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A Progress Study of Lobotomized and Control Patients.

Previous reports in the literature have crystallized quite well the results effected by frontal lobotomy in the treatment of the major psychoses. The authors' present investigation, which deals particularly with dementia praecox, gives further support to previous conclusions. Apparently one can anticipate that some 50 to 60 per cent. of appropriately selected patients will exhibit significant improvement following frontal lobotomy, with approximately equal division between levels of moderate improvement and of marked improvement. There appear to be relatively few relapses with the passage of time—at least within a 2-year period—and, statistically, these relapses are compensated by other cases that exhibit their optimal improvement after a year or more of post-operative interlude. In general, results are somewhat better in affective disorders and other nonschizophrenic conditions than in dementia praecox. Among the latter, best results are observed in the mixed and paranoid subgroups. Symptoms related to tension and depressive states, emotional aggressiveness and hyperkinetic behavioristic features are most amenable to lobotomy. This lends support to the implication emphasized by other investigators that the clinical results of psychosurgery are attributable to its influence on emotionally charged psychic phenomena, presumably through interruption of appropriate thalamic radiations. The authors' discharge rate of some 37 per cent. agrees closely with the statistics of other large series of cases. The most frequent significant complication, convulsive seizures, appears to occur in some 10 to 15 per cent. of patients. It is generally accepted that this is not a burdensome complication; it is readily controlled by anticonvulsant therapy. Operative mortality appears to range around 2 to 3 per cent.

The problem of controls has been of particular interest to the authors in their study. It was decided that the most satisfactory controls would be patients who, like the operative group, had been selected for lobotomy according to currently recognized clinical criteria, but on whom operation could not be performed because of refusal of permission by the family. The two groups were well matched from the standpoint of various factors, especially in the pertinent features of diagnostic grouping and symptomatology. Although the mean duration of hospitalization was somewhat lengthier in the control group, the difference was not sufficiently pronounced to exert a significant effect on the final results. The great majority of both groups had been hospitalized longer than two years—a temporal point that appears to be critical from the standpoint of recovery spontaneously or by the aid of therapeutic measures other than lobotomy.

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In contrast to the operative group, there was practically no change in the status of the control group at the termination of the two-year observation period. Only 3 per cent. exhibited significant improvement—none at a level superior to moderate improvement. No significant long-term improvement was achieved in this chronically ill control group by the use of shock therapies. Only 2 per cent. were able to leave the hospital, and one of these patients required rehospitalization within a relatively short time. It seems evident, particularly with respect to dementia praecox, that the course of the illness will be well crystallized before the end of the second year of hospitalization. Improvement, either by spontaneous means or by the use of shock therapies, is rare after this point, and it would seem fruitless to delay psychosurgery in appropriate cases much beyond this time. Comparative results in the authors' two groups lead to the inevitable conclusion that lobotomy exerts a beneficial effect that is not achieved by other means in cases of chronic mental illness. (Authors' abstr.)

Changes in the Body Weight of Schizophrenic Patients Following Prefrontal Lobotomy.

1. In this series of schizophrenic patients there was no consistent group change in weight prior to the sixth month after lobotomy.

2. At the sixth post-operative month the patients as a group showed a small but significant weight increase. This arose principally from a marked weight gain on the part of a small group of patients.

3. The marked weight gains that occurred in certain patients post-operatively led, for the most part, to a resumption of a normal weight rather than to the development of obesity.

4. Separate analyses of the improved and unimproved groups indicated a trend toward weight gain in the improved patients, and a trend toward weight loss in the unimproved patients.

5. The post-operative retraining program did not appear to be responsible for the weight changes after lobotomy.

6. These findings indicate that an increase in weight does not necessarily follow the operation of prefrontal lobotomy. It is suggested that those patients who do gain weight on a controlled diet do so as a result of the improved appetite that accompanies amelioration of their mental symptoms. There is no indication from these observations that lobotomy produces any metabolic change leading to abnormal weight increase. The findings, instead, would confirm the prevalent belief that obesity following lobotomy results from uncontrolled eating during the post-operative period. (Authors' abstr.)

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Dandy's Striatal Theory of " The Center of Consciousness " : Surgical Evidence and Logical Analysis Indicating Its Improbability.

In 1946 Dandy marshalled evidence to support the theory that the cerebral " center of consciousness " is located in the anterior striatum—specifically, in the oral portions of the head of the caudate nucleus and the putamen. He maintained that a lesion of these structures on one or both sides is followed by complete and permanent loss of consciousness.

Of 38 patients with Parkinsonism and 5 with torticollis on whom the author operated within the past decade 27 were subjected to removal, under direct vision, of portions of the anterior striatum corresponding to or exceeding the limits of the " center " described by Dandy. Three of the 27 patients died after operation and necropsy confirmed the existence of the intended lesions. Of the remaining 24 patients the post-operative period of none was characterized by enduring " unconsciousness." In 14 instances the surgical lesions were produced on the right side, in 9 on the left, and in 1, on both sides.

An analysis of the factual data presented by Dandy and the *modus operandi* by which he formulated the anterior striatum theory suggests that (*a*) in its present form the problem is not scientifically solvable ; (*b*) the clinical material employed was inept for its intended purposes ; (*c*) inferences were commonly mistaken for facts ; (*d*) unwarranted assumptions were frequently made ; (*e*) numerous variables inhering in the problem were overlooked or arbitrarily discounted, and (*f*) the fallacies of *petitio principii* and *non sequitur* were exercised.

The currently available data render the anterior striatum theory of the " center of consciousness " improbable. (Author's abstr.)

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Glucose Tolerance in Chronic Schizophrenia and Senile States.

Twenty-eight patients with chronic schizophrenia were compared with 10 patients with senile psychosis and studied with a modified Exton-Rose glucose tolerance test.

Of the patients with chronic schizophrenia, 67·9 per cent. showed abnormal, diabetic-like responses, as compared with 80 per cent. of the group with senile psychosis.

The mean values for the two groups reveal a severer disturbance in the senile patients.

It appears that this biochemical disturbance is related not only to stress, tension and anxiety but also to the ageing process. (Authors' abstr.)

Effect of Electroshock on the Blood-pressure in Psychotic Patients.

1. Immediately following the administration of electro-shock to psychotic patients, there are sharp systolic hypertension and diastolic lability. Both the systolic and the diastolic blood pressure return to preshock levels within 10 to 20 minutes. Patients with different psychoses seem to have similar blood-pressure responses.

The atypical blood-pressure responses of a hypertensive psychotic patient are described.

2. The delayed effects on blood pressure produced by the administration of elsctroshock in normotensive psychotic patients are as follows :

(*a*) Systolic and diastolic hypotension is present after 6 to 10 electroshocks have been given.

(*b*) Thereafter both systolic and diastolic blood pressures tend to return to the preshock levels and may not reach them until two weeks after the administration of the last electroshock. This phase is characterized by a widely divergent range of basal blood pressures.

Similar, but more pronounced, effects have been found in five hypertensive psychotic patients.

3. Changes in vascular reactivity in response to the cold pressor test attributable to electroshock treatments have not been observed in psychotic patients.

(Authors' abstr.)

Anticonvulsant Drug Therapy of Bahavior Problem Children with Abnormal Electroencephalograms.

Twenty-one boys with behavior problems of varied causations, 6 to 13 years of age, with various electroencephalographic abnormalities, in residential treatment in a children's psychiatric ward, received one or more anticonvulsant drugs, including diphenylhydantoin (dilantin), methylphenylethylhydantoin (mesantoin), trimethadione (tridione) and phenobarbital. Their behavior was noted fairly independently by a number of observers throughout the course of therapy. With minor exceptions the results were almost uniformly disappointing in producing any significant improvement in behavior. An attempt is made to explain the psychodynamics involved in the improvement of behavior disorders under drug administration in out-patient use, and a hypothesis is offered for the rationale of amphetamine therapy in the behavior disorders. (Author's abstr.)

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Use of Methylphenylsuccinimide in Treatment of Petit Mal *Epilepsy.*

The data show that N-methyl-a-phenylsuccinimide (PM 334) is equal to, if not superior to, trimethadione (tridione) in therapeutic efficacy in the group studied and has the advantage of being relatively nontoxic. Animal tests likewise indicate that PM 334 is much more active than trimethadione. In the author's experience, N-methyl-a-phenylsuccinimide has also proved more efficacious in that group of cases in which standard medicaments gave only indifferent to fair results.

Complete control of seizures was obtained for a period of from 4 to 31 weeks, with an average of 12 weeks for the group, in 30 per cent. of the total case-load on an average daily dose of 2·4 gm. Practical control was secured in 30 per cent. of the cases, this group showing an average reduction in attacks of 90 per cent. below the pre-experimental frequency for 13 weeks. Thirty-two per cent. of the total case-load showed an average reduction in attacks of 50 per cent., while only 8 per cent. of the entire group was not helped at all over an average period of seven weeks. (Author's abstr.)

