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A Study of the Effect of Evipan on the Flicker Fusion Intensity in Brain Injuries.

The results of all the investigations with the evipan test in brain injuries of various genesis (acute traumas, virus infections, intoxications, active chronic processes) can be summarized as follows :

The evipan test is positive in active, extensive, diffuse brain injuries ; the evipan test can probably yield valuable information with regard to the degree of severity of acute traumatic, toxic, and infectious brain injuries and of the activity of chronic pathological cerebral processes. (Author's abstr.)

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Thyroid Function in Mental Disease Measured with Radioactive Iodine, I^{131}.

This is a report of a study in progress on thyroid function in patients with mental disease, and in controls, as measured by the uptake of the radioactive isotope of iodine, I^{131}, by the thyroid gland, and compared with serum protein-bound iodine, basal metabolic rate, and plasma cholesterol. These 4 tests represent a combination of the best and most widely accepted methods for evaluating thyroid status known to-day.

Data are given on 36 subjects, 24 patients and 12 controls, and include a total of 61 basal metabolic rates, 66 plasma cholesterols, 65 serum protein-bound iodines, and 78 I^{131} uptake determinations. The largest diagnostic category studied is schizophrenia. The number of patients in all other categories is insufficient to establish any trends.

The average basal metabolic rates are somewhat low in the authors' subjects, the average plasma cholesterols somewhat high. The serum protein-bound iodines fall compactly within the normal range. The uptake of I^{131} is widely distributed, with uptakes below 10 per cent. and above 40 per cent. in several cases but, with the exception of one patient with an uptake of 60 per cent., they fall for the most part within the normal range. In no case did the uptake curves on the authors' subjects resemble the types found in myxedema or thyrotoxicosis. Most important, so far no significant difference has been found between patients and controls by clinical evaluation, and as measured by both old indirect and new direct tests of thyroid function.

The authors' results contrast with many reports in the past of low basal metabolic rate compared with normal controls, and of low plasma cholesterol in schizophrenic patients. Perhaps their more nearly normal findings are due to selection of a group for study with short duration of illness and short length of hospitalization. The significance of reports in the past on patients chronically ill and hospitalized for prolonged periods is open to question. On the other hand, the number of subjects they have studied, particularly control subjects, is still small, and it may or may not be that when a larger sample has been accumulated there will be a shift in trends.

The authors find no change in thyroid function as measured by the above tests in patients during or after insulin shock, electroshock, combined shock, or psychotherapy. Thyroid medication, however, produced profound alterations in findings on all 4 tests in the 2 patients on whom study has been completed.

It should be pointed out that there has been insufficient analysis of *rate* of I^{131} uptake; the authors have dealt in this paper primarily with the maximum con-

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centration of I^{131} accumulated in the thyroid gland after a test dose. Since the data presented in this paper were analysed, results possibly suggestive of some abnormality have been found on 2 depressed manic-depressive patients. (Both patients had a marked drop in their radioactive iodine uptake curve as they improved during electroshock therapy. One patient had an abnormally high initial uptake, the other a high normal uptake. The rate of uptake in the patient with the high normal curve was markedly delayed.) Studies of this diagnostic category, of anorexia nervosa, and of psychoneurosis, of analysis of varying rates of I^{131} uptake and effects of thyroid medication are being pursued further, and will be reported at a later date. (Authors' abstr.)

MARCH.

*Adrenal Cortical Responses to Stress in Normal Men and in Those with Personality Disorders. *Pincus, G., and Hoagland, H.* 641
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Adrenal Cortical Responses to Stress in Normal Men and in those with Personality Disorders.

1. Six indices of adrenal cortical activation have been compared in groups of normal male subjects and schizophrenic male patients when they were subjected to a variety of stresses. The indices are changes in output of urinary sodium, potassium, uric acid, 17-ketosteroids and neutral reducing lipids, together with changes in the number of circulating lymphocytes. The stresses have been the target ball frustration test, operation of a pursuit meter (each test lasting one hour), the effects on the authors' indices of adrenal cortical extract and of pituitary adrenocorticotrophin.

2. Responses of the authors' 6 adrenal cortical indices and also eosinophile responses to injected adrenocorticotrophin were determined for groups of male and female psychoneurotic patients and compared to normal controls.

3. The tests all involved significant numbers of patients and controls, and the results have been treated statistically.

4. The authors' data indicate a highly significant failure of normal adrenal stress responses in the schizophrenic population as compared with the control population.

5. The failure occurs principally at the level of the ability of the adrenal cortex to respond to adrenocorticotrophin.

6. This failure was not corrected by a dietary supplement rich in proteins and vitamins.

7. These findings are discussed in relation to the etiology of schizophrenia.

8. Psychoneurotic patients, in contrast to schizophrenics, respond in a normal fashion to injected adrenocorticotrophin. (Authors' abstr.)

Carbohydrate and Lymphoid Studies in Schizophrenia.

A series of studies have been carried out in schizophrenic patients and normal controls that indicate that (1) there is a reduction of tolerance to glucose in this psychosis ; (2) the response of the adrenal cortex to stimulation by the ingestion of glucose is generally deficient, as exemplified by measurements of various blood and urinary variables known to be pertinent to adreno-cortical activation.

(Authors' abstr.)

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Studies of Adrenal Cortical Activity in Psychoneurotic Subjects.

The use of a cumulative index of adrenal cortical activity has been described.

This has been applied to the estimation of adreno-cortical activity after (1) small doses of A.C.T.H. in anxiety states, (2) injection of saline and venipuncture, (3) controlled thermal pain, and (4) electro-convulsive therapy.

In all these experiments the data indicate activation of the adrenal cortex.

It is suggested that the greater the patient's anxiety and tenseness the greater the activation of the adrenal cortex by the test situation.

The use of pretreatment sodium amytal seems to decrease the response of the adrenal cortex to E.C.T. (Authors' abstr.)

Hallucination and Imagery Induced by Mescaline.

Mescaline produces altered visual experiences of several types, whose vividness and degree of distortion is proportionate to the size of the dose. There are no sharp boundaries dividing abnormal sensibility, illusions, and hallucinations. Subjects who gave fewer responses of the type " I see it," when asked to imagine situations were more likely to hallucinate than other patients. Visual responses declined still further after administration of mescaline in a degree more closely related to the amount of drug given than to the vividness of hallucinatory alterations, even in those experimental subjects who reported virtually no alteration in actual vision. The fall in reported visual imagery was not found in control subjects.

(Authors' abstr.)

Cytochrome C : Effects of Intravenous Administration in Presenile, Senile and Arteriosclerotic Cerebral States.

Theoretically and experimentally the vital role played in cellular metabolism by the cytochromes as respiratory tissue enzymes is recognized and appreciated (14). This apparently also applies to tissue activity in the nervous system, particularly during growth, differentiation, and regeneration following injury. Cytochrome C, a commercially available preparation, was selected for clinical trial in cases of presenile and senile states, with or without evidence for nervous system arteriosclerosis. The authors fully recognize that there are other equally important enzyme systems involved in cellular metabolism, notably riboflavin or flavoproteins and pyridine nucleotides. The latter has the important nicotinic acid amide component serving as a reversible hydrogen acceptor, and is indispensable for the action of a great many dehydrogenases. However, catalytic action of Cytochrome C is still a link in part of the oxidation going on through these systems. The relation of cellular oxidations to lipid phosphorylation is also thought to be through oxidations by the cytochrome system (11). Cytochrome C, therefore, seemed to be a good choice for trial (15, 16).

Clinical improvement was noted in a majority of cases observed in regard to memory, orientation, irritability, interest, confusion and behavior. Only slight changes were observed in the electroencephalographic recordings, and these changes may be insignificant. Psychometric examination showed qualitative improvement in keeping with clinical improvement and a trend toward higher scores.

The changes noted in these patients during the trial period are quite in contrast to the results obtained in the problem of treatment of the senile states for the previous 3 years on the psychiatric service. During that period 27 cases were diagnosed as senile reactions. Of these, 6 were improved and, of these 6 cases, 4 were treated with electro-shock. The remaining 21 cases were referred to State institutions, domiciliaries, nursing homes, or sent home as unimproved. These cases were given the routine supplementary vitamine therapy, symptomatic care, special diets, and routine activity programs which were also part of the program for the cases reported.

Total duration of mental illness, as judged by reviewing the literature, in the senile psychotic state tends to be from 1 to 3 years, generally less than 2 years, and when improvement takes place it most generally does so within 2 or 3 months' time. Because of the heavier and increasing burden to mental hospitals, any aid to hasten possible improvement and the care of the aged seems justifiable when psychological and physical factors combine to incapacitate the individual.

The authors wish merely to report these studies as observations, making no

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claims beyond the theoretical about specific action or changes produced by this enzyme. They feel encouraged, though, by the clinical changes noted during the short observation period. The biochemist can give the authors little help in interpreting these observations beyond theoretical speculation, but neither can they tell them what happens to cellular metabolic processes in nervous tissue as a result of electro-shock or insulin therapy. The authors, nevertheless, use such therapy because it works. The pharmacologists express themselves freely that the role of cytochrome in cellular respiration is well established, but they are very sceptical that injected cytochrome can be utilized as such by the body tissues. However, practically no work has been supplied by either the pharmacologists, the experimental biologists or pathologists that would indicate Cytochrome C to be of any utility in the therapy of pathological tissue states such as those in which we are interested.

More promising and encouraging are apparent results from Cytochrome C, noted by the authors in their trial of it in acute toxic inflammatory reactions of the nervous sytem, about which they hope to report separately at a later date.

