60; while for drugs effective in parkinsonism the ratio was greater than 40. Several exceptions to the above were found.

RICHARD F. RILEY (Chem. Abstr.)

Formation of Ammonium Ion in the Cerebrum in Fluoroacetate Poisoning. Benitez, D., et al. [*Am. J. Physiol.*, **176**, 488 (1954).]

The concentration of NH_4 ion in cerebral tissue of dogs was increased nearly 7-fold during the course of fluoroacetate poisoning. It reached a maximum at about 60 minutes, and epileptiform seizures supervened at approximately the same time. The cerebral origin of the NH_4 ion was indicated by the relatively low levels in the blood. The precursor of the NH_4 ion is unknown. The cerebral NH_4 ion concentration was increased during seizures induced by pentamethylenetetrazole, but the levels attained were lower than those reached in fluoroacetate-poisoned animals during the preconvulsive stage. Infusion of NH_4Cl induced cortical seizures in 2 animals and cortical depression without seizures in 3 animals. Subdural injection of NH_4 salts did not induce excitation of the cortex.

E. D. W. (Chem. Abstr.)

The Effect of the Monohydroxybenzoic Acids on the Respiration of Rat Brain Homogenates. Patel, Chandulal A., and Heim, Harold C. [*J. Am. Pharm. Assoc.*, **43**, 251 (1954).]

The respiration of rat-brain homogenate was inhibited by salicylate but not by m- or p-hydroxybenzoate when succinate was the substrate, was inhibited by all 3 when lactate was the substrate, was stimulated by salicylate but not by the other 2 when pyruvate or glucose was the substrate, and was stimulated by all 3 when glutamate was the substrate.

DAVID B. SABINE (Chem. Abstr.)

The Chemical Diagnosis of Alcoholic Intoxication. Prag, J. J. [*S. African J. Med. Sci.*, **18**, 141 (1953).]

Investigations have been made of the normal blood alcoholic concentration in abstainers, moderate and heavy drinkers, all with the same dose of alcohol. The rates of combustion, absorption, and elimination in normal individuals with different doses of alcohol are also analyzed. Investigations of 100 cases of drunk drivers indicate that the ratio of blood alcohol to urine alcohol is 1·00:1·31, that motor abnormality is the most important sign in diagnosing intoxication, that the smell of alcohol on the breath is of least importance, that dilation of the pupils is an inconsistent sign, that the degree of intoxication is parallel to the motor and psychological abnormality, and that over 0·15 per cent alcohol in the blood is a strong indication of intoxication and below 0·05 per cent. the person is sober. A comparison of the clinical state of intoxication with the maximum blood alcohol concentration proves that the maximum drunkenness is present long before the blood alcohol reaches its maximum. Sugars increase the degree of intoxication, but assist in sobering the individual more quickly as they increase the rates of combustion and elimination of alcohol. 17 references.

W. R. HENN (Chem. Abstr.)

The Influence of Excitation of the Central Nervous System on the Metabolism of Substances in the Muscles. Epshtein, S. F. [*Ukrain. Biokhim. Zhur.*, **25**, 247 (1953).]

A single injection of pervitin (or cardiazole) reduced the acid-soluble P compounds fraction in the skeletal muscles; acid-insoluble fraction was increased, and the same was true on repeated injections. The general intensity of P metabolism was increased; NH_3 and glutamine were not changed in the muscle but were increased in the blood. Acid-soluble fraction in the heart muscles was reduced considerably with an appreciable increase of the acid-insoluble fraction. The results would indicate that the stimulation of the central nervous system with pervitin or cardiazole does not cause any apparent work for the muscles but results in some changes in the processes of metabolism. It could be expected that the excitation might reflect to a greater degree on the chemical processes of the muscles in action.

B. GUTOFF (Chem. Abstr.)

Organic Aspects of Periodic Catatonia. V. Type B. Gjessing, R. [*Arch. Psychiat. Nervenkrankh.*, **191**, 191 (1953).]