Lesions of Transorbital Lobotomy.

Transorbital lobotomy produces minor lesions of the skull and dura. The cortex is usually traumatized very little. The distinctive lesions are within the white matter, the incision severing the thalamofrontal radiation just lateral to the anterior horn of the lateral ventricle, although sometimes penetrating the ventricle and lacerating the caudate nucleus. There is sometimes a hemorrhagic cavity in the frontal white matter, which evolves into a cyst with pigmented walls. Wallerian degeneration can be traced into the frontal lobe, and also through the internal capsule into the pons. Retrograde degeneration on the thalamus is milder than that seen after prefrontal lobotomy.

From the pathologic standpoint, transorbital lobotomy is a clean-cut, selective operation for severing the thalamofrontal radiation. (Authors' abstr.)

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*An Experimental Study of the Hippocampal Connexions of the Cingulate Cortex in the Rabbit. *Adey, W. R.* 233

The Familial Incidence of Disseminated Sclerosis and its Significance.

(1) The slow recognition of a genetic factor in the aetiology of disseminated sclerosis has been due to a number of causes, including the low familial incidence, the lack of published material, and the difficulty in distinguishing the progressive form of disseminated sclerosis from familial spastic ataxia and paraplegia.

(2) 184 families in which more than one case of disseminated sclerosis occurred have been collected from the literature. In this paper a further 33 families are recorded.

(3) In a series of 168 consecutive cases of disseminated sclerosis seen by the authors during a period of eighteen months there were 12 instances of one or more relatives being similarly affected. In an earlier series of 142 patients, in which the inquiry was more limited, the family history was positive on 8 occasions. Therefore in a total of 310 cases the familial incidence was 6·5 per cent. The case histories of affected members of families are recorded.

(4) The incidence of disseminated sclerosis in the sibs of 168 cases and in the parents of 310 cases is shown to be significantly higher than that expected on the basis of a random distribution of the disease.

(5) A few additional pedigrees of particular interest are described, including the occurrence of the disease in a mother and four of her daughters, and an example of the disease occurring by direct transmission in three generations.

(6) The clinical features and relative frequency of certain familial degenerative disorders of the spinal cord and of disseminated sclerosis are compared.

(7) The present study supports the view that a genetic factor is present in disseminated sclerosis, and that there is evidence pointing to both a dominant and a recessive mode of inheritance.

(8) A comparison is made between disseminated sclerosis and some other diseases in which a genetic factor plays a role in the aetiology. It is concluded that the aetiological factor or factors causing disseminated sclerosis may act more readily in the presence of an inherited disposition towards this disease.

(Authors' abstr.)

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An Experimental Study of the Hippocampal Connexions of the Cingulate Cortex in the Rabbit.

(1) An experimental study has been made in the rabbit of the connexions of the limbic cortex with the hippocampal region, using the silver staining method of Glees to demonstrate degenerating fibres and terminals following cortical ablation.

(2) It has been found that there is a strong connexion from the posterior cingulate and retrosplenial areas to the subiculum and presubiculum. The fibres run as two distinct laminae vertically downwards through the substance of the presubicular and subicular cortex.. The superficial weaker lamina is situated in the outermost layer of the cortex. The broader and deeper lamina shows numerous degenerating terminals in the presubicular and subicular cortex.

(3) Following lesions in the posterior cingulate and retrosplenial cortex degenerating fibres can be seen in sagittal sections in the upper part of the presubiculum and the upper part of the dentate gyrus. Their course to the dentate gyrus and presubiculum resembles closely that of the perforating temporo-ammonic tract of Cajal.

(4) A commissural connexion between the posterior cingulate and retrosplenial regions of one side and the corresponding regions of the opposite side has been demonstrated passing through the dorsal part of the splenium of the corpus callosum.

(5) Lesions in the anterior cingulate cortex produced severe degeneration in the cingulum extending posteriorly around the splenium of the corpus callosum to the upper part of the subiculum and presubiculum. Terminal degeneration was seen around the cells of the subiculum and presubiculum.

(6) Terminal degeneration in the posterior cingulate cortex was seen in laminae I and IV following lesions in the anterior cingulate cortex.

(Author's abstr.)

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Anterior Cingulate Gyrus and Corpus Callosum.

(1) Irritative and partly destructive lesions (not section) of the anterior corpus callosum cause a state of emotional excitability, confusion, motor unrest, irritability and often convulsions.

(2) As destruction of the corpus callosum progresses laterally the anterior cingulate gyri are undermined and their projection systems are destroyed.

(3) Undermining of the anterior cingulate gyri in the human subject, when the corpus callosum has been softened, causes complete apathy with akinesia and mutism.

(4) In all probability the anterior cingulate gyri have the same function in the human subject as in the monkey; it is, among other things, the cortical area for emotional expression.

(5) Since all action is emotionally motivated, absence of emotional expression leads to absence of all activity. When the corpus callosum is, in addition, degenerated but not severed the individual has the mechanism of movement interfered with: he has apraxia. (Author's abstr.)

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Diffuse Thalamic Projection to Cortex : an Anatomical Critique.

A fallacy is pointed out in Morison and Dempsey's claim to have excluded by experiment the possibility that diffuse activation of cortex from the thalamus occurs by way of the specific projection nuclei ; they only excluded the primary neurones of sensory relay nuclei. The argument by exclusion that there must be a non-specific projection system from thalamus to cortex therefore no longer holds.

Review of morphological aspects of the intralaminar nuclei and the reticular nucleus, which have been postulated to make up such a diffuse thalamo-cortical projection system, reveals evidence suggesting that none of these nuclei possesses a direct diffuse projection to neocortex. There is, however, circumstantial evidence pointing to the possibility that the " centromedian complex " of intralaminar nuclei diffuses activity within the thalamus, and hence can act as a distributing centre for widespread activation of the cortex by way of the corticopetal connections of some of the specific projection nuclei. The evocation of cortical recruiting responses from the neighbourhood of the smaller rostral and medial intralaminar nuclei may be attributable to activation of nerve-fibres of passage coursing between the centromedian nucleus and regions rostral to the thalamus and between left and right centromedian nucleus.

There are several morphological objections to regarding the reticular nucleus and the centromedian nucleus as two parts of one system. (Author's abstr.)

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Cingulate-cerebellar Mechanisms in the Physiological Pathogenesis of Epilepsy.

(1) The effects of electrical stimulation of the anterior cingulate gyrus are described.

(2) Respiratory, motor and electroencephalographic effects are observed and include suppression and facilitation in each category. Respiratory effects consist of arrest and hyperpnoea. Motor effects consist of arrest of spontaneous motor movement and facilitation in the form of a jerk of the muscles of the face. With increasing intensity of stimulation, the jerking involves progressively the muscles of the neck, forelimbs, trunk and hindlimbs, in that order.

(3) Electroencephalographic suppression has been reported in detail previously. After-discharge may also be produced by stimulation of the anterior cingulate gyrus, but not of the pre- or sub-callosal areas nor of the posterior cingulate gyrus. Optimum parameters of stimulation are: frequency, 30 per second, pulse duration, 11 to 16 msec., and intensity, 2 to 3 volts. The stimulus is applied for 10 seconds and the after-discharge persists 5 to 30 seconds after cessation of stimulation. It usually shows a characteristic 3-per-second spike and wave configuration, although the rate may be 12 to 18 per second. It is transmitted preferentially to the cerebellum, where it may be amplified and at a faster rate. It is seen less often in the lateral cerebral hemispheres, has been recorded from the hippocampal formation, or may remain localized.

(4) Electrical stimulation of the uncus elicits local after-discharge, which spreads preferentially to the temporal tip and posterior orbito-frontal areas, but may involve the anterior cingulate gyrus and cerebellum as well.

(5) Electrical stimulation of the cerebellum does not elicit local or transmitted after-discharge.

(6) Dilantin elevates the threshold of motor cortex to the point of unresponsiveness at maximal stimulation but does not alter the threshold of the anterior cingulate gyrus.

Triodine elevates the threshold of the motor cortex and of anterior cingulate gyrus slightly.

(7) The similarities are reviewed between the effects of stimulation of the anterior cingulate gyrus and the clinical seizures of the *petit mal* triad. It is suggested that *petit mal* triad seizures are attributable to discharge in a system which includes the anterior cingulate gyrus and cerebellum as well as the anterior and mid-line thalamic nuclei.

(8) A functional integration in this system of the hippocampal formation and entorhinal areas afferent to it is suggested. (Authors' abstr.)