(Authors' abstr.)

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Frontal Lobotomy and Electrical Stimulation of Orbital Surface of the Frontal Lobes : Effect on Respiration and on Blood Pressure in Man.

The effect of lesions and of stimulation of the frontal lobes in man on respirations and on blood pressure was studied in 19 psychiatric patients. The effect of frontal lobotomy on blood pressure was noted in 10 patients. The effect of transcortical electrical stimulation of the orbital surface of the frontal lobes on blood pressure and respirations was observed in 9 patients. The results may be summarized as follows :

1. There was no consistent change in blood-pressure levels after frontal lobotomy, several patients being followed up for one year after operation.

2. Electrical stimulation of the orbital surface of the frontal lobes produced an elevation of blood pressure in 6 of 9 patients and a cessation or diminution of respirations in expiration in 7 of 9 patients. These responses occurred together during a given stimulus in 2 patients. In 4 patients elevation of blood pressure occurred independently of a change in respirations. In 5 of 7 patients the changes in respirations were independent of a change in blood pressure during a given stimulus.

3. While the magnitude of elevation of blood pressure was not striking, the average elevation for the 6 patients was 3·5 times as great as the maximal spontaneous variation for the systolic blood pressure, and 3·4 times as great as the maximal spontaneous variation for the diastolic blood pressure.

4. The authors' crude method of identifying the stimulus area did not permit them to be certain of the location of the responses. The responsive areas appeared to be along the posterior orbital aspect of the orbital surface. These findings confirm for the first time in man the results of animal studies.

The significance of these observations as regards the cortical control or regulation of blood pressure or respiration will have to await more precise studies of the anatomy and physiology of these areas. (Authors' abstr.)

Psychiatric Aspects of Vagotomy. IV. Phantom Ulcer Pain.

Psychiatric studies of patients with peptic ulcer treated by vagotomy revealed that one of the sequelae of this operation is a syndrome characterized by the persistence of symptoms of ulcer, in spite of roentgenologic evidence of healing of the lesion.

The hypothesis is proposed that the persistence of ulcer pain in such circumstances represents a phantom sensation (" visceral phantom pain ").

In support of this hypothesis certain clinical and theoretic data are presented. It is suggested that in certain circumstances a visceral lesion, such as peptic ulcer, may become part of the patient's body image. An organic procedure which then leads to the disappearance of the lesion may thus be followed by the appearance of phantom sensations, in this instance, phantom pain simulating " ulcer pain." Psychologic factors which may predispose to the development of this syndrome are briefly discussed. (Author's abstr.)

Longevity in Multiple Sclerosis.

It is noted that in these 3 cases of long duration the multiple sclerosis was primarily of the spinal type for the greater part of the course. In all 3 cases manifestations of the disease remained limited chiefly to the spinal cord for about twenty years. Although the so-called spinal type bears a good prognosis, eventual dissemination throughout the neuraxis can be expected. (Authors' abstr.)

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Blood Chemistry of Schizophrenic Patients Before, During and After Insulin Shock Therapy: Preliminary Studies.

Blood chemistry determinations were performed on 24 young men with schizophrenia before, during and after insulin shock therapy. The results are summarized as follows:

1. Values for serum potassium, sodium, chlorides and magnesium and blood levels of glucose and total reducing substances were normal before and after insulin therapy. The glucose and total reducing substances of the blood were sharply reduced during coma.

2. The lactic acid levels of the blood were variable, being either low or high in a few cases before and after insulin treatment. Pyruvic acid was essentially normal. The lactic acid-pyruvic acid ratio had a wide range.

3. Of the phosphate fractions, serum inorganic phosphorus was generally increased before and after treatment. Blood inorganic phosphorus was increased in a few patients before treatment, but was normal in all patients after treatment. Values for adenosine triphosphate phosphorus after treatment were higher than the values before treatment, many of which were below normal. The total organic acid-soluble phosphorus was somewhat increased after treatment, many of the pretreatment results being below normal. Hexose phosphate phosphorus levels were variable, and were essentially the same before and after treatment. Diphosphoglyceric acid phosphorus was normal before and after treatment. The only phosphate fractions to show a significant change during deep coma were the inorganic phosphorus of the blood and serum, which dropped.

4. Of the hepatic function tests performed, the sulfobromophthalein sodium test (with one exception), the alkaline phosphatase determination and the thymol turbidity test all gave normal results before treatment. After treatment the values for the thymol turbidity test were increased in a few cases. The results of the cephalin flocculation test were positive before treatment in several cases, in some of which they became normal after treatment. (Authors' abstr.)

Neurofibromatosis (von Recklinghausen's Disease of the Nervous System): Analysis of the Total Pathological Picture.

The basic lesions are multiple foci of hyperplasia and neoplasia of the supportive or protective derivatives of the ectoderm.

The neuroglia, myelin, meninges, capsule cells and connective tissue of the cerebrospinal ganglia, the supportive tissue of the nerves and the protective and supportive tissue of the epidermis participate in the disease process.

The basic tissue is not exclusively of neural crest origin or of connective-tissue origin, as would be indicated by certain discussions in the literature.

To the protective and supportive elements is frequently added a vascular component, which may occur as independent vascular lesions or as vascularized supportive lesions.

Hyperplasia and tumor formation of parenchymatous elements occur rarely, and are chiefly in the form of chromaffin tumors of the adrenal glands and hyperplastic nerve bundles (neuromatosis).

Neurofibromatosis is related to the other neurocutaneous disorders.

(Author's abstr.)

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Studies on Headache. I. Effects of Carbon Dioxide-Oxygen Mixtures Given During Preheadache Phase of the Migraine Attack. II. Further Analysis of the Pain Mechanisms in Headache.

The preheadache phenomena of migraine, visual disturbances, paresthesias and dysarthria are associated with, and probably due to, cranial vasoconstriction. These phenomena can be modified or abolished by certain agents which produce cranial vasodilatation.

A series of patients were given a 10 per cent. carbon dioxide-90 per cent. oxygen mixture by face mask during the preheadache or early headache phase. This mixture abolished the preheadache phenomena and aborted the headache in most of the trials. Ten per cent. carbon dioxide in air was less effective, having a shorter and more transient effect.

There was a lowering of the pain threshold in the intracranial vessels without headache in certain stressful circumstances. The "jolt threshold" was low before and after certain intracranial vascular headaches in a setting of stress and fatigue. After the ingestion of a moderate amount of alcohol, headache could be induced by inverting the subject 60 degrees from the horizontal.

Local vasodilatation of a segment of the temporal artery was produced by iontophoretic application of metacholine chloride and by histamine. Pain was not induced in 64 trials, even though pronounced vasodilatation and edema of the vessel wall were obtained. It is inferred therefore that, in addition to dilatation and edema, other factors are probably necessary for the production of vascular headache of the migraine type.

Certain of the chain of bodily changes leading to migraine headache are evident. Days or hours before the headache there is a change in vascular reactivity followed by vasoconstriction. This is followed by vasodilatation, which is painful, owing in part to a lowering of pain threshold in the vessels. The vasodilatation may be an attempt on the part of the body to restore the homeostasis of cranial circulation. (Authors' abstr.)

Studies on Headache: Distention of the Rectum, Sigmoid Colon and Bladder as a Source of Headache in Intact Human Subjects.

Headache did not result from experimental distention of the bladder or large bowel in human subjects with intact segmental reflexes. It is inferred that in normal human subjects with constipation or with urinary retention the mechanism of any associated headache is probably not directly related to the visceral distention or to contraction of the large bowel. Moreover, minimally painful distention of the bladder and large bowel in normal human subjects does not result in significant autonomic effects. It is probable, therefore, that the constipation and headache associated with it are not causally related to the distention. (Authors' abstr.)

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Histologic Study of the Brains of Monkeys After Experimental Electric Shock.

Five monkeys were given courses of electric shock treatments comparable to those used in human convulsion therapy. An additional monkey served as a control. After the last treatments of the experimental animals all were killed, and the brains fixed by an improved technic of intravascular perfusion and fixation to prevent the development of post-mortem artefacts in the brain and spinal cord.

Histologic study of sections of the central nervous system, stained by precisely controlled neurologic methods, revealed no difference between the experimental and the control animals. There were no neuronal changes, glial proliferation, areas of demyelination or evidence of old or recent hemorrhages in either series. No structural alteration was demonstrated after experimental electric shock.

(Authors' abstr.)

The Current Path in Electric Convulsion Shock.

A brief discussion of mental symptoms occurring with pernicious anemia is given. A review of the available literature showed no case in which electric shock therapy had been used in conjunction with liver therapy.

A case of pernicious anemia with psychotic reaction which was treated with electric shock therapy is reported. Prompt improvement was noted.

(Author's abstr.)

Behavioral and Physiologic Changes Under Stress After Operations on the Frontal Lobes.

In a setting of lowered tension and steadier heart rate, under stress, the patients who had undergone operations on the frontal lobes showed increased responsiveness to external stimulation. These findings support the hypothesis which the present study was designed to test.

Objective evidence of lowered tension after operation was found in the measurement of finger movement and in the measurement of muscle potentials from the neck. Muscular tension and steadiness of heart rate reflect the subject's physiologic state or the setting in which his responses to stimulation occur. Evidence that they may be to some extent an index of what one may call the " anxious set " was presented in a previous paper.

In the present study the increased potency of external stimulation was objectively demonstrated. After operation, withdrawal of the head from heat occurred more frequently, and the magnitude of the galvanic skin response was higher.