In 2 patients with periodic catatonia of the synchronous-syntonic (SS.) type the acute onset of the reaction phase occurred about midway between maximum and minimum N retention, in contrast to previously described patients in whom the change occurred at the maximum (Type A) or minimum (Type C). The response (stupor or excitement) in the reaction phase is related to the position on the N-retention curve where the onset occurs. Two normal young men were subjected for about 2 months to the same regime which G. has used in long-continued (frequently 1 year or more) studies of patients, including confinement in bed, a consistent liquid diet, and daily or frequent determining of a large number of chemical constituents of blood and excreta, particularly N-containing compounds. It required about 1 month for a metabolic steady state (consistent N balance, etc.) to be reached. There were no cyclic fluctuations in the excretion of N-containing compounds such as are characteristic of SS. periodic catatonics.

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VI. Environmental Factors. Gjessing, R. [*Ibid.*, 220.]

A high-fat diet of consistent compound (milk, eggs, cream, sugar, vitamins, NaCl, and trace elements) has been used G.'s studies since 1928. There was no correlation between physical activity and of the cyclic fluctuations in N balance.

VII. Evaluation of the Findings. 1. Gjessing, R. [*Ibid.*, 247.]

The very large number of data obtained in G.'s study of periodic catatonia during many years leads to the following conclusions: O consumption is always higher in the reaction phase (stupor or excitement) than in the relatively normal intervals. Despite the use of a standardized diet and consistent protein intake the N excretion in the urine varies in phases which have the same length as those of the psychic periods, but the point on the N-balance curve at which the psychic change occurs varies in different patients. The difference between minimum and maximum total N retention varies from about 15 to 30 g. Urea accounts for most of the variation; the excretion of ammonia N, uric acid, creatinine, and amino acids is usually normal. The range of variation of the blood nonprotein N is much increased, and the average concentration is usually above normal. Acidosis occurs during the periods of excess N excretion and alkalosis during the periods when N is being retained. NaCl excretion is less during the reaction phases than during the intervals between them. In 2 periodic catatonics it required 6 to 8 weeks for the establishment of N balance after a change to a low-protein (I) diet, and after 6 to 8 months on this diet it required 5 months for the re-establishment of N balance on a high-protein diet. The decreased excretion of N on the (I) diet was accounted for almost entirely by urea: other N-containing compounds of urine were little affected. The cyclic changes in psychic state were not affected by the (I) diet and the correlated changes in N retention continued at the lower level.

VIII. Evaluation of the Findings. 2. Gjessing, R. [*Ibid.*, 297.]

The cyclic changes in periodic catatonia are ascribed to variations in thyroid function. There is also evidence of abnormal liver function in the reaction phase: Increased excretion of urobilin and other urinary pigments and increased concentration of bile pigment in serum.

W. M. SPERRY (Chem. Abstr.)

Vascular Diseases of the Brain. Adams, Raymond D., and Eecken, Henry M. Vander. [*Ann. Rev. Med.*, **4**, 213 (1953).]

A review. Some biochemical factors are covered. 186 references.

THERESA SEVERN (Chem. Abstr.)

2. Pharmacology and Treatment

Some Physical Mechanisms in Narcosis. Mullins, L. J. [*Chem. Revs.*, **54**, 289 (1954).]

Narcosis by chemically inert molecules appears to take place when a constant fraction of the total volume of some nonaqueous phase in the cell is occupied by narcotic molecules. If the narcotic behaves ideally in this nonaqueous phase, the thermodynamic activity of the narcotic multiplied by its molal volume is a constant, about 1 ml./mole. Higher values of thermodynamic activity for narcosis as one ascends a homologous series may be due to an increase in the activity coefficient of the narcotic in the nonaqueous phase, corresponding to an increased difficulty of inserting larger and larger molecules into this phase. The nonaqueous phase resembles a highly polar liquid. If the molecules of this phase are considered to be reasonably large, the liquid must be held together by H bonding. In peripheral nerve the nonaqueous phase has a highly polar structure, but in the central nervous system it has a considerably less polar structure and therefore one that can accommodate less polar molecules more easily. The possibility of creating lattice defects in the nonaqueous phase by inserting molecules equivalent in size and polarity to those of this phase but different in shape makes possible an explanation of the physiological action of convulsants. Narcosis and convulsant action operate independently, in that convulsants will overcome the effects of narcotics and vice versa. The experimental evidence available does not support any definitive mechanism for the action of narcotics. In the case of excitable structures it is unlikely that a proposal of enzymic inhibition can be supported by experimental data if an enzyme is to be regarded as a protein structure made up only of amino acids, since such an enzyme will have a structure totally unlike the phase to which narcotics can be shown to be partitioned. If the enzyme is modified by being encased in a lipide envelope, it is conceivable that access of enzyme to substrate could be impeded by a narcotic. 58 references.