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Ictal and Non-Ictal Psychiatric Disorders in Temporal Lobe Epilepsy.

Analysis of 458 cases with electroencephalographic evidence of focal seizure discharges reveals that the anterior temporal region is more vulnerable than any other area to the type of injury which results in focal discharging lesions. Ninety-five per cent. of 163 cases with focal seizure activity in the anterior temporal lobe had clinical psychomotor seizures. This is eight times as great as the association between psychomotor seizures and epileptic foci in other parts of the cortex. Psychiatric disorder was more than three times commoner in cases with focal seizure activity in the temporal lobe than in cases with a focus in any other cortical area. The epileptic and psychiatric components of psychomotor epilepsy are independent, and though physiologically antithetic they are anatomically associated. Non-ictal psychiatric disorder is not temporally associated with electroencephalographic abnormalities, but the seizure discharge provides a clue to the anatomic locus of the psychiatric disorder.

The present data suggest that the temporal lobe subserves a hierarchy of neuronal functions. These are divisible into (*a*) sensation, (*b*) perception, (*c*) evaluation, and (*d*) judgment. The middle and posterior temporal cortex are chiefly concerned with (*a*) and (*b*) and the anterior temporal region with (*c*) and (*d*). Specific psychiatric symptomatology depends on the type of disorder, minor differences in locus and degree of involvement of specific neurones. Misevaluations resulting from disorder in posterior temporal regions result in distortions of the meaning of specific afference streams; for example, hallucinations, micropsia, *déjà vu*. Misinterpretations of the total afferent stream (experience) results in such symptoms as depression and psychopathy. (Author's abstr.)

Chemical Analysis of Spectrophotometric Findings in the Cerebrospinal Fluid.

(1) Ultraspectrophotometry and chemical determination of the ascorbic acid content of the cerebrospinal fluid were carried out simultaneously in 40 cases.

(2) In a part of the material the ascorbic acid and protein content of the C.S.F. accounted for its selective absorption with the peak at 2650 A. These were cases without definite structural alterations of the central nervous system or with preponderant lesions of the white matter, cases studied one or more years after cerebral injury or in the early stage of an affection of the cerebrum.

(3) In certain pathologic cases (particularly tumors, some convulsive disorders, recent cerebral concussion) a definite difference was found between the selective absorption of the C.S.F. at 2650 A and the sum of the extinction coefficients corresponding to the ascorbic acid and to the protein content.

(4) Reasons are given supporting the view that this difference is due to the appearance of purine or pyrimidine compounds in the C.S.F.

(Authors' abstr.)

JULY.

Autonomic Changes Paralleling Psychologic Changes in Mentally Ill Patients. *Funkenstein, D. H., et al.* 1
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The Syndrome of Sensorimotor Induction in Combined Cerebellar and Labyrinthine Injury. *Halpern, L.* 137
*Electroshock Therapy in Schizophrenia. *Palmer, D. M., et al.* 162

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Electroshock Therapy in Schizophrenia : a Statistical Survey of 455 Cases.

Four hundred and fifty-five male veteran schizophrenics were treated with a single series of electroshock treatment with the following results :

(1) One hundred and ninety-eight patients or 43·5 per cent. showed either marked or moderate improvement.

(2) Seventy of these 198 relapsed before they could be discharged.

(3) One hundred and twenty-eight patients were discharged with marked or moderate improvement following electroshock. This was a discharge rate of 28·1 per cent.

(4) Forty-eight of the 128 discharges (or 37·5 per cent.) had relapses after they left the hospital, leaving the number of discharges, after a period ranging from 42 to five months, at 80 (or 17·6 per cent.) remaining discharged.

(5) There was a definite relationship between length of illness and remission following shock. Those who remained discharged had a mean illness period of 15 months, while those who remained hospitalized had been ill slightly over 39 months (mean value).

(6) Hebephrenics appeared to respond somewhat less favorably than catatonics.

(7) Those who responded well to electroshock were significantly younger in age than those who did not improve, but further analysis showed that the patients who responded satisfactorily had been ill a shorter period and that illness duration, and not age, was the important prognostic factor.

(8) Whites responded more favorably than negroes, both in terms of hospital discharge and in not suffering relapse after leaving the hospital.

(Authors' abstr.)

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*Electrical Activity of the Human Brain During Artificial Sleep. II. *Wyke, B. D.* 137

Electrical Activity of the Human Brain During Artificial Sleep.

The cyclical changes induced in each of the major subdivisions of the human brain surface by progessive barbiturate sedation are described.

Evidence is presented to show that during the onset of sleep the brain does not respond in an overall uniform fashion.

It is suggested that while in the waking human brain different cortical areas do not usually possess well-defined electrical identities, during the onset of sleep they pass through a period when they may assume more or less independent patterns ot electrical behaviour, the pattern of electrical activity at each stage of sleep being characteristic of the particular region.

(Authors' abstr.)

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Thalamo-cingulate Fasciculotomy.

Occasional undesirable sequelae following psychosurgery indicate the need for a less extensive procedure which may accomplish its purpose without the complication of post-operative personality impairment or epilepsy.

An effort is being made to accomplish this by interruption of the thalamo-cingulate projection because of the evidence of its relationship to emotion, and the fact that the procedure spares a substantial part of the anterior thalamic radiation.

A simple procedure has been described, which seems capable of interrupting these impulses, through a small incision at an easily identified landmark.

(Author's abstr.)

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*A Psychometric Examination of Latent Homosexuality in Alcoholism. *Botwinick, J., and Machover, S.* 268
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The Inhalation of Ethyl Alcohol by Man: I. Industrial Hygiene and Medicolegal Aspects. II. Individuals Treated with Tetraethylthiuram Disulfide.

1. A search of the literature pertaining to the inhalation of alcohol by man indicated that the presently accepted value for the maximum allowable concentration in the air was based on vague qualitative observations, and that it was erroneous from the standpoint of industrial safety and hygiene and of no value for medicolegal purposes.

2. Qualitative observations were made of the effects of varying concentrations of alcohol in the air at various rates of ventilation. It is concluded that concentrations greater than 40 mgm. per litre are intolerably irritating, while at concentrations between 10 and 20 mgm. per liter work might be carried on, albeit not in comfort.

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3. Determinations of the percentage of alcohol absorbed from the inspired air showed that 62 per cent. of the alcohol is absorbed.

4. Human subjects were exposed to various concentrations of alcohol in air for periods up to 6 hours, at various rates of ventilation. Determinations of the resulting concentrations of alcohol in the blood indicated a simple relationship for calculating the maximum allowable concentration under various conditions of work. A maximum allowable concentration of 7 mgm. per liter is proposed, which is about 4 times the accepted value.

5. It was shown that intoxication can result from the inhalation of alcohol under certain conditions, and an expression has been given for calculating the concentration which may be expected to develop in the blood provided four facts are known: the concentration of alcohol in the air, the rate of ventilation of the individual, the individual's weight, and the duration of the exposure.

6. Observations on patients under treatment with tetraethylthiuram disulfide showed that the maximum safe concentration for T.E.T.D.-treated individuals is 2 mgm. of alcohol per liter of air. (Authors' abstr.)

Psychiatric Implications of the Treatment of Alcoholism with Tetraethylthiuram Disulfide.

1. In a series of 42 patients treated with tetraethylthiuram disulfide, 8 developed psychotic episodes. Five of these episodes were transitory and reponded promptly to the withdrawal of T.E.T.D. and the use of mild sedation. Three were relatively prolonged.

2. The projective, hostile individual who feels threatened by help and who has difficulty in forming interpersonal relationships is usually not a desirable candidate for treatment with T.E.T.D.

3. A history of psychotic episodes, or an indication of incipient psychosis, contraindicates treatment with T.E.T.D.

4. Borderline schizophrenic adjustments, as well as character neuroses with transitional schizophrenic components that may be easily overlooked, should be particularly watched for. In the authors' present series the psychotic reactions developed in these two groups of patients. It is possible, of course, that an unidentified element of selection in the authors' series may differentiate it from other reported groups.

5. Individuals who show a capacity to develop sustained interpersonal relationships and who show some utilizable dependency traits appear to be suitable candidates for treatment with T.E.T.D. The incidence of therapeutic success is highest when T.E.T.D. treatment is employed with individuals selected on the basis of psychiatric criteria of suitability, including a demonstrated ability to utilize psychotherapy. The implications of T.E.T.D. are almost always linked inseparably with the implications of psychotherapy.