Thus, by means of objective behavioral and physiologic determinations, the authors have found differences which parallel the clinical observation that in some cases pathologic anxiety is reduced after operations on the frontal lobes. Moreover, it appears that such a change in psychiatric status may probably be understood in terms of the same formulation which was advanced to account for the observed reduction in intelligence following operative procedures on the frontal lobes.

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Results of Spinal Pyramidotomy in the Treatment of the Parkinsonian Syndrome.

The results of spinal pyramidotomy were evaluated in 22 cases of the Parkinsonian syndrome which could be followed for more than 12 months after the operation. The condition immediately after the operation and at the time of the last follow-up examination is described.

Of the various manifestations of the Parkinsonian syndrome, only the alternating tremor could be favourably influenced. In one-third of the cases there was complete disappearance of tremor ; in an additional third the tremor was remarkably reduced, and in the last third the results were considered failures.

Reduction of motor strength, present in all cases immediately after the operation, subsided in the majority of cases, but was still demonstrable to a smaller or larger degree in some cases.

This surgical procedure can be considered not a specific treatment of Parkinsonism, but a symptomatic treatment for tremor. Patients have to be selected carefully. The operation can be recommended without restriction to patients with severe distressing alternating tremor if akinetic symptoms and rigidity are not pronounced. In advanced conditions with disabling rigidity and severe tremor the usefulness of the extremities may not be improved by the operation, but the patient usually feels more comfortable after relief from the tremor, even though no more active.

The possibility of the persistence of reduction of motor strength after the operation has to be considered with this operation, as well as other operations for the relief of tremor, but the average disability appears to be less following spinal than following cortical and subcortical operations ; there is no danger of convulsions, and there is a substantial difference in mortality in favour of pyramidotomy

In the present series the results of unilateral operations are presented. The authors have also had favourable experiences with the use of a unilateral pyramidotomy combined with a homolateral cortical operation, as reported by Scott, and also with bilateral pyramidotomies, as first reported by Pimenta. The authors' experiences have been too few and the time interval has been too short to permit definite conclusions concerning the results, beyond the fact that both types of operation are feasible, are not particularly dangerous and promise good results. Ebin's proposal to sever the direct as well as the indirect corticospinal fibres also appears to have merit. (Authors' abstr.)

Experimental Demyelination by Means of Enzymes, Especially the Alpha Toxin of Clostridium Welchii.

Sections or blocks of spinal cord and brain of laboratory animals were incubated in *Cl. welchii* filtrate (consisting principally of alpha toxin), or in various snake venoms, and were then prepared for histologic study. In addition, *Cl. welchii* filtrate was injected intracerebrally into rabbits and intravenously into dogs, rabbits and mice.

In the *in vitro* tests, demyelination, as indicated by the Spielmeyer or the Weil stain, was produced by *Cl. welchii* filtrate, cobra venom and rattlesnake venom.

Fatty degeneration, as shown by the oil red O stain, was found in the cobra venom preparations, but not in the *Cl. welchii* filtrate preparations. Free phosphate ions, as detected by Gomori's phosphatase stain, were found in the *Cl. welchii* filtrate preparations, and a new use for this histochemical technic was introduced. Whereas previously, according to this technic, the presence of an enzyme in a tissue has been detected by the addition of a substrate, in the present modification the presence of a substrate (lecithin) in the tissue is detected by the addition of an enzyme (lecithinase) capable of attacking it.

In the *in vivo* tests the intravenous injections produced no loss of myelin.

It is maintained, therefore, that not only can the myelin sheath be broken down by enzymatic action, but also that it can be broken down in more than one way, that is, that " demyelination " may not always be precisely the same process. (Authors' abstr.)

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Topographic Distribution of Plaques in the Spinal Cord in Multiple Sclerosis.

Spinal plaques have a predilection for a distinct localization. In the posterior columns they always lie in the center, in the lateral columns, in the center and posterior two-thirds, and in the ventral columns, symmetrically on both sides of the anterior median fissure.

The changes begin in the center of the columns, where the diameter of the white matter is greatest. These changes appear around the radial veins. The plaques are of extraordinary length, but small in diameter. As the plaque grows, it first spreads towards the central gray matter, where fusion of plaques from the posterior, lateral and ventral columns takes place. Finally, the lesion reaches the surface of the spinal cord. This mode of progression may be explained by differences in the venous drainage. (Author's abstr.)

Histamine Therapy in Acute Ischemia of the Brain.

Early vasodilatation is considered the logical method of salvaging ischemic areas of the brain.

Histamine phosphate given intravenously in a speed of 0·02 mgm. per minute produces a consistent dilatation of the arterioles, capillaries and venules of the brain.

This is most conveniently accomplished by administering 2·75 mgm. of histamine diphosphate dissolved in 500 c.c. of isotonic fluid and given by intravenous drip over a period of two hours.

No change in the arterial or venous blood pressure occurs in man with this speed of intravenous infusion of histamine.

Histamine infusions were given once to three times daily, and nicotinic acid administered orally to patients with acute ischemia of the brain.

Twenty-five patients have been followed sufficiently long to evaluate the results of such therapy. One death occurred from an intercurrent uremia. Twenty patients had definite improvement in all affected fields, 3 had improvement in some fields, and 2 had no apparent change during histamine therapy.

Compared to the usual mortality and improvement rates without vasodilatation therapy, these results indicate that histamine therapy was of benefit to these patients.

Intravenous infusion of histamine as described is a safe, readily available, and easily administered method of vasodilatation in case of acute ischemia of the brain. (Author's abstr.)

Changes in Behaviour Following Frontal Lobectomy in Dogs and Cats.

There is a species difference between dogs and cats in the reaction to various stimuli and in general behaviour after removal of the frontal lobes.

The most typical phenomenon observed in dogs after prefrontal or frontal ablation was the " reaction to restraint " without any manifestations of rage.

The intensity of the " reaction to restraint " increased with progressively larger removals of the frontal lobes and with simultaneous ablation of the olfactory bulbs and tracts. This reaction was associated with autonomic hyperactivity, the intensity of which increased in proportion to the amount of frontal brain tissue ablated.

Ablation of a region of the cortex in the dog, corresponding in part to the island of Reil and the orbital surface in man, induced only hyperactivity.

Prefrontal and frontal ablations never produced a rage reaction in cats, but, on the contrary, made them more friendly or indifferent. A more extensive removal of the frontal pole (anterior to the coronal plane through the ansate sulci) abolished the usual reaction to nociceptive stimuli. (Authors' abstr.)

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Study of Efferent Connexions of the Frontal Lobe in the Human Brain after Leucotomy.

1. Brains of patients with a short survival time after leucotomy have been examined with a silver method to trace corticofugal fibres to their termination in subcortical nuclei.

2. After leucotomy lesions restricted to prefrontal areas surprisingly few fibres from the severed areas terminate in the dorsomedial nucleus of the thalamus. Experimental findings asserting that the prefrontal cortex projects to other thalamic or extrapyramidal nuclei are not confirmed for the human brain.

3. When the leucotomy lesions extend into the white matter which underlies dysgranular and agranular cortex of the frontal lobe, terminal degeneration is present in the mammillary body, the dorsomedial and ventrolateral group of nuclei of the thalamus, the globus pallidus, zona incerta, Forel's field, red nucleus and subthalamic nucleus.

4. It has been possible to demonstrate that the cortical fields projecting to these centres are confined to the rostral part of Brodmann's area 6, and to dysgranular areas of the frontal cortex such as Brodmann's areas 8 and posterior 9 (Economo's area FC).

5. Fibres from the frontal cortex which terminate in the mammillary body may represent the anatomical pathway previously suggested by Ward and McCulloch on physiological evidence.

6. The extent and importance of frontal projections to the ventrolateral group of thalamic nuclei in the human brain is emphasized. A projection from the rostral cingular gyrus to the anterior nucleus of the thalamus could not be demonstrated.

7. Of the extrapyramidal nuclei, the finding of a direct corticopallidal pathway is of particular interest.

8. Fibres from the frontal cortex were seen to terminate in the red nucleus after lesions which certainly exclude areas 4 and 4 s.

9 Degeneration of fibres of the fronto-pontine tract in the most medial part of the peduncle was present after lesions anterior to the premotor cortex.

(Author's abstr.)

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The Spontaneous Electrical Activity of the Human Thalamus.

1. Simultaneous records have been made of the electrical activity of the cortex, subcortical white matter, and the basal grey matter, notably the optic thalamus. These records were accompanied by E.E.G.'s, E.C.G.'s and other observations. They were made with an electrode needle presenting four point electrodes each 2 cm. apart from its neighbour down the length of the needle. The metal tube of the needle was earthed and insulated, thereby acting as an electrical screen to the independent and isolated electrodes. The electrode needle was introduced with the usual technique for a ventricular puncture, and the positions of the electrodes were determined by ventricular radiology. The methods are fully described.

2. Twenty-one subjects with diverse conditions, including organic brain damage and *grand mal* epilepsy, were studied. The encephalograms were modified in different ways during the periods of recording.

3. In most circumstances the thalamogram is featureless, whatever is occurring in the electroencephalogram.

4. Slow rhythms ($\frac{1}{2}$–2 a second) occur when the thalamus is damaged by a tumour, and also occasionally when there is organic cortical damage.

5. Episodes of fast rhythms (16–22 a second) arise in the thalamus in a small proportion of subjects.

6. No relationship appears to exist between the spontaneous rhythms which may be seen in the thalamus in patients with organic brain damage, and the spontaneous rhythm of the cortex.