LOUISE DELLEY (Chem. Abstr.)

Current Status of Vitamin Therapy in Nervous and Mental Disease. Peterman, Robert A., and Goodhart, Robert S. [*J. Clin. Nutrition*, **2**, 11 (1954).]

The status of vitamin therapy in neurologic disorders is reviewed.

L. E. F. (Chem. Abstr.)

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Clinical Evaluation of Primidone (Mysoline), New Anti-convulsant Drug. Sciarra, Daniel, et al. [*J. Am. Med. Assoc.*, **154**, 827 (1954).]

A new compound, primidone (5-phenyl-5-ethylhexahydropyrimidine-4, 6-dione), was administered to 121 patients with one or more types of convulsive seizures. Its anticonvulsant effect could be evaluated in 72 patients who were observed for periods ranging from 1 to 18 months. In all but 7, primidone was given in conjunction with one or more of the standard anticonvulsant drugs. Seizures were completely controlled in 10 per cent., reduced in frequency in 43 per cent., and unchanged in 47 per cent. The greatest benefit occurred when the seizures were of the grand mal, psychomotor, minor, or focal types. No improvement was noted in any of the patients with petit mal. Side-effects occurred in 65 patients, but none were serious. Drowsiness and ataxia were the 2 most frequent symptoms and made it necessary to discontinue the administration of primidone in 25 patients.

EDWARD J. VAN LOON (Chem. Abstr.)

Effects of Reserpine, a New Alkaloid of Rauwolfia Serptina on the Central Nervous System of the Animal. Meier, Rolf, et al. [*Compt. rend.*, **238**, 961 (1954).]

Reserpine, given at doses ranging from 0·03 to 1·0 mg. per kg. orally or intravenously, produces hypotension of long duration and marked sedation. This sedative action, as measured by the postural reflexes, is not similar to that found with phenobarbital and NaBr. At more elevated dosage levels of reserpine, the sedation never reaches the narcosis stage, but the duration of the sedation is increased. Reserpine, in addition to a sedation, produces a miosis, a hypothermia, and central inhibition. Thus reserpine acts differently than other known sedatives.

N. R. STEPHENSON (Chem. Abstr.)

Mechanism of Action and Metabolism of Antiepileptics. Toman, J. E. P., and Taylor, J. D. [*Arzneimittel-Forsch.*, **4**, 175 (1954).]

A review with 164 references.

K. SCHOEN (Chem. Abstr.)

Effect of Central Paralyzants in Animals Deprived of the Cerebral Cortex. Werner, G. [*Naunyn-Schmiedebergs Arch. exptl. Pathol. Pharmakol.*, **222**, 168 (1954).]

The effect of pentothal-Na and Largactil in cats is considerably enhanced after removal of the cerebral cortex. Bilateral superficial incisions at the base of the frontal lobes closely in front of the chiasma cause sham rage, but the sensitivity to the drugs is not increased.

A. E. MEYER (Chem. Abstr.)

Action of Some Medicinal Products to Increase the Permeability Towards the Brain Determined by the Action of Acetylcholine. Garattini, S., et al. [*Atti soc. lombarda sci. med. biol.*, **8**, 399 (1953).]

Acetylcholine shock renders the blood-brain barrier permeable to electropositive dyes, such as Bismarck brown, toluidine blue, and methyl violet, but does not change the permeability of electro-negative dyes. Acetylcholine shock does not modify the fixation of procaine in the brain; it increases considerably the penetration of penicillin.

A. E. MEYER (Chem. Abstr.)

Synergy Between Procaine and Strychnine. Strychnine Increasing the Permeability of the Blood-brain Barrier. Garattini, S., et al. [*Atti soc. lombarda sci. med. biol.*, **8**, 396 (1953).]