6. Five of the eight psychotic responses in the authors' series occurred several weeks after the patient's discharge from the hospital, and indications of mounting anxiety usually had been observable during the earlier T.E.T.D.-alcohol reaction tests. This anxiety, together with parallel signs, can be used in helping to forsee and to handle complications that may arise in the future use of T.E.T.D. Of the three other breakdowns, one emerged shortly after the third T.E.T.D.-alcohol test in the hospital (4 weeks after the beginning of T.E.T.D. medication), one occurred at the first T.E.T.D.-alcohol test, and the third was manifested prodromally during the first test. These findings, along with other considerations, suggest that psychodynamic factors may be responsible. At this stage in the authors' investigation they have been unable to rule out completely possible physiological components that might have contributed to the production of emotional manifestations. Considerable further psychiatric, medical and physiological studies will be necessary before a final evaluation and correlation of these factors can be made.

(Authors' abstr.)

Psychotic Phenomena Provoked by Tetraethylthiuram Disulfide.

Tetraethylthiuram disulfide may give rise to specific psychotic phenomena when taken in doses unnecessarily high for the individual patient.

This can be avoided by continuous observation of the patient for the special, relatively mild, side effects precursory to the state of psychosis. Even in patients

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highly sensitive to T.E.T.D. a carefully adjusted minimal dosage may prove to be of therapeutic value. (Authors' abstr.)

Tolserol in the Treatment of the Post-alcoholic State.

Tolserol in doses of 2 to 2·5 gm. per day is of decided benefit in the management of the post-alcoholic state. It markedly reduces or eliminates tremulousness and gastrointestinal symptoms, and improves the subjective state of the patient. It has a lesser effect on sleep. This rapid improvement in the post-alcoholic state facilitates better psychotherapeutic management and reduces the necessity for prolonged hospitalization. (Authors' abstr.)

A Psychometric Examination of Latent Homosexuality in Alcoholism.

1. The purpose of this study was to examine by means of interest tests the hypothesis that regards alcoholism as a condition involving some homosexual component.

2. The M-F and " I " scales of the Terman and Miles Attitude Interest Analysis Test and a mimeographed version of the M-F Scale of the Minnesota Multiphasic Personality Inventory were administered to 39 patients in the alcoholic ward of the King's County Hospital. These scales were given to the same patients in 31 cases.

3. The mean M-F scores were not statistically different from the means of the normative populations employed in the standardization of the tests. There was, however, a significant difference between the " I " score means. These differences point to the " normality " of the experimental alcoholic population in regard to sexual interest pattern.

4. It is concluded that in so far as the tests used in this study measure homosexuality, latent or otherwise, homosexuality cannot be an essential factor in alcoholism, although it may play a dynamic role in individual cases.

(Authors' abstr.)

RASS. STUD. PSICHIAT.

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1. Biochemistry, Pathology, etc.

Cholinesterase of Red Cells in Mental Diseases. Barbato, L., and Terrana, V. [*Acta neurol (Naples)*, **5**, 429–37 (1950).]

The cholinesterase content of red cells is lower in women than in men, is substantially lower in catatonic, hebephrenic and simple schizophrenia and in biopathic or cerebropathic phrenasthenias, has a trend to decrease in progressive paralysis, and is normal in paranoid schizophrenia, in dysthymias, and other phrenasthenias.
C. SCANDURA (Chem. Abstr.).

Cholinesterase in Encephalitic Parkinsonism. Barbato, L. (*Univ. Palermo, Italy*), *and V. Terrana.* [*Lavoro neuropsichiat.*, **7**, 9 *pp.* (1950 (reprint).]

In 19 patients the cholinesterase of red cells was low (5·04 in men, 4·80 in women, in c.c. 0·01 N NaOH per c.c. blood as in method of following abstract). The

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decrease was greater in patients to whom belladonna was administered. Red blood cells taken from the side attacked by the syndrome showed lower values than cells from the other side. C. SCANDURA (Chem. Abstr.).

Factors Affecting Acetylcholine Found in Excised Rat Brain. Elliott, K. A. C., and Henderson, Nora, (McGill Univ., Montreal, Can.). [*Am. J. Physiol.*, **165**, 365–74 (1951); *cf. C. A.*, **44**, 10179*b*.]

The amount of acetylcholine (I) found in rat whole brain does not change rapidly after excision; in cortex it falls with time. Less (I) is found in brains of small than of large animals. Freezing in liquid air causes loss of (I). This does not occur in brains from eserinized animals. The (I) content of brains of eserinized animals is elevated. Virtually all the (I) in brain is in the bound form. Acid, mechanical disturbance, freezing, hypotonic suspension medium, and high K concentrations accelerate liberation from the bound form. The release of (I) from the bound form appears to be reversible. The possibility is discussed that bound (I) is not necessarily an intermediate in the production of free (I), and that the (I)-synthesizing system may be located on the cell surface.

E. D. WALTER (Chem. Abstr.).

The Presence of a Reticulocytogenic Factor in the Cerebrospinal Fluid (CSF). Agostini, Luciano (Univ. Perugia, Italy). [*Riv. Biol. (Perugia)*, **42**, 339–55 (1950) (*English summary*).]

Normal rabbits intravenously injected with 1 c.c. centrifuged CSF taken from bled rabbits showed a high reticulocytosis in the peripheral blood. This did not occur when the CSF was taken from normal rabbits. Therefore there may be a reticulocytogenic factor in the CSF. C. SCANDURA (Chem. Abstr.).

The Precipitation of Cerebrospinal Fluid Globulin by Zinc Sulfate. Donovan, Alfred M., Foley, Joseph M., and Moloney, William C. (Boston City Hosp., Boston, Mass.). [*J. Lab. Clin. Med.*, **37**, 374–81 (1951).]

The method is based on that described by Kunkel (*C. A.*, **42**, 1620*i*) for the study of serum proteins. Results of the test correlate well with the presence of neurosyphilis and multiple sclerosis. The procedure may be useful in measuring the degree of activity of the disease process in multiple sclerosis.

FRED H. SNYDER (Chem. Abstr.).

Chlorides in Spinal Fluid in Normal and Pathological Conditions. Trautman, S., and Ambard, L. [*Bull. acad. natl. med.*, **135**, 105–7 (1951).]

Capillary ultrafiltration supplies the meningeal space with a fluid closely resembling plasma in electrolyte concentration. In the process of circulation fluid is selectively filtered out of the system, leaving a higher concentration of Cl in the remaining fluid. A similar condition exists in the aqueous humor of the eye.

A. E. MEYER (Chem. Abstr.).

Glutamic Acid and Intelligence Quotient. Delay, Jean, and Pichot, P. [*Bull. Acad. natl. méd.*, **135**, 112–17 (1951).]

Modification of the metabolism of the nerve cells improves the intelligence output. A. E. MEYER (Chem. Abstr.).

Cell Content of Cerebrospinal Fluid. Bedford, T. H. B. [*Brit. J. Pharmacol.*, **3**, 80–3 (1948).]

The cell content of the cerebrospinal fluid was determined 24 hours after the introduction of procaine, amylocaine and amethocaine into the cisterna magna of dogs; the effects were compared with those produced by distilled water, isotonic NaCl, and Ringer solution. Isotonic NaCl solution, 1 per cent. procaine, and amylocaine-HCl in distilled water excited reactions of approximately equal intensity. Ringer solution caused a more intense reaction than distilled water, but less than that of isotonic NaCl solution. The result of these experiments raises doubts about the advisability of using simple NaCl to render isotonic solutions required for introduction into the subarachnoid space. B. A. (Chem. Abstr.).

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Significance of Glutamic Acid for the Metabolism of Nervous Tissue. Weil-Malherbe, H. (Runwell Hosp., Wickford, Essex, Engl.). [*Physiol. Revs.*, **30**, 549–68 (1950).]

The 3 enzymic reactions involving glutamic acid (deamination, transamination, amidation) may perhaps be integrated into a system for the deionization and removal of intracellular NH_3. Glutamic acid is the only amino acid oxidized in the brain to any appreciable extent by a specific enzyme. Transamination of glutamic acid serves as a buffer system which takes up the sudden influx of NH_3 and ensures its gradual disposal during restitution. The amidation reaction is formulated as follows: glutamic acid + NH_3 + ATP → glutamine + ADP + H_3PO_4. Glutamic acid is known to maintain respiration of nervous tissue. It may also be essential for sustaining its function. Glutamic acid may exert its special activity through its effect on permeability of the nerve cell membrane. The latter may become increased, allowing diffusion from the cell, which can be prevented by the joint action of glucose and glutamic acid. As far as the effect of glutamic acid in hypoglycemia is concerned, the evidence seems to point to an adrenergic stimulation. Similarly, the effect of glutamic acid in the treatment of *petit mal* or of mental deficiency is believed to be by an adrenergic mechanism just as in the case of amphetamine (sympathomimetic amines). In fact, a comparison of their effects manifests such a degree of parallelism as to suggest a fundamental identity of the underlying mechanism. S. Morgulis (Chem. Abstr.)