7. No reflection of induced changes in cortical rhythms can be seen in the thalamogram.

8. Although in some circumstances rhythms recorded from the cortex can be picked up from deeper structures, there is usually a striking independence of thalamic and cortical activity.

9. This preliminary survey suggests that with the methods so far available, exploration of the electrical activity of the basal grey matter has no immediate application to the routine investigation of organic brain disorder. The results can, however, be used as a baseline for the experimental study of abnormal states of behaviour, including epilepsy. (Authors' abstr.)

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Basal Lead Studies in Epileptic Automatisms.

In a study of a selected group of 24 patients with epilepsy, the basal electroencephalogram was of particular interest in those cases with a history of automatisms. This report is concerned with the clinical and electroencephalographic findings in the 12 patients who were subject to this type of seizure. Among this group, spike activity was present in 10 instances and could be localized to the temporal or basal regions. In 7 instances the origin of the spike activity appeared to be nearer the electrodes at the base than at the scalp. The tendency for this activity to occur bilaterally has been emphasized. Of all the electrodes now applied to the outer cranium the nasopharyngeal and tympanic lie nearest the basilar parts of the rhinencephalon. Such anatomical considerations must be taken into

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account in inferring the origin of the spike activity in the majority of the cases reported here. Some of the therapeutic and neurophysiological problems pertaining to the findings in these studies have been discussed.

(Authors' abstr.)

Metrazol Activation of Seizure Discharge in Epileptics with Normal Routine Electroencephalograms.

1. Slow intravenous infusion of 5 per cent. metrazol evoked seizure discharges in 47 per cent. of 57 epileptics who had normal routine E.E.G.

2. Rhythmic, repetitive discharges were characteristic of patients with " idiopathic " epilepsy, whereas arhythmic, asymmetric discharges characterized the group classified as symptomatic epilepsy. (Authors' abstr.)

Augmentation of Evoked Electro-cortical Activity During Spindle Bursts.

Several types of evoked electro-cortical activities have been observed to undergo pronounced augmentation during spindle bursts, and depression during the interburst period. The alternation is attributed to a periodic waxing and waning of background excitability, of which the burst may be a manifestation rather than a cause. (Authors' abstr.)

Studies on Diffusion Respiration. VII. The Cortical Electrical Activity of Dogs.

1. The behaviour of the cortical electrical activity of dogs held in apnea by an overdose of Pentothal sodium for 45 min. under conditions permitting diffusion respiration has been studied.

2. The E.E.G. exhibited initial slowing followed by periodic suppression, and finally complete and continuous suppression. Continuous suppression appeared at an average of 19 min. of respiratory arrest and lasted until the apnea was artificially terminated, or for an average of 26 min.

3. The CO_2 content of the blood progressively increased throughout the apnea, and at the 45th min. of respiratory arrest the average venous blood pH had fallen from a control of 7·29 to the low value of 6·69.

4. The E.E.G. of all animals returned to normal within one week following the experiment. (Authors' abstr.)

Effects of Di-Isopropyl Fluorophosphate (D.F.P.) on Electroencephalogram and Cholinesterase Activity.

1. The intra-carotid injection of D.F.P. produces electrical changes in the corticogram of the unanesthetized rabbit which, within limits, are proportional to the amounts of the anticholinesterase administered.

2. The decrease of cholinesterase activity in various parts of the brain is correlated with the degree of abnormality produced in the electrocorticogram. This relationship fails, however, when the *grand mal*-like electrical patterns develop, as the cholinesterase activity has previously fallen to a minimum.

3. It is suggested that in the production of the *grand mal*-like electrical pattern multiple factors may be involved. (Authors' abstr.)

Cumulative Effects of Minimal Cortical Stimulations.

Five effects of local cortical faradic stimulation are described: (*a*) afterdischarge; (*b*) spreading depression of the normal cortical activity; (*c*) a fast, low potential activity during the depression; (*d*) convulsoid activity, and activity resembling that recorded during experimental seizures, which may be present during the spreading depression and may replace it; (*e*) changes in the resting electroencephalogram. Changes in strength and duration of the stimulus affect mainly the afterdischarge. Repetition of a stimulus at 5- to 10-minute intervals enhances the afterdischarge and the fast, low potential activity. It is the only way in which the convulsoid activity has no peripheral motor equivalent.

(Authors' abstr.)

The Identity of Spreading Depression and " Suppression."

1. That type of electrical change characterized by the appearance of reduced electrical activity at the point of cortical stimulation, thence to appear in successive

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fashion in contiguous areas of cortex, requiring minutes for such spread, has been identified in the literature with " suppression of electrical activity," a property ascribed only to certain " suppressor areas." Experimental evidence herein presented has shown that this phenomenon is actually due to the spreading depression of Leão, and cannot be distinguished from it by any presumed criteria of differentiation.

2. Spreading depression can be produced at times, under ill-defined conditions, by strychnine as well as by other methods of stimulation (chemical, electrical or mechanical) from any area of the cortex in cat and monkey.

3. The mechanism by which the changes of electrical activity, known under the general heading of spreading depression, are produced, is essentially cortico-cortical ; further, it does not require neural continuity but only neural contiguity.

4. The type I or type II spreading depression of electrical activity is accompanied by a decrease in cortical excitability, as judged by decrease in cortically induced movements, and by a depression of strychnine spikes and sensory evoked potentials.

5. Stress has been laid upon the importance of considering mechanisms functioning independently of neuro-anatomical connections, as being of significance in function, either normal or abnormal. In particular, possible relationships between the phenomenon of spreading depression and the spread by contiguity of a focal epileptic discharge have been suggested. (Authors' abstr.)

Thalamocortical Activity During Spreading Depression.

Simultaneous recordings from cortex and thalamus were made during the spread of Leão's depression along the cortex of the rabbit. Twenty-six experiments were selected for report, all carried out upon animals under light anesthesia. Unique slow potentials, previously described by Leão (1944) as locally appearing concomitants of the process, were detected in the thalamus ; and the sites of coincident appearance in cortex and thalamus correlate well with the anatomical projections between the thalamic nuclei and the cortex of the rodent. Outcroppings of fast paroxysmal discharge were similarly localized to corresponding cortical and thalamic points and support the linkages reported. Results obtained by the strychnine activation method also correlate.

Spread of depression or its associated slow potential discharges, originating at a point in the cortex and invading thalamic regions in succession, does not spread cortex to thalamus to cortex, but from successively activated cortical areas to their corresponding thalamic nuclei.

Other subcortical centers were not investigated. (Authors' abstr.)

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VOL. II. 1948.

*E.E.G. Studies of Changes Induced by Electric Shock in Man : II. *Wada, T.* 304

Electroencephalographic Studies of Changes Induced by Electric Shock in Man. II : Supplementary Observations.

The author reports electroencephalographic sequelae to electric shock rendered by bifrontal and ear hole application in 30 cases of psychosis, principally schizophrenic in character. He considers that the sequence of E.E.G. change in convulsion

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following electric shock is similar to that obtained with convulsions of other etiology. In non-convulsive response to shock the E.E.G. recorded paralleled the level of consciousness attained. When ear hole application of shock is made, waves resembling those obtained in epileptic equivalent states occur, and the author suggests this as evidence that psychomotor activity in the E.E.G. is a manifestation of subcortical discharge. He believes he can relate the change in the electro-encephalogram incident to shock therapy to the phenomena of facilitation and extinction observed in experimental studies of Adrian, Dusser de Barenne, *et al.*

(Courtesy of Biol. Abstr.) (Psychol. Abstr.)

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Electroshock Convulsions and Memory : The Interval Between Learning and Shock.

From the data it may be concluded that for these two subjects :

1. The effect of electroshock on learning and retention is slight or undetectable until a cumulative effect which appears suddenly and shows generally in the patient's behavior makes the subject unable to attain the criterion of learning.

2. The cumulative effect of electroshock convulsions on memory is reversible following cessation of shocks : the number of repetitions for learning and relearning gradually returns to the level preceding the electroshock convulsions.

3. The cumulative effect of electroshock convulsions on memory is apparently the same for material learned one hour before as for material learned just prior to electroshock.

4. The hypothesis that an electroshock convulsion, administered during a learning activity, would result in complete amnesia for that material is untenable.

5. Whether or not an electroconvulsive shock impairs learning ability and retention, then, depends on the number of shocks previously administered.

(Authors' abstr.)

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Multiple Sclerosis (Encephalomyelitis Disseminata Periaxialis) and the Vegetative Nervous System.

In both the gastrospasm and the enterospasm encountered in multiple sclerosis the most significant fact is the disharmony between kinetic and tonic impulses. That means a breach of the fundamental law of the gastro-intestinal innervation. The lack of pains in total gastrospasm and the involvement of the entire organ are important features. In view of the complex innervation of the viscera, due to the antagonism of the vegetative nerves and to the automatic function of these organs, it is most difficult to arrive at a precise concept of how the various components operate. In addition to the nerves, the author has further to consider hormonal influences arising from the endocrine organs and from the intestinal mucosa (enterogastrone ?). The difficulties in the experimental study of the vegetative " centers " appear to be, to-day, insurmountable. A certain insight may derive from close clinical and anatomic studies. Virchow's cellular pathology, with its tendency of localizing, has won triumphs in the field of cerebral and spinal diseases. On the other hand, the better the close interrelationship of the inner organs and their domination by central factors is understood, the lesser the justification of a specialistic attitude. The outcome of Virchow's ideas is vanishing, and the necessity of considering the body as a unit is imperative. (Author's abstr.)

An Evaluation of Vitamin E Therapy in Diseases of the Nervous System.