Both compounds act synergistically in producing convulsions. This is supposedly caused by intensive fixation of procaine in the cerebellum. Cerebellectomy increases the sensitivity of guinea pigs to strychnine. Strychnine increases the fixation of procaine in the brain.

A. E. MEYER (Chem. Abstr.)

Neurological Symptoms and Differential Diagnosis of Chronic Barbiturate Intoxication. Zigeuner, R., and Jaklitsch, H. [*Med. Monatsschr.*, **8**, 81 (1954).]

The electroencephalic findings are analyzed. Therapy consists in intravenous injections of procaine which not only combat the symptoms but also prevent the appearance of the withdrawal syndrome.

A. E. MEYER (Chem. Abstr.)

In Vitro Action of Barbituric Acid, 2-thiobarbituric Acid, and Some of Their Derivatives on Glycolysis in the Tissue of the Central Nervous System and of the Liver in the Rabbit Fetus and Young Rabbit. Santarato, R. [*Arch. sci. biol.*, **37**, 598 (1953).]

The action of barbiturates and thiobarbiturates on nervous and hepatic tissue of the fetuses of rabbits close to term and of newborn animals is fundamentally different than the effect on these tissues in adult rabbits. They inhibit the enzyme activity decisively. The cerebral tissue turns to adult response at about the 90th day of life, the liver tissue at the 40th day.

A. E. MEYER (Chem. Abstr.)

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The Influence of Depression of the Central Nervous System (Narcosis) on the Contents of Adrenaline in the Adrenal Glands of White Mice. Kulins'kii, V. I. [*Ukrain. Biokhim. Zhur.*, **25**, 278 (1953).]

There were 3 stages in the change in the value of adrenaline content under ether narcosis: 1st, sharp drop (>50 per cent.); 2nd, gradual increase, up to the 30th minute, reaching 150 per cent.; and 3rd, slow, progressive drop, reaching 65 per cent. of normal within 2 hours. The narcosis also tended to change the ratio of free and loosely bound (with protein) adrenaline. The adrenaline was estimated by the quantity fluorescent method (modification of Frenkel, *Ukrain. Biokhim. Zhur.*, **23**, 348 (1951).)

B. GUTOFF (Chem. Abstr.)

The Experimental Neuro-stimulating and Convulsant Effects of Theophylline and Some of its Derivatives. Mercier, G., et al. [*Trav. soc. pharm. Montpellier*, **9**, *No.* 2, 14 (1949).]

The analeptic and convulsant effects of theophylline and some of its soluble derivatives have been determined and compared. The compounds used were the Na salt of theophylline (I), 7-(2-hydroxyethyl)theophylline (II), 7-(2,3-dihydroxypropyl)theophylline (III), theophylline ethanolamine (IV), and 7-(2-diethylaminoethyl)theophylline (V). Dogs under chloralose anesthesia were perfused intravenously with (I) to (V) at the rate of 1·6, 1·8, 2·0, 2·44, and 2·55 mg. per kg. of body wt. per minute, respectively. The total amounts administered were recorded at the moment of awakening, at the onset of mild irregular convulsions, at the onset of frequent convulsions, and at the onset of incessant convulsions. (III) produced no awakening from the anesthesia and no convulsions. (I), (II), (IV), (V) produced awakening after the mean administration of 27, 32, 21, and 20 mg., respectively; they produced irregular convulsions after the mean administration of 34, 57, 24, and 26 mg., respectively; and they produced frequent convulsions after the mean administration of 53, 90, 48, and 34 mg., respectively; (I), (IV), and (V) produced incessant convulsions after the mean administration of 85, 77, and 58 mg., respectively: (II) produced no incessant convulsions. In addition measurements were made of the mean percentage increases in respiratory rate and the mean percentage decreases in arterial pressure after the administration of 1 g. per kg. of body wt. of each compound. (I) to (V) produced, respectively, 150, 72, 42, 57, and 83 per cent. increases in respiratory rate, and 42, 10, 10, 32, and 18 per cent. decreases in arterial pressure. Stimulating and convulsant activities for these compounds increase in the following order: (II), (I), (IV), (V), indicating that OH groups in the side chain decrease activity while NH_2 groups increase activity.

CONSTANTINE J. GILLESPIE (Chem. Abstr.)

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