Relation Between the Adaptation-tropic Filaments of Sympathetic Nervous System and the Adrenals. Senkevich, I. V. (Kazan Sect., Acad. Sci). [*Fiziol. Zhur. S.S.S.R.*, **36**, 558–65 (1950).]

The source of sympathin in animals appears to be adrenaline circulating in the blood. In the absence of sympathin the sympathetic nervous system loses the ability to transmit through its adaptation-tropic fibres the impulses to the appropriate tissues. G. M. Kosclapoff (Chem. Abstr.).

Effect of Vegetative Nervous System on the Recoil Reflex. Gumenyuk, I. G. (Dnepropetrovsk State Univ.). [*Fiziol. Zhur. S.S.S.R.*, **36**, 552–7 (1950).]

Deposition of a NaCl crystal on the thalamic region of the brain causes the disappearance of the recoil reflex, caused by Faradic stimulation of the central end of sciatic nerve. The phenomenon is reversible. Ergotoxin in 1 : 1000 concentration does not affect the reflex, but it removes the blocking effect of the thalamic region on this reflex. The NaCl effect is manifested through the sympathetic nervous system. G. M. Kosolapoff (Chem. Abstr.).

The Effect of Estrogen on the Phosphate Turnover in the Hypophyseal-diencephalic System. Borell, U., and Westman, A. (Karolinska Sjukuset, Stockholm) [*Acta Endocrinol.*, **3**, 111–18 (1949).]

Normal and hypophysectomized rats were treated with estradiol monobenzoate administered by intramuscular injection. P^{32} in 5 per cent. glucose solution was given 40 minutes before decapitation. The radioactivity and total phosphate of the blood, cerebellum, tuber cinereum, adenohypophysis and ovaries were determined. In normal rats estradiol monobenzoate in comparatively high doses increased the P^{32} turnover in the adenohypophysis and tuber cinereum. In hypophysectomized rats it had no significant effect on the tuber cinereum.
Elva G. Shipley (Chem. Abstr.).

Effect of Treatment with Adrenocorticotropic Hormone (ACTH) or Cortisone on Anatomy of the Brain. Castor, C. William, Baker, Burton L., Ingle, Dwight J., and Li, Choh Hao (Univ. Michigan, Ann Arbor). [*Proc. Soc. Exptl. Biol. Med.*, **76**, 353–7 (1951).]

In rats, administration of ACTH caused chromatolysis in the cells of the paraventricular hypothalamic nucleus. Cortisone affected this nucleus but induced more widespread chromatolysis and vacuolation of thalamic and hypothalamic nerve cells. L. E. Gilson (Chem. Abstr.).

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The Effects of Increased Potassium Concentration on the Metabolism of Rat Cerebral Cortical Slices. Lipsett, Marie Nieft, and Crescitelli, Frederick. (*Univ. of California, Los Angeles*). [*Arch. Biochem.*, **28**, 329–37 (1950).]

The Qo_2 of thin slices of cortical tissue in a glucose substrate was increased 75 per cent. by the addition of 0·1 M KCl. The effect of K was less marked in the presence of lactate and pyruvate substrates and absent with α-ketoglutarate and succinate. The addition of glutamate, citrate, α-ketoglutarate, or succinate (all participants in the tricarboxylic acid cycle) to the glucose substrate abolished the effect of K. Aspartic acid, methionine and glutamine caused no inhibition. In lactate and pyruvate media the K response was greater, on a percentage basis, at 25·5° than at 37·5°. With these substrates, glutamate inhibited the effect of K at the lower but not at the higher temperature. NaF and 2, 4-dinitrophenol inhibited the K effect, while NaN_3 did not. FRED H. SNYDER (Chem. Abstr.).

Microchemical Studies of the Nervous System. VIII. Changes in the Cystine Content of Nerve During Degeneration. May, Raoul Michel, and Thillard, Marie Jeanne (*Sorbonne, Paris*). [*Bull. soc. chim. biol.*, **32**, 977–82 (1950); *cf. C. A.*, **43**, 5461*i*).]

During degeneration of the severed sciatic nerve of the rabbit the cystine content nearly doubled during the first 10 days, then slowly decreased. The relative increase in cystine was much greater than the increase in protein content of the nerve during the same period. L. E. GILSON (Chem. Abstr.).

Microchemical Studies on the Topical Distribution of Trace Elements in the Brain. Bertha, H., Malissa, H., and Pohl, F. (*Tech. Hochschule, Graz, Austria*). [*Mikrochemie ver. Mikrochim. Acta*, **36/37**, 988–96 (1951).]

Besides K, Ca, Na, Mg, and P, all the spectrograms show the presence of Al and Cu in the brain although their distribution in different parts of the brain is not yet known. Pb, Zn, Sr, Ag, Be and Ti also appear in the regions examined. The existence of separate cells in certain sections of the brain makes it seem possible that special elements may be required for the exercise of special functions. No definite conclusions can be drawn now. W. T. HALL (Chem. Abstr.).

The Effect of Some Antihistamines and Calcium Preparations in Disturbances of the Vascular Permeability in the Brain. Broman, Tore (*Lund, Sweden*). [*Intern. Arch. Allergy Applied Immunol.*, **1**, 299–305 (1951).]

Antihistamines and Ca preparations either separately or together were unable to prevent or contribute to the healing of disturbances of vascular permeability in the brain produced chemically or serologically. There is a possibility that these substances might even exert an unfavourable effect so that a site of disturbance of permeability becomes a site of punctate hemorrhage.

JULIAN H. LEWIS (Chem. Abstr.).

The Histochemistry of the Corpora Amylacea of the Central Nervous System. Bravi, Giovanni, (*Univ. Pavia, Italy*). [*Atti soc. ital. sci. nat. e museo civico storia nat. Milano*, **86**, 14–22 (1947).]

Human brains from victims of late stages of syphilis that had been preserved in formalin for 10 years to a few hours were used. Tissue was taken from the subependymal zone of the lateral ventricles and of the third ventricle, sectioned, frozen and fixed in paraffin. Sturmer (*Histol. Histopathol. Arch.*, **5**, No. 3, 417) recorded tests showing the presence of carbohydrates in " corpora amylacea " (CA) found in such sections. Immediate study in water after staining with 0·5 per cent. toluidine blue for a few minutes showed metachromasia clearly in some of the larger CA, especially in the nucleus. A feeble test of the same sort was obtained in the nuclei of the larger CA of preparations mounted 10 hours in glycerol. This reaction shows that the composition of the CA is not homogeneous, even though doubt has been raised that it proves the presence of polysaccharide sulphates. The technique of Bignardi (*Boll. soc. med.-chir. Pavia*, **54** (1940), as well as that of Bignardi and Casella (*Boll. soc. med.-chir. Pavia*, **55**, No. 6 (1941), after 240 hours, gave a positive test for metachromasia which is more characteristic of amyloid than of mucoprotein. Tests for lipides (including phosphatides) were negative. The cortex or pheripheral

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part of the larger CA and the entire smaller ones are composed of undifferentiated material, from which, as the CA grow, the organized materials of the nucleus are formed. The nuclei of the larger CA have in addition to the characteristics of the cortex the ability to react as H_2SO_4-esters of the higher polysaccharides.

E. L. GREEN (Chem. Abstr.).

Oxygen Consumption of the Cerebrum. Coviân, F. Grande. (Univ. Madrid). [*Rev. clín. españ.*, **39**, 1–17 (1950).]

L. E. GILSON (Chem. Abstr.).

Biochemical Studies on the Action of the Nerve. II. The Distribution of Cholinesterase in Animal Brains. Okinaka, Shigeo, Yoshikawa, Masaki, and Gotô, Jûya. (Univ. Tokyo). [*Igaku to Seibutsugaku (Med. and Biol.)*, **18**, 38–40 (1951); *cf. C. A.* **45**, 1181*c*.]

Cholinesterase activities in various parts of brains of rats, rabbits and dogs were determined with results closely agreeing with those of Nachmansohn (*C. A.* **33**, 7322[8]). The enzyme activity was fairly constant in one part of brain in one species of animal, although significant differences were observed between the enzyme activities of various parts of one animal or of one part of various species. The enzyme activities in the brains of rats inoculated with Yoshida's sarcoma showed no appreciable difference from those of normal rats, although the enzyme activities in the liver and serum were lowered by 20–30 per cent.

M. N. (Chem. Abstr.).

Glutamic Acid Decarboxylase in Brain. Roberts, Eugene, and Frankel, Sam. (Washington Univ., St. Louis, Mo.,) [*J. Biol. Chem.* **188**, 789–95 (1951); *cf. C. A.*, **45**, 3431*g*.]