Vitamin E, as present in wheat germ oil and natural mixed tocopherols, contains myotrophic and neurotrophic factors and is of importance in regulating capillary permeability. It influences favorably muscle growth in the young, and aids in increasing muscle strength and muscle tone. It has been found of value in selected cases of muscular hypotonia and muscular hypoplasia in the young. In cases of anterior poliomyelitis and infectious polyneuritis with residual muscular weakness it was found useful in hastening return of normal muscle function when combined with other methods of treatment.

It appeared to produce arrest or slowing down of progression of demyelinization when used in combination with the B complex group of vitamins in certain demyelinization states, including tabes dorsalis, amyotrophic lateral sclerosis and multiple sclerosis.

It should be given a trial in all cases of amyotrophic lateral sclerosis in the female, and is of some value in the spinal cases of amyotrophic lateral sclerosis in the male. It produced regeneration of atrophied musculature in one case of amyotrophy associated with tabes dorsalis and one case associated with multiple sclerosis when combined with intraspinal pyridoxine thiamine therapy and oral vitamin B complex.

In cases of congenital non-obstructive hydrocephalus it produced arrest or slowing down of progression of head enlargement. A number of children with progressive hydrocephalus have developed normally after receiving wheat germ oil for varying periods of time. It is suggested that congenital disturbance of the hematoencephalic barrier is probably responsible for many cases of hydrocephalus in the young, and that vitamin E is of value in restoring to normal the spinal fluid secretion-absorption mechanism in such cases.

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In view of the non-specific beneficial effect of vitamin E on muscle tone and muscle tissue proliferation in the young it should be included, preferably in the form of wheat germ oil, as a necessary vitamin supplement in the diets of all infants and children manifesting defective maturation of their neuromuscular apparatus. (Author's abstr.)

The Use of Ephedrine Sulfate in the Control of Enuresis in Schizophrenic Regression.

Ephedrine sulfate, 0·048 gm., was administered daily during a testing period to 28 regressed schizophrenics to determine its effect on the enuresis manifested by each of these patients.

The results were presented and theories of the rationale of therapy were advanced. (Authors' abstr.)

MARCH.

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Positive and Negative Aspects of Hypothalamic Disorders.

The author must compare the effects of chronic hypothalamic affections in man with experimental results. His material illustrates the great variety in the clinical picture. These variabilities are caused (*a*) by differences in the localization and extent of the pathological process, (*b*) by their nature and the tempo of their development, and (*c*) by the age of the patient. Accompanying disturbances in the brain outside the hypothalamus may also play a role.

Clinico-anatomical observations seldom offer opportunities to connect functional disturbances with the damage of special hypothalamic nuclei. Hence the task of the clinician regarding the problem of functional localization is more difficult

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than that of the physiologist. Clinical observations may, however, increase our insight into these relations, provided that they are carefully controlled by microscopical investigation. In comparing experimental results with those of clinicopathology one has to realize that the functional disorders that occur after experiments on animals are caused by acute lesions, in which the chains of neurones are suddenly interrupted. Observations in man, however, were on cases in which the pathological process developed slowly from the onset, so that compensation by other parts of the central nervous system might take place. To-day the best experimentally analysed syndrome is diabetes insipidus, but we have seen that, in man, bilateral destruction of the supra-optic nuclei does not always cause polyuria and polydipsia.

The author believes that the dorso-medial, ventro-medial and lateral nuclei of the tuber exert an important influence on vegetative functions, but up till now it is not proved that the different types of disordered metabolism correspond with lesions of distinct " centres." Hess (1948), whose method of electrical stimulation with very weak currents gives the most accurate results, also came to the conclusion that there is some localization of function in the hypothalamus, but that it is not limited to circumscribed " centres."

In order to explain the contradiction between the acute experimental and the chronic clinical facts in the central vegetative nervous system, one has to consider the relations in the somatic nervous system, where we meet the same difficulty. An acute lesion in man, for example, causes severe disturbances in motility or in sensibility which for the most part, after a time, gradually disappear. The theory of diaschisis of von Monakow (1905, 1914), which deepened the author's insight into cerebral localization of function, has to be applied also to the hypothalamus. Von Monakow pointed out that the various neurones are intimately connected : if one part suddenly drops out, this results in a functional reaction in all the parts of the brain linked up with the damaged area. But this reaction disappears after some weeks, and only the remaining symptoms have value for localization. Many facts shown by modern neurosurgery favour this conception. Foerster (1936), for example, showed that whereas excision of small parts of the anterior central gyrus in man causes total paralysis of the corresponding extremity, motility recovers very soon. Removal of circumscribed parts of the posterior central gyrus evokes loss of cutaneous and deep sensibility in the corresponding part of the body, but again recovery takes place, and after some time the usual methods of clinical examination fail to show any diminution of sensory function. Seen in this light, the results of the experimental method and of clinical pathology do not contradict each other. They only prove that there is a refinement in the functional localization in the brain, and not least in the vegetative central nervous system. Economic reasons incite Nature to follow frequently-used pathways. For the security of vital functions many fuses are placed in the central nervous system. If one of these breaks down, others redouble their activity.

At the present day scientific investigation is focused on the hypothalamus, but vegetative functions are also represented in other parts of the brain, for example in the cerebral cortex, although here they are spread more widely. The different negative cases in hypothalamic affections point clearly in the direction of this functional luxury. Positive and negative aspects have therefore to be studied with equal care. (Author's abstr.)

The Effects of Diisopropylfluorophosphonate in Schizophrenia and Manic-Depressive Psychosis.

In 17 schizophrenic patients, 9 manic-depressive patients and 10 normal subjects, the effects of D.F.P. given intramuscularly in doses of 1 to 2 mgm. daily have been studied. Observations have been made of the effect of the drug on the cholinesterase activity of the blood, and on the physical and mental state of the patients. Electroencephalographic studies have also been carried out. The mean values for red cell and plasma cholinesterase activity obtained before D.F.P. treatment were not significantly different in the three groups of subjects. Administration of the drug produced marked inhibition of both types of cholinesterase activity, and the levels of inhibition were comparable in the two psychotic groups.

When D.F.P. was administered for a period of seven days, in a total dosage of 13 mgm., characteristic physical effects were produced, particularly on the gastro-

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intestinal tract and on the cardiovascular system. These were considerably less marked in schizophrenic than in manic-depressive and normal subjects. There was a marked difference in the blood-pressure responses of the two psychotic groups. The possible significance of these findings is discussed.

A number of electroencephalographic changes are described, the most characteristic of which is lowering of amplitude associated with diminution of alpha activity. Approximately 24 hours after the withdrawal of D.F.P., however, an increase of amplitude with increased dominance and spread of the alpha rhythm was seen. No evidence of an epileptogenic action of the drug was observed. The incidence of E.E.G. changes was much greater in normal and manic-depressive subjects than in schizophrenic subjects. Atropine in doses of 1–5 mgm., subcutaneously, produced changes in the E.E.G. almost indistinguishable from those of the early stages of sleep, and did not counteract the effects of D.F.P. on the E.E.G.

The mental changes produced by the drug are illustrated by case-records. A characteristic depressive effect was observed in manic-depressive patients and in normal subjects. In a number of schizophrenic patients, on the other hand, an activation of the psychosis occurred which was not associated with disturbances of consciousness. (Authors' abstr.)

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*Site of Action of Myanesin in the C.N.S. *Kaada, B. R.* 89

Electronarcosis. II. Inhibition of Electrical Activity of Cerebral Cortex Following Application of Pulsed Stimulus to Diencephalon.

1. The application of a pulsed current directly to the diencephalon is followed by the appearance of continuous or spindled slow waves (10–18 per sec.) in the motor area of the cerebral cortex. The waves are bilateral in phase, but frequently of different amplitude. This state may progress to the complete inhibition of electrical activity. Occasionally spikes similar to those obtained from single wave or muscle fibers appear at a frequency of 10–18 per sec. These spikes are probably the expression of the activity of one or more cells which escape inhibition.

2. In a very limited area of the frontal lobes the effect of the stimulus is to accentuate the slow rhythms.

3. The area which, when stimulated, produces the inhibition of the cerebral cortex is close to the mammillary bodies next to the center controlling the electrical activity of the upper part of the spinal cord. (Authors' abstr.)

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Electronarcosis. III. Inhibition of Cortical Electrical Activity Following Local Application of Pulsed Stimulus.

1. The application of a pulsed stimulus directly to the motor cortex alters the cortical electrical activity: the most important phenomenon is inhibition of such activity.

2. In the anterior part of the occipital lobe, after stimulation of the homolateral motor cortex, the same electrical signs are seen as in the contralateral motor cortex, the wave potentials being out of phase.

3. Stimulation of the anterior frontal area is without effect on its electrical activity: when the stimulation is applied on the motor cortex the normal alpha waves increase in amplitude. This increase of the slow rhythm may be due to a functional isolation of the frontal cortex to which impulses from the motor area are interrupted because of the inhibition. (Authors' abstr.)

After-potentials and Excitability of Spinal Motoneurones Following Antidromic Activation.

When motoneurones are activated by an antidromic volley, they generate after-potentials which have been recorded either with ventral root leads or with a micro-electrode in, or close to, the motor nucleus. Probably the early phase of after-negativity is in part due to a catelectrotonus of uninvaded motoneurones, and in part to a true after-potential of invaded motoneurones. The subsequent after-positivity (duration about 100 m.sec.) is a true positive after-potential of the invaded motoneurones.