Glutamic acid decarboxylase was demonstrated in homogenates and acetone powders from mouse brain. The enzyme is a typical decarboxylase. It requires pyridoxal phosphate as coenzyme and is inhibited by semicarbazine and NH_2OH. When excess glutamic acid and pyridoxal phosphate are present the reaction is of zero order and the activity is proportional to the quantity of enzyme used.

FELIX SAUNDERS (Chem. Abstr.).

Phosphate Transport and Turnover in the Brain. Sacks, Jacob, Culbreth, Geo. G., and Damast, Barbara. (Brookhaven Natl. Lab., Upton, N.Y.). [*Am. J. Physiol.*, **165**, **251–6** (1951).]

A comparison was made of the distribution of intracisternally and intravenously injected tracer phosphate between brain, blood plasma, and muscle in cats. In 4 hours after the injection into the cisterna magna, about 60 per cent. of the tracer appears to be absorbed into the general circulation. There is a very rapid interchange of phosphate between the cerebrospinal fluid and the brain substance, with a high rate of incorporation of the tracer into the phosphocreatine and the labile P of the adenosine triphosphate (ATP) of the brain. The apparent turnover rate of the phosphocreative and ATP of brain following the intravenous injection of the tracer is higher than the turnover rate of these compounds in resting muscle. The intravenously injected tracer becomes available to the brain substance for turnover by secretion into the cerebrospinal fluid.

E. D. WALTER (Chem. Abstr.).

Tetanus Intoxication and its Effect on the Metabolism of Central Nervous Tissue, Asakura, Shintarô, Takaki, Masahiko, Kinashi, Atsuo, and Higashiyama Akira. (Osaka Univ.). [*Osaka Daigaku Igaku Zasshi*, **2**, 395–405 (1950).]

Reducing sugars, acetone bodies, pyruvate and α-ketoglutarate in the spinal fluid and blood of rabbits poisoned with tetanus were estimated. The amount of glucose and total acetone bodies in both blood and spinal fluid increased as the tetanus paralysis proceeded. The rate of increase in spinal fluid was greater than that in blood. The increase in β-hydroxybutyrate and acetoacetate accounted for most of the increase in the acetone bodies. Acetoacetate began to increase before β-hydroxybutyrate increased. Pyruvate and α-ketoglutarate increased in parallel with the intoxication. The increase of α-ketoglutarate was earlier in the spinal

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fluid than in blood, as was that of pyruvate. The return of these metabolites to normal levels was much earlier than the recovery from paralysis.

ITIRO TYUMA (Chem. Abstr.).

Multiple Sclerosis: A Correlation of its Incidence with Dietary Fat. Swank, Roy Laver. (*McGill Univ., Montreal, Can.*). [*Am. J. Med. Sci.*, **220**, 421–30 (1950).]

An epidemiologic study of multiple sclerosis in Europe and unreported clinical studies indicate that a diet high in fat, although not the cause of multiple sclerosis, may contribute to a high incidence of the disease by accelerating it in susceptible individuals. MARION HORN PESKIN (Chem. Abstr.).

The Localization of Cerebral Tumors with Radioactive Derivatives of Fluorescein. Belcher, E. H., and Evans, H. D. [*Brit. J. Radiology*, **24**, 272–9 (1951).]

It is possible to detect lesions concentrating $(I)^{131}$ with the scintillation counter described, provided that the concentration of activity in the lesion is 10 times that of normal brain, and the size of the lesion is greater than a certain minimum volume depending on its depth. The syntheses of diiodo^{131} fluorescein and of dibromo^{82} fluorescein are described. G. L. CLARK (Chem. Abstr.).

Presence of Histamine in Extracts of the Central Nervous System. Cicardo, Vicente H., and Stoppani, A. O. M. [*Pubs. centro invest. tisiol.* (*Buenos Aires*), **13**, 153–65 (1950).]

The mechanism of the action of brain extracts on arterial pressure, respiration and pupillary diameter in the dog was studied. The active reagent of the action of the extracts has the following properties: (*a*) It is inhibited by antihistaminic benadryl to the same extent as histamine; (*b*) it is not affected by atropine; (*c*) like histamine, it is not precipitated by Pb salts, but it is precipitated by Ag in alkali solution of $Ba(OH)_2$ and by phosphotungstic acid in acid medium, while the hypotensor action of the active fractions is inhibited by benadryl. The hypotensor agent is extracted from the cerebral tissue by alkali, acetone, and CCl_3CO_2H. These findings indicate that histamine is the principal reagent of the pharmacological action of the extracts of the central nervous system of the dog. The histamine equivalent of the nervous tissue is approximately 15–20 γ/gm. of the fresh tissue. The hypotensor effects of brain extracts, peduncles and bulb are similar, while the effects obtained with cerebellar extracts are less marked. The hypotensor action of brain extracts of different types of animals are analogous.

W. R. EICHLER (Chem. Abstr.).

The Decerebration Rigidity of Bufo arenarum as Test for Curarizing Substances. Patetta, M. A. (*Facultad med., Montevideo, Uruguay*). [*Arch. soc. biol. Montevideo*, **16**, 91–4 (1949) (pub. 1950).]

The rigidity shown by decerebrated *Bufo arenarum* disappeared after subcutaneous injection of crude curare, flaxedil, or intocostrin T in a few minutes. This reaction is recommended as a test for curarizing substances.

F. FROMM (Chem. Abstr.).

The Neuropathology of Antibiotic-induced Peripheral Nerve Paralysis. Woodhall, Barnes, Broadbent, Thomas R., and Javer, Jerome (*Duke Univ., Durham, N. C.*). [*Surg. Forum, Proc. 36th Clin. Congr. Am. Coll. Surgeons*, 1950, 394–9 (pub. 1951).]

Reports of paralysis and neuritis from injections of antibiotics are discussed. The sciatic nerve of the cat was injected subepineurally with 100,000 units of Na, K, or Ca salts of penicillin or 25–75 mgm. of dihydrostreptomycin sulfate, or otherwise treated with other agents used in injecting antibiotics intramuscularly. Histological studies were made after 10 and 60 days. The penicillin salts had a toxic effect upon the peripheral nerve axon, which might lead to axonal degeneration. With sesame oil or peanut added as a carrier, toxicity was increased. The dihydrostreptomycin sulfate had an even more marked effect. Tween 80, pectin, and carboxymethylcellulose had little effect. Care must be taken to avoid major peripheral nerve segments when antibiotics are injected intramuscularly.

W. C. TOBIE (Chem. Abstr.).

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Effect of Adenosinetriphosphoric Acid on the Chronaxy of the Motor Zone of the Cerebral Cortex. Babskiĭ, E. B., and Malkiman, I. I. [*Doklady Akad. Nauk S.S.S.R.*, **74**, 1135–7 (1950).]

Suboccipital administration of adenosine triphosphate (as Na salt) to dogs leads to the following results: Repeated use of small doses (10–20 mgm.) lowers the rheobase by 20–45 per cent. and the chronaxy by 40–60 per cent. within 3–5 minutes, after which both begin to return to substantially normal levels within about 80 minutes. Use of large doses (30–50 mgm.), however, causes a convulsion stage, after which the sensitivity of the cortex declines (rheobase rises) and the chronaxy is extended; maximum values reach 120–45 per cent. and 130–60 per cent., respectively after some 30 minutes, after which a decline to normal gradually takes place. Larger doses cause convulsions and death. Administration of 15–20 mgm. into the blood-stream gives qualitatively the same results as the suboccipital method, but the effect is seen after 1–2 hours; this occurs only in intra-arterial administration; the intravenous method gives no changes in the cortex. It appears that ATP plays a significant role in determination of the level of sensitivity of the cortex and in the rapidity of response to a stimulus.

G. M. Kosolapoff (Chem. Abstr.).

Blood Flow and Oxygen Consumption of the Human Brain in Diabetic Acidosis and Coma. Kety, Seymour S., Polis, B. David, Nadler, Carl S., and Schmidt, Carl F. (*Univ. of Pennsylvania, Philadelphia*). [*J. Clin. Invest.*, **27**, 500–10 (1948).]

Studies of blood gases, electrolytes, acid-base balance, respiration, blood pressure, cerebral blood flow and cerebral O consumption are reported in 14 patients in severe diabetic coma, 6 of which were in deep coma. Respiratory minimum volume was well correlated with arterial pH. Coma was associated with, and probably the result of, a 40 per cent. reduction in cerebral utilization of O, which occurred in spite of a generally augmented cerebral blood flow and normal arterial O saturation. The depression in cerebral O consumption is partly related to the acidosis, and more significantly to the ketosis, although other factors as yet poorly defined are undoubtedly operating. The results establish the feasibility of applying these techniques to diabetic coma, and open the possibility of further defining the biochemical derangements in the living human brain by study of new specific metabolic components. John T. Myers (Chem. Abstr.).

Anaerobic Glycolysis of the Warm-blooded Brain in situ. Thorn, Werner (*Univ. Kiel, Ger.*). [*Biochem. Z.*, **321**, 361–7 (1951).]

Since at the moment of decapitation there is still O available in the brain (0·3 volume per cent. in solution, the O as oxyhemoglobin also creatin phosphate as a source of energy), it is calculated that there is enough energy available to meet the resting needs of the brain over the first 10 seconds. Within 7 to 25 seconds the anaerobic glycolysis exceeds by far the values obtained *in vitro* with carcinomas. The anaerobic glycolysis is the same whether the animal is awake or under urethan narcosis. Within the 7–25-second period the maximum rate of glycolysis is 70–90 mgm. per cent. per minute, but between 20 and 100 seconds the lactic acid production proceeds at a uniform rate of 33 mgm. per cent. per second. After 100 seconds glycolysis slows down chiefly because of lack of substrate. The maximum glycolysis may coincide with the convulsions associated with ischemia.

S. Morgulis (Chem. Abstr.).

Effect of Ascorbic Acid on the Gaseous Metabolism of the Animal Brain. Uzbekov, G. A. (*Med. Inst., Stavropol*). [*Biokhimiya*, **16**, 104–7 (1951).]

Vitamins B_1, B_2 and nicotinic acid can correct the unbalance in carbohydrate and gas metabolism of the animal brain brought about by a prolonged carbohydrate diet (*Trudy Stavropol'skogo Medinstituta*, **3**, 115 (1949)). When the dog is saturated with ascorbic acid (I) by daily subcutaneous injection of 20 mgm. (I)/kgm., the O content increases in the arterial blood and decreases in the venous blood. The coefficient of O utilization in the brain rises from 28 to 52 per cent. The hemoglobin content of dog blood increases from 13·6 to 13·9 per cent. The amount of (I) produced by the dog is apparently insufficient for the maximum utilization of the biochemical processes. H. Priestley (Chem. Abstr.).

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Determination of Anaerobic Glycolysis of Rabbit Brain in situ. Bredow, Wolfgang and Thorn, Werner (Univ. Kiel, Ger.). [*Biochem. Z.*, **321**, 357–60 (1951).]

Rabbit heads were either frozen with liquid air after variable periods following decapitation or the brain was separated into two halves, one being frozen immediately (control), the other after a determined interval. In both series it was observed that there was an increase in bisulfite-binding substances. Methods for determining lactic acid are discussed. The fact that there is actually a rise in lactic acid has been further corroborated by the observation that following an intravenous injection of CH_2ICOOH there was no increase. S. MORGULIS (Chem. Abstr.).

Isolated Nuclei from Cells of the Cerebral Cortex. Preparation and Enzyme Content. Richter, D., and Hullin, R. P. (Neuropsychiatric Research Centre, Whitchurch, Cardiff, Engl.). [*Biochem. J.*, **48**, 406–10 (1951).]

Nuclei were isolated from cerebral cortex by differential centrifugation. They were found to contain a high concentration of alkaline phosphatase. This bears out previous studies showing an intense alkaline phosphatase reaction of the chromosomes. This enzyme is probably responsible for P exchange in desoxyribonucleic acid. The acid phosphatase is present in equal concentrations in nucleus and cytoplasm of the nerve cell, but its biochemical significance is not understood. Cholinesterase was also found in high concentration. The cytochrome oxidase activity is minute, but is approximately of the same order of magnitude as in the cytoplasm. The carbonic anhydrase activity of the nuclei is roughly about one third of that of cytoplasm but, as is pointed out, the physiological significance of the enzyme is not sufficiently known to interpret this finding correctly.

S. MORGULIS (Chem. Abstr.).

2. Pharmacology and Treatment.

Effects of Pentobarbital, Amobarbital, and Barbital on Oxygen Consumption of Brain Slices. Westfall, B. A. (Univ. of Missouri, Columbia). [*J. Pharmacol. Exptl. Therap.*, **101**, 163–6 (1951); *cf. C. A.*, **43**, 7139*d*.]

Pentobarbital (0·3 mgm. per cent.), amobarbital (1 mgm. per cent.), and barbital (2 mgm. per cent.) slightly increased the O consumption of rat brain slices. Considerably higher concentrations decreased O consumption.

L. E. GILSON (Chem. Abstr.).

A 24-hour Periodicity in the "LH-Release Apparatus" of Female Rats, Disclosed by Barbiturate Sedation. Everett, John W., and Sawyer, Charles H. (Duke Univ., Durham, N. C.). [*Endocrinology*, **47**, 198–218 (1950).]

The specific neurogenic stimulus which is essential for the ovulatory discharge of LH (luteinizing hormone) and which activates the hypophysis between 2 and 4 p.m. on the day of proestrus, and a 24-hr. rhythm of excitability in the neural component of the LH-release apparatus, have been confirmed. Nembutal will prevent the ovulatory activation of the hypophysis when administered at 2 p.m. during proestrus. Follicles persist for 2 to 3 days when nembutal is repeated on successive afternoons at the same critical hour. On the second and third days a supplementary injection is required at 3·30 and 4 p.m. If treatment is omitted or postponed until after 4 p.m. on either of these three days, pituitary activation occurs and ovulation will follow. Amytal, dial, barbital and phenobarbital produce similar results. Blockage of LH release with barbiturates on successive days discloses a follicular cycle which ends in atresia approximately two days before the onset of the next proestrus. ELVA G. SHIPLEY (Chem. Abstr.).

Effect of Barbiturates on Oxidative Phosphorylation. Brody, Theodore M., and Bain, James A. (Univ. of Illinois Med. School, Chicago). [*Proc. Soc. Exptl. Biol. Med.*, **77**, 50–3 (1951).]

Thiopental, pentobarbital and amobarbital lower the phosphate uptake/O uptake ratio obtained in particular tissue preparations from liver and brain respiring on a pyruvate substrate. This depression is obtained at concentrations of the drugs which have only a slight effect on the O uptake of the preparations, and which

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approximate those necessary *in vivo* to produce surgical anesthesia. It may be that such an uncoupling of phosphorylation from oxidation is one way in which barbiturates act to produce anaesthesia. L. E. GILSON (Chem. Abstr.).

The Metabolism of Tetraethylthiuram Disulfide (Antabuse, Aversan) in the Rat, Investigated by Means of Radioactive Sulfur. Eldjarn, L. (Univ. Oslo, Norway). [*Scand. J. Clin. Lab. Invest.*, **2**, 198–201 (1950); *cf. following abstract.*]

Approximately 80 per cent. of ingested antabuse (I) (tagged with S^{35}) is absorbed from the intestinal tract of the rat, the remaining 20 per cent. being excreted in the feces. Only 60 per cent. of intraperitoneally injected (I) is recovered in the urine and feces in the following 15 days. (I) accumulates primarily in the adrenals, liver and spleen. BERNARD KLEIN (Chem. Abstr.).

The Metabolism of Tetraethylthiuram Disulfide (Antabuse, Aversan) in Man. Investigated by Means of Radioactive Sulfur. Eldjarn, L. (Univ. Oslo, Norway). [*Scand. J. Clin. Lab. Invest.*, **2**, 202–8 (1950); *cf. preceding abstract.*]

Ninety per cent. of antabuse (I) is absorbed from the intestine, the remainder is excreted in the feces. The greater part of (I) is oxidized by the organism and excreted in the urine as part free and part sulfated, although small amounts are excreted unchanged or in reduced form as diethyl dithiocarbamate (II). Twenty per cent. of absorbed (I) remains in the body after 6 days. The optimum plasma concentration of (I) is 0·5–1·0 mgm. per cent. and exists almost entirely as free (I) and after 6 hours two-thirds is reduced to (II). The suggestion is made that the physiological effect may be due to the (II) anion. B. KLEIN (Chem. Abstr.).

Anticonvulsive Action and Molecular Structure of Some Heterocyclic Pentagonal Compounds. VIII. Influence of Opening of the Cycle. Hazard, René, Cheymol, Jean, Chabrier, Peirre, and Smarzewska, Klaudia, [*Compt. rend.*, **232**, 658–60 (1951); *cf.* C. A., **44**, 3613*i*.]