Three types of testing stimulation (monosynaptic orthodromic, antidromic, and direct) have been used for investigating the changes in excitability of the motoneurones that are associated with these after-potentials. The deepest depression of excitability is invariably found at 10–20 m.sec. after the antidromic activation of motoneurones. As the testing interval is shortened there is always a phase of lessened depression—even of facilitation—while with lengthening intervals a gradual recovery to normal excitability is observed at 80–140 m.sec. Rarely a later prolonged depression is observed. Evidence is given that the phase of lessened depression at short intervals is in part attributable to the supernormality associated with the negative after-potential of invaded motoneurones, and in part to facilitation produced in uninvaded motoneurones by their catelectrotonic depolarization. In general the depression corresponds closely in its time course to the positive after-potential and is thus homologous with the subnormal state of peripheral nerve, though both the potential and the depression are much larger than with peripheral nerve.

At very short intervals the testing stimuli evoke responses only in those motoneurones not invaded antidromically. It is shown that such motoneurones can fire a reflex discharge down their motor axons as soon as 0·7 m.sec. after the arrival of the antidromic impulse at its site of blockage—presumably the axon hillock.

Even during the depth of the depression, a testing orthodromic volley sets up a synaptic potential showing little or no depression, but a large depression is observed at very short intervals after the antidromic volley (less than 6 m.sec.).

The relatively supernormal and the subnormal phases of excitability make it difficult to estimate the duration of the refractory period, but the absolutely refractory period is less than 1·3 m.sec., and the total duration of absolute plus relative refractoriness is 4–6 m.sec., which is in good agreement with values for blood-perfused mammalian nerve.

In the discussion it is shown on experimental grounds that the positive after-potential and the associated subnormal phase are located on the soma and proximal dendrites, i.e. in the area covered by synaptic knobs, and not, for example, in the dendritic terminals or interneurones. Explanations are offered for the recurrent discharge which is set up from a few motoneurones by an antidromic volley.

Previous attempts to test the effect of an antidromic impulse on the prolonged synaptic excitatory state (facilitation potential) are shown to be unsatisfactory. Every possible precaution is taken to make a new experimental investigation satisfactory, and the results do suggest that the prolonged facilitation state is extinguished when a motoneurone is invaded by an antidromic impulse. However, an alternative explanation is possible, and it is argued that a definitive result is only possible with the investigation of single motoneurones. (Authors' abstr.)

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Dorsal Column Conduction of Group I *Muscle Afferent Impulses and their Relay through Clarke's Column.*

The largest afferent fibers, serving muscle, for the most part terminate in the upper lumbar and lower thoracic segments. During this relatively truncated course in the dorsal columns, after supplying myotatic reflex collaterals to the motoneurons, these fibers came into relation with the cells of Clarke's column, where a relay is established for the projection to the cerebellum of stretch-evoked activity.

Conduction velocity of impulses in the primary afferent fibers is strikingly non-linear. A volley engendered in the large afferent fibers of muscle has an initial velocity approximating 110 M. per sec. Once these fibers have entered the spinal cord velocity drops to about two-thirds the initial value. Further changes, occurring typically in the third and first lumbar segments, bring velocity to less than one-quarter the initial value. Less spectacular changes attend impulse conduction by the larger cutaneous afferent fibers. Impulses in the dorso-lateral tract conduct at a uniform velocity that compares with the initial velocity of impulses in the presynaptic afferent fibers from muscle.

The synaptic articulations which the large afferent fibers form with motoneurons and with the cells of Clarke's column differ characteristically, considerable summation being requisite for transmission in the motor nuclei, but not in Clarke's column.

Postsynaptic response in the dorso-lateral tract begins with a discharge relayed, with little time delay, at the caudal end of Clarke's column. Following this monosynaptic discharge is a series of discharges occurring with progressively increasing randomness. The mechanism of the later discharges is not known.

(Authors' abstr.)

Cortical Inhibition of Gastric Motility.

1. The effect of cortical electrical stimulation on gastric motility has been reviewed and studied in dogs.

2. Inhibition of pyloric antral motility occurs from the "insular-orbital" region and the sub-genual portion of the anterior cingulate gyrus.

3. No augmentation of antral motility was produced in this series by stimulation anywhere on the exposed cortex.

4. A functional relationship between the orbital surface and the anterior cingulate gyrus has been suggested, and the phylogenetic relationship of part of the "orbital surface" of the dog to the Island of Reil in man has been pointed out.

(Authors' abstr.)

Effect upon Blood Pressure of Electrical Stimulation of Tips of Temporal Lobes in Man.

1. Electrical stimulation of the tips of the temporal lobes has been found to produce an elevation of blood pressure in a patient under pentothal anesthesia.

2. Significant elevations occurred both in the systolic and diastolic blood pressures.

3. The blood-pressure responses were obtained using 10 cycles per sec., a pulse duration of 10 m.sec., and from 5 to 20 volts.

4. Suggestions are made of possible connections between the tips of the temporal lobes and the hypothalamus which might mediate the blood-pressure responses.

(Authors' abstr.)

Threshold of Action Potentials in Ear of Guinea-Pig.

A method is described for determining the threshold of auditory action potentials in the cochlea of the guinea-pig for frequencies below 1,000 cps. The method depends on cancelling the aural microphonic by a signal derived from the electrical current that produces the sound stimulus.

The action-potential threshold in decibels for tones below 1,000 cps. is a linear function of the logarithm of the frequency. The slope of this line varied from — 28 db. per octave in fresh preparations to — 1 db. per octave in animals treated with a large dose of quinine.

The "threshold" of the aural microphonic (intensity needed for a μ1 v. response) when the intra-aural muscles are relaxed seems to be practically independent of

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frequency from 1 to 5,000 cps., provided the microphonic at each frequency is measured close to its source. To make such measurements in the middle frequency range the action potentials must be suppressed. This can be done, with very little effect on the aural microphonic, by an appropriate dose of quinine. Less complete differential reduction of action potentials may occur "spontaneously," apparently as a result of the operative procedures involved in implanting electrodes in the cochlea.

In a fresh preparation the over-all "threshold of cochlear response" is determined by the aural microphonic at high and at low frequencies, but by action potentials over the middle frequencies. The apparent "threshold" curve is irregular because of re-enforcement or partial cancellation of the two components. The interaction varies with frequency and with the position of the electrodes.

The relationships to frequency of the action-potential threshold and of the microphonic differ widely (up to 28 db. per octave), and vary independently. The differential sensitivity of the ear with respect to frequency is determined in part by physical acoustic properties of the ear as a whole. For frequencies at least up to 1,500 cps., however, this sensitivity is even more importantly determined by a process closely related to the excitation of the nerve impulses, and subsequent to (or quite independent of) the aural microphonic. (Authors' abstr.)

Site of Action of Myanesin (Mephenesin, Tolserol) in the Central Nervous System.

1. The site of action of myanesin (mephenesin, tolserol) in the central nervous system has been studied in cats and monkeys.

2. In therapeutic doses of the drug (10–40 mgm./kgm. i.v.) the spinal mono- and multisynaptic reflex discharges were unaffected, as were the patellar, flexion, and crossed extension reflexes. With increased dosage the multisynaptic reflex discharges were depressed before the monosynaptic ones. Correspondingly, the flexion and crossed extension reflexes were found more susceptible to the drug than the patellar reflexes. In accordance with earlier observations it was found that hyperactive spinal reflexes (produced with light chloralose anesthesia or by injection of strychnine) were promptly reduced to normal with clinical doses of myanesin. The great enhancement of the multineuron discharge following the injection of strychnine could also be effectively counteracted with myanesin.

3. Facilitation and inhibition of the knee-jerk from stimulation of the brain stem reticular formation were reduced or abolished by myanesin in amounts of 20–30 mgm./kgm. The stimulus threshold for obtaining these effects was measured before and after the administration of the drug. In most experiments the two systems were about equally depressed, while in some preparations with very hyperactive reflexes facilitation was somewhat more reduced than inhibition.

4. Similar facilitation and inhibition obtained from the anterior lobe of the cerebellum were reduced with smaller doses of myanesin (10–20 mgm./kgm.). Cortically induced movements were reduced by doses of 15–35 mgm./kgm.

5. Spontaneous cortical and subcortical potentials were unaffected by clinical doses of myanesin. The repetitive discharges of the evoked cortical potentials were abolished with smaller doses of the drug than was the primary complex. Cortical after-discharges in chloralosed animals were reduced.

6. It is concluded that the more complex multisynaptic pathways are particularly vulnerable to myanesin. Such pathways are presumably involved in disorders which respond to myanesin, such as spasticity, rigidity, certain involuntary movements, *petit mal* epilepsy, and possibly certain types of pain.

(Author's abstr.)

MARCH.

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*After-potentials and Excitability of Spinal Motoneurones Following Orthodromic Activation. *Brooks, C. McC., et al.* 157
*Excitation of Single Nerve Fiber by Action Current from Another Single Fiber. *Tasaki, I.* 177

Electronarcosis. IV. Effects of Square Wave Application to Motor Area Following Destruction of Diencephalon.

1. After the diencephalic center has been destroyed by diathermy, stimulation of the cortex with interrupted current is without effect: after a few minutes the normal electrical activity of the cortex slowly decreases and the cortex is insensible to electrical, mechanical or chemical stimuli.

2. The phenomena described in the first paragraph of the Summary may be interpreted as due either to (*a*) fatigue of cellular elements of the cortex, whose activity is not controlled by the inhibitory diencephalic center, or (*b*) random activity such that the number of neurones in question being very great, the algebraic sum of their electrical manifestations tends to equal zero.

3. Electrical silence follows passage of the interrupted current, whatever may be the position of the recording electrodes on the skull.

4. After this stage electrical activity is resumed, characterized first by very rapid waves, which later increase in amplitude and appear in groups. During this period the patient has mental confusion and often catatony.

(Authors' abstr.)

Electronarcosis. V. Faradic Stimulation of Motor Area Following Diencephalic Diathermy.

1. If the motor cortex is stimulated with an inductorium instead of an interrupted current, wave potentials of the strychnine type appear, and a partial inhibition, similar to that obtained with the interrupted current, occurs.

2. In an animal in which the diencephalic centre has been destroyed, faradic stimulation of the motor cortex is without effect; on the contrary, strychnine solutions applied to the cortex give rise to the appearance of strychnine waves. The application of interrupted current in the presence of strychnine does not produce inhibition, as when the diencephalic centre is intact, but only a local excitation.

3. In conclusion, a demonstration has been presumably given of a centre extending from the frontal part of the diencephalon back to the pons. This centre has a regulatory function on all parts of the central nervous system, from the telencephalon to the spinal cord, and it has a segmentary structure and the segments may be independently stimulated both directly or reflexly.

(Authors' abstr.)

Some Connections of the Orbito-fronto-temporal, Limbic and Hippocampal Areas of Macaca mulatta.

1. By means of the technique of physiological neuronography some of the connections of the rhinencephalic and limbic areas of *Macaca mulatta* have been investigated in an attempt to extend reports of previous studies.

2. The following areas can be recognized by differences in their firing patterns: trigonal, subcallosal and medial orbital, precallosal cingulate, supracallosal anterior cingulate, supracallosal posterior cingulate, retrospinal, posterior orbital and anterior insular, temporal polar, periamygdaloid, and entorhinal. An attempt has been made to correlate these with cytoarchitectural differences and with subcortico-cortical connections whenever possible. Some of the connections of the hippocampus and amygdala were also investigated.

3. The cortico-cortical interconnections of these areas suggest that they fall into three groupings: (i) The trigonal, subcallosal and medial orbital, precallosal cingulate, posterior orbital and anterior insular, temporal polar, periamygdaloid and entorhinal areas are heavily interconnected. This group may be referred to as the orbito-fronto-temporal region. (ii) The second group includes the projection areas of the three divisions of the anterior thalamic nucleus. There are three of these areas: supracallosal anterior cingulate, posterior cingulate, and retrosplenial. According to previous studies, these areas are closely related to the

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cortex surrounding the cingulate sulcus and to certain aspects of the lateral surface of the hemispheres. They are functionally interconnected by extremely short fiber systems. This group may be referred to as the limbic region. (iii) Finally, the consideration of the hippocampal formation as a separate region is tentative until its relation to the orbito-fronto-temporal and the limbic areas is further clarified and any possible connections with the lateral neocortex investigated.
(Authors' abstr.)

Recovery of Skilled Motor Functions after Small Repeated Lesions of Motor Cortex in Macaque.

1. Small lesions in the thumb or hand area of the motor cortex revealed that no definite area within the internal capsule can be assigned to the cortico-spinal fibres coming from a particular subdivision of area 4. Moreover, small lesions in the hand area caused degeneration down to the lumbar region, suggesting that subdivisions of area 4 connect with several spinal levels.

2. It was found that small lesions to area 4 produced a contralateral paralysis and inability to perform a delicate skilled motor act, such as opening a puzzle box. This paralysis was followed by a considerable degree of recovery and a return of motor skill.

3. When, after recovery, area 4 was again exposed, parts adjacent to a lesion in the hand area gave hand responses which were not detectable at the earlier operation. Undercutting of these subdivisions caused a recurrence of paralysis and loss of motor skill in the previously recovered arm.

4. It is suggested that the motor cortex does not function as a mosaic but has a tendency when a lesion occurs to act in a less differentiated and more primitive manner, which may be made possible by the plurisegmental connections of area 4 described in our experiments. (Authors' abstr.)

Course of Spinothalamic and Medial Lemniscus Pathways in Cat and Rhesus Monkey.

1. Stimulation of the sciatic and saphenous nerves of cat and rhesus monkey initiated potentials in the medulla oblongata, midbrain, thalamus and internal capsule which were characterized by an initial, rapidly conducted spike which was followed occasionally by slower spikes.

2. A large portion of the afferent pathways from the saphenous nerve passed lateral to the inferior olive.

3. The afferent impulses from both the sciatic and saphenous nerves traversed the midbrain in a restricted area corresponding to the medial lemniscus, and then entered the nucleus ventralis posterolateralis.

4. Impulses following sciatic and saphenous nerve stimulation ascended in the same relative positions on both sides of the brain stem.

5. The components of the medial lemniscus from the gracilis and cuneatus nuclei completely crossed to the opposite medial lemniscus and thalamus.
(Authors' abstr.)

After-potentials and Excitability of Spinal Motoneurones Following Orthodromic Activation.

Motoneurones innervating a particular muscle (usually gastrocnemius) have been subject to orthodromic activation by a single synchronous volley that was set up by stimulation of group 1 afferent fibres of that muscle. When the volley was so small and/or the anaesthesia so deep that no reflex discharge was evoked, the negative synaptic potential recorded from an emerging ventral root was followed by an after-positivity persisting for about 100 m.sec. When a reflex discharge was superimposed on the synaptic potential, there was a corresponding increase in the after-positivity.

A testing monosynaptic orthodromic volley has been used for investigating the changes in excitability of the motoneurones that were associated with these after-positivities. When the conditioning and testing volleys were set up in the same muscle afferent fibres (group 1 only), the deepest depression of excitability occurred at 10–30 m.sec. (complete suppression of the testing reflex response), and initially, recovery occurred along much the same time course as after antidromic activation of motoneurones. However, unlike the latter, this phase of

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recovery was always incomplete and followed by prolonged slow recovery of excitability, which was still incomplete at the longest test interval of 660 m.sec.

A similar, but less intense, depression with two-stage recovery was observed after a conditioning volley which was so small that it evoked little or no reflex discharge. However, when this reflexly subliminal volley was in a different (synergic) nerve from the testing volley, little or no reflex depression was usually observed.

It is concluded that the initial phase of depression is attributable to a subnormal state of motoneurones during the positive after-potential that follows their response to the conditioning orthodromic volley, and is recorded after electrotonic spread to the ventral root. It is evident that the reflex discharge of an impulse should set up an after-potential and depression similar to that following antidromic invasion of that motoneurone.

It is shown that the after-positivity and associated depression following reflexly subliminal activation is, according to the electrical hypothesis, likewise attributable to the positive after-potential following the local responses of the subsynaptic areas of a motoneurone. On the available evidence the prolonged phase of depression is located in the presynaptic pathway. (Authors' abstr.)

Excitation of Single Nerve Fiber by Action Current from Another Single Fiber.

By the method of bridge-insulator, action currents from an isolated nerve fiber were led to another fiber without appreciable leakage. In many cases it was observed that an impulse initiated in the primary fiber jumped to the secondary fiber at the insulated region. Application of a hypertonic NaCl solution upon the region of electrical contact of the two fibers facilitated the jump of impulse. It was shown that a concentrated NaCl solution reduces the membrane resistance of the nerve fiber and prolongs the action current. (Author's abstr.)

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Experience with Topectomy for the Relief of Intractable Pain.

1. Following Pool's lead in the surgery of mental disorders, bilateral topectomy of the 9, 10, 46 region was performed, since 1947, on 25 patients suffering from different kinds of unbearable pain.

2. Results are generally good with a bilateral cortical excision of a total of about 20 to 25 gm. Unilateral topectomy failed often. Some results have lasted nearly 2 years to date.

3. Different classes of unbearable pain are analysed. The action of topectomy is beneficial on both organic unbearable pain or the so-called " psychic " pains. Indications for other operative procedures are discussed.

4. An objective technique of measuring unpleasant and unbearable pain is given. Such a condition is called *souffrance*, and its close relationship with anxiety is shown. A step is taken in bringing a mental condition up (or down) to a physiological phenomenon.

5. Possible mechanisms and localizations involved are briefly discussed.

(Author's abstr.)

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Experiences with Unilateral Prefrontal Lobotomies for Pain.

1. In a series of 16 cases of intractable pain treated by unilateral lobotomy, lasting relief was obtained in 50 per cent. of the series.

2. In some instances, at least, unilateral lobotomy gives effective relief when the pain is diffuse, when it is due to direct nerve involvement, or when it occurs in the upper extremities or head.

3. The authors' experience has suggested that complete unilateral leucotomy is more effective than a medial incision that does not include the superior lateral quadrant.

4. The most impressive advantages of the unilateral operation are the minimal surgical risk and the absence of marked post-operative mental change.

5. Pain was subsequently controlled satisfactorily by making the operation bilateral in 3 cases. Other pain-relieving operations were successfully used in several additional cases.

6. On the basis of this small series of cases, the authors feel that unilateral lobotomy has a definite place in the treatment of intractable pain, and deserves further trial. Subsequent operation on the second side may always be added if necessary. (Authors' abstr.)

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General Survey of Insulin-treated Patients after Five Years.

A long-term follow-up of schizophrenics who were treated with insulin shock therapy reveals the following :

(1) There is no apparent difference between males and females in correlations between diagnosis, condition after treatment or, at present, duration of illness prior to treatment, or the length of time and adjustment outside of the hospital after release.

(2) Chronic cases are more benefited by intensive coma treatment than by light treatment combined with personal care.