In explaining their anticonvulsant properties, Goodman *et al.* (*C. A.*, **43**, 4763*f*) advanced the theory that the hydantoins and barbiturates are transformed in the organism by opening of the cycle into an active linear chain, whereas the *acylureas* show a similar activity on forming a cycle *in vivo*. When the hydantoins and thiohydantoins were paired with their corresponding acylureas, and tested for protection against pentrazole and electric shocks, it was found that Goodman's theory holds for the hydantoins and thiohydantoins, but not for phenacetylurea. Diphenylhydantoin, which is inactive in pentrazole crisis, is very effective in electric shock, inversing its effect in the molecule corresponding to an open cycle. The cyclization of monophenylacetylurea is very active in both tests, while monophenylhydantoin is inactive in both crisis.

DOROTHY A. MEYER (Chem. Abstr.).

Antagonism and Synergism Between Narcotics and Sympathomimetic Amines in their Action on Central Nervous System of Vertebrates. III. Role of Sympathetic Nervous System on Narcotic Action and Phenylalkylamine Action on Central Nervous System of Cold-blooded Animals. Ya, S. [*Arbuzov. Fizio. Zhur. S.S.S.R.*, **36**, 496–509 (1950); *cf. C. A.*, **43**, 7141*g*.]

In a study of normal and sympathectomized frogs the minimum a.c. current that caused tetanic convulsions was determined. In normal animals the increased value of the minimum current under influence of the chemical agents places the latter in the following descending order of activity: pervitin, phenamine, ephedrine, sympatol, adrenaline; in sympathectomized frogs the order is pervitin, phenamine, adrenaline, ephedrine, sympatol. Duration of action of narcotics in intact animals is lowered by small and moderate doses of phenylalkylamines (more effective with chloral hydrate than with medinal). Antagonism to narcotics is strongest with phenamine, pervitin, and ephedrine; at high dosages narcotics and phenylalkylamines are synergistic. In sympathectomized animals the antagonism is weak and at medium or high dosage only synergy is observed.

G. M. KOSOLAPOFF (Chem. Abstr.).

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Selective Inhibition of Brain Respirations by Benadryl. Carlisle, Edith M., and Crescitelli, Frederick (Univ. of California, Los Angeles). [*Science*, **112**, 272–3 (1950).]

The O consumption of slices of rat cerebral cortex respiring in a Krebs-Ringer phosphate solution (pH 7·35) was studied with glucose and L-glutamate as substrate, and with and without benadryl-HCl(I) and histamine. With glucose, the addition of (1) exerted no effect on O consumption, but with L-glutamate respiration was completely blocked. The selectivity was specially striking when (I) was used in concentration range 9f 0·0004–0·0018 M. The endogenous respirations (no added substrate) behaved, in response to (I), not like respiration in glucose but like respiration in L-glutamate. Results similar to the above were obtained with pyribenzamine-HCl and with histadyl. N-amyl carbamate, dl-amidone and morphine did not show the selective action of (I), the same inhibition being obtained in both glucose and L-glutamate media. Histamine-2 HCl in 0·03 M concentration did not influence the O respiration of brain slices in glutamate, nor prevent the inhibition of respiration by (I). The possibility exists that some metabolic step in the oxidation of L-glutamate is blocked.

JULIA O. HOLMES (Chem. Abstr.).

Effects of Repeated Convulsions from Electroshock on Some Blood Enzymes. Tripodo, Cesare (Univ. Bari, Italy). [*Riv. biol. (Perugia)*, **42**, 485–502 (1950).]

In rabbits electro-shocked every day for 40 days (1) the amylase power of blood (determinations by the Wohlgemuth method) decreased 50 per cent. in 3 of 5 cases from the 20th day of treatment up to the 20–30th day after cessation of shocks; (2) the phosphatase power of blood (Roberts method, *C. A.*, **24**, 3269) decreased irregularly during the 10–20th days, normal values being restored and surpassed, respectively, at the end of and 30 days after the treatment; (3) the P content of blood (Briggs method, *C. A.*, **18**, 2183) decreased from 3·7 to 2 mgm. per cent. within the 20th day, normal values restored and surpassed (26·85 per cent.) after the treatment; (4) the tributyrinase power of plasma (Scoz and Guzzi method, *C. A.*, **36**, 7044[6]) decreased between the 7th and 14th day, normal values restored, surpassed (up to 41·98 per cent.) and again restored, respectively, on the 21st day, 16–30 days after, and 60 days after the shock treatment. C. SCANDURA (Chem. Abstr.).

Inhibitory Action of Carbon Dioxide on Experimental Convulsions. III. Experiments on Cryoepilepsy in the Frog: Mechanism of the Inhibitory Action of Carbon Dioxide on Convulsions. Moussatché, H. [*Mem. inst. Oswaldo Cruz*, **48**, 227–37 (1950) *(in English)*; *cf. C. A.* **38**, 1032[8].]

Frogs whose intercellular fluid pH is lowered by perfusion below the pH obtained after CO_2 inhalations sufficient to inhibit cryoepilepsy are still subject to such convulsions. It is therefore likely that CO_2 has a specific inhibitory action on the nervous centers and does not inhibit cryoepilepsy merely by lowering intercellular fluid pH. KARL F. URBACH (Chem. Abstr.).

Anticonvulsants and their Effect on Mouse Convulsions, Cheymol, Jean, and Thuillier Jean (Faculte med., Paris). [*Arch. intern. pharmacodynamie*, **83**, 593–601 (1950).]

Drugs were tested against strychnine, pentrazole, picrotoxin, and thujone convulsions in mice. They were effective in decreasing order: 5, 5-dimethyl-2, 4-dithiohydantoin, phenobarbital, 3, 5, 5-trimethyl-2, 4-oxazolidinedione, phenylacetylurea, and 5, 5-diphenylhydantoin. The protection provided by the first was almost complete, and at 100 mgm./kgm. there were no toxic symptoms. Diphenylhydantoin was almost useless. Picrotoxin convulsions were the most resistant to the action of these protective drugs.

M. L. C. BERNHEIM (Chem. Abstr.).

Central Nervous Function and Changes in Brain Metabolite Concentration: Characteristic Glycogen Increment Patterns Produced by Convulsant Drugs. Chance, M. R. A. (Univ. Birmingham, Engl.). [*Brit. J. Pharmacol.*, **6**, 1–7 (1951); *cf. J. Explt. Biol.*, **27**, 311 (1950).]

Low variance associated with the determination of glycogen (I) in mouse brain during procedures which bring about changes in the amount of (I) permitted accurate

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estimations of relative changes in different parts of the brain. The accumulation of (I) in mouse brain, which takes place during convulsions, was determined in cortex, midbrain, medulla, spinal cord, central lobes and the lateral lobe of the cerebellum at various times during seizures induced by dl-amphetamine, caffeine, dibenamine, insulin, leptazole, coramine, picrotoxin, Na diphenylhydantoin and strychnine. In general, the most marked increases in (I) were found in cortex, mid-brain, and medulla. The resulting patterns showed differences in the rates of increment and recovery for different parts of the brain and for different drugs. These patterns were interpreted as indicating the distribution of nervous activity in the brain arising from drug stimulation.

RICHARD F. RILEY (Chem. Abstr.).

Effect of Amphetamine on Conditioned Behaviours. Yoshii, Naosaburo, Sasaki, Hiromasa, and Hiraoka, Keizo (Osaka Univ.). [*Med. J. Osaka Univ.*, **2**, 151–4 (1950).]

Small doses of amphetamine (I) caused an increase in conditioned salivary secretion (but not of unconditioned salivary secretion) in the dog. Larger doses of (I) inhibited the conditioned salivary secretion. (I) heightens excitability level of conditioned reflex center and decreases the fatigue produced by the repetition of the reflex performance. Large doses of (I) cause the experimental animal to take neither food nor water. DON SCOTT (Chem. Abstr.).

Effect of Sodium Salicylate and Acetylsalicylate on Metabolism of Rat Brain and Liver in Vitro. Fishgold, J. T., Field, J., and Hall, V. E. (Stanford Univ., Stanford, Calif.). [*Am. J. Physiol.*, **164**, 727–33 (1951).]

Na salicylate, added to the medium in which slices of rat cerebral cortex are suspended, increases the O consumption in concentrations up to 0·56 millimols per l., and decreases it in higher concentrations. Na acetylsalicylate is without effect. Anaerobic glycolysis of brain tissue was not affected either by salicylate in moderate concentrations. Liver slice O consumption is not changed by concentrations of Na salicylate up to 0·62 millimols per l., but is increased by comparable concentrations of Na acetylsalicylate. Possible mechanisms for the different metabolic response of brain and liver tissue to the salicylates are discussed, and the bearing of the results on a hypothesis of temperature regulation attempting to relate antipyretic action to changes in brain metabolism is considered.

E. D. WALTER (Chem. Abstr.

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