(3) Those who showed the most improvement at the completion of treatment have also shown the greater ability to remain in the community.

(4) Acute cases appear to have a better prognosis than chronic cases. The five-year prognosis is poor for both acute and chronic, the acute cases still doing better than the chronic.

(5) Some chronic patients who were ill over three years have made as good outside adjustments as have some of the patients with short histories of illness before treatment was initiated.

(6) A certain percentage of chronic cases does respond favorably to insulin-coma therapy. (Authors' abstr.)

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VOL. LXXIII. 1948.

*Electrical Potentials of the Corpus Striatum and Cortex in Parkinsonism and Hemiballismus. *Meyers, R., and Hayne, R.* 10
*Spreading Depression of Electrical Activity in the Cerebral Cortex Following Local Trauma and its Possible Role in Concussion. *Echlin, F.* . . 199

Electrical Potentials of the Corpus Striatum and Cortex in Parkinsonism and Hemiballismus.

The experimental group consisted of 11 patients, 10 with paralysis agitans and 1 with hemiballismus, the control group consisting of 11 patients without identifiable " organic " diseases of the brain. The authors passed into the corpus striatum and environs a special needle, equipped with 8 ring-type "pick-up" electrodes, through a burr hole in the anterior vertical region of the skull in unanesthetized patient. E.E.G. tracings were analysed in respect to frequency, voltage and relative polarity of waves. Wave frequency of the corpus striatum and contiguous area is greater than that of cerebral cortex ; no consistent relationship was demonstrable between the polarity of the striatal and neighboring electrical potentials and those of the cerebral cortex ; certain portions of the striatal region tend strongly to exhibit a sustained, corresponding polarity of their respective action potentials ; " voluntary " movements of the upper and lower limbs and stimulation of the cutaneous surfaces of these members with the point of a pin do not produce perceptible wave changes ; certain tracings obtained from patients afflicted with paralysis agitans are characterized by frequencies of striatal waves appreciably greater than those seen in control subjects.

F. C. SUMNER (Psychol. Abstr.).

Spreading Depression of Electrical Activity in the Cerebral Cortex Following Local Trauma and its Possible Role in Concussion.

Weak faradic stimulation or tapping locally of the cortex with a glass rod causes a marked decrease in the spontaneous electrical activity of the cortex at the stimulated point which spreads outward, and within 3 to 6 minutes involves the entire cortex of the hemisphere stimulated. Leão has called this phenomenon " spreading depression." Recovery takes place within 5 to 10 minutes. The present author reports his study of spreading depression in rabbits under nembutal anesthesia, and points to the striking similarity between the E.E.G. findings in rabbits showing " spreading depression " in cerebral cortex, and those shown to occur following experimental concussion. It is concluded that the

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E.E.G. findings in concussion may be largely explained on the basis of a " spreading depression " of electrical activity initiated from innumerable points in cerebral cortex simultaneously. F. C. SUMNER (Psychol. Abstr.).

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1. Biochemistry, Physiology, Psychiatry, &c.

Variation in Acetylcholine Content of the Brain with Physiological State. Richter, Derek, and Crossland, James. [*Am. J. Physiol.*, **159**, 247–55 (1949).]

The acetylcholine content of the rat brain depends on the physiological state. It is increased in Na pentobarbital anaesthesia and in sleep; it is reduced in emotional excitement, in electric stimulation, and in convulsions. It thus appears to vary inversely with the degree of activity of the brain.

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

Specificity of the Trimethylammonium Group in Acetylcholine. Holton, Pamela, and Ing, H. R. [*Brit. J. Pharmacol.*, **4**, 190–6 (1949).]

The effect of replacement of the N-methyl groups of acetylcholine by Et groups and by acetoxyethyl groups was studied, by using the cat's blood pressure, guinea-pig ileum, frog heart, and frog rectus muscle. The replacement of one Me group of acetylcholine by Et reduces the activity of the compound. The replacement of 2 Me groups produces a much greater reduction proportionally. The replacement of 3 Me groups altered the pharmacological effect, and produced paralysing nicotine-like effects on the cat's blood pressure and superior cervical ganglion. It also antagonized acetylcholine in the frog heart and the rabbit auricles. The replacement of 1 or 2 Me groups by acetoxyethyl reduced activity more than replacement by Et. This suggests that 2 *N*-Me groups play an important part in the structural specificity of the acetylcholine molecule, and a form of attachment by means of 2 Me groups, as well as by the acetoxy group, is suggested. The 1, 2, and 3-N-ethyl substituted compounds were hydrolyzed at the same rate as acetylcholine by the cholinesterases of dog's caudate nucleus and cobra venom, but less rapidly when horse serum was used. The 3 enzyme preparations hydrolyzed both ester groups of bisacetoxyethyldimethylammonium iodide, and, more slowly, tri(acetoxyethyl)methylammonium iodide. LA VERNE L. KIESSLING (Chem. Abstr.).

Influence of Acetylcholine on the Resting Potential of Striated Frog Muscle. Bartels, Heinz. [*Arch. ges. Physiol.* (*Pflugers*), **250**, 277–94 (1948).]

Muscle-sections responded to 10^{-3} acetylcholine (I)/100 c.c. Ringer solution (II) only if they contained nerve endings, in which case the resting potential became more negative. The potential changes developed exponentially, reaching half the maximum value in about one minute, then reaching the maximum value (an average of 4–5 mv. under the most favourable conditions) in 5 or 10 minutes, and taking at least 30 minutes to return half-way to the control value. The duration of the tonic contraction induced by (I) was dependent on the dose of (I), and was shorter than the time taken to reach the maximum negative potential. Previous and concurrent treatment with prostigmine (III) increased the sensitivity of the sartorius muscles of frogs collected from January to March to the point where 10^{-5} gm. (I)/100 c.c. (II) was effective. The optimum concentration of (III) for this effect was 10^{-3} gm. (I)/100 c.c. With frogs collected from April until July, 10^{-3} gm. (I)/100 c.c. was necessary to produce an effect with or without (III), but in general the lowering of potential was somewhat greater for these frogs.

MARSHALL E. DEUTSCH (Chem. Abstr.).

Effect of Vitamin B_1 on Acetylcholine. Laos, Pablo A. [*Rev. facultad farm. y bioquim., Univ. nacl. mayor San Marcos* (*Lima, Peru*), **10**, 50–9 (1949).]

Twenty mgm. of *acetylcholine* (I) in contact with dog blood loses its hypotensor effect within 3 minutes due to hydrolyis by cholinesterase. When (I) is added to

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mixtures of blood and vitamin B_1 which stood for 10 and 30 minutes respectively, (I) becomes ineffective only after 12 and 60 minutes respectively. Apparently cholinesterase is inhibited by vitamin B_1.

J. H. WEISBURGER (Chem. Abstr.).

The Quantitative Relationship of Antagonism Between Acetylcholine and a Synthetic Curare (2559 *F*). *Guarino, Salvatore, and Bovet, Daniele.* [*Rend. ist. super. sanita*, **12**, 215–36 (1949); *cf. C. A.* 1603*d*.]

On the basis of the wide dosage applicable, 2559 F (triiodethylate of 1, 2, 3-tri-(2-diethylaminoethoxy)benzene) was shown to be suitable for the estimation of the acetylcholine/curare antagonism on the rectus abdominis muscle of the frog.

VINCENT C. PETRILLO (Chem. Abstr.).

Relations Between Acetylcholine Synthesis and Metabolism of Carbohydrates and D-Glucosamine in the Central Nervous System. Harpur, R. P., and Quastel, J. H. (*Montreal Gen. Hosp. Research Inst., Montreal, Can.*). [*Nature*, **164**, 779–82 (1949).]

Extracts of acetone-dried brain powder can produce adenosinetriphosphate (I) from the glycolysis of glucose and fructose for the synthesis of acetylcholine (II). Glucose and fructose inhibit (II) synthesis in brain extracts. (II) synthesis is inhibited by similar concentrations of D-glucosamine, which may also be phosphorylated by brain extracts at the expense of (I). The fall of (I) concentration, because of the hexose phosphorylation, may be responsible for the inhibitory action on (II) synthesis. N-Acetylglucosamine competes with D-glucosamine and fructose for the phosphorylase involved in the reaction with (I), but N-acetylglucosamine is not phosphorylated. N-Acetylglucosamine prevents the dephosphorylation of (I) by D-glucosamine and fructose, and N-acetylglucosamine stops the inhibition of (II) synthesis. The affinity of glucose for the phosphorylase far exceeds that of fructose and D-glucosamine, and little or no relieving action of N-acetylglucosamine is found on the glucose inhibition. Diphosphopyridine nucleotide, which by enabling glycolysis to take place causes (I) to be produced at a rate comparable with the rate of its breakdown, is destroyed by a diphosphopyridine nucleotidase present in brain extracts. An extract of acetone-dried brain powder, when added to a medium containing glucose and (I), normally shows little or no glycolysis or (II) formation. If the action of the diphosphopyridine nucleotidase is inhibited by nicotinamide in the above system, a high rate of glycolysis and (II) synthesis results. In an anaerobic system (cysteine-nicotinamide-extracts of acetone-dried brain powder containing (I)) glucose can be replaced by fructose for (II) synthesis. In this complete system (II) synthesis closely follows glycolysis. CHESTER HARGREAVES (Chem. Abstr.).

The Parallelism Between the Curarizing Action of Certain Synthetic Curares and the Antagonostic Effects of Acetylcholine. Marotta, Maria. [*Rend. ist. super. sanita*, **12**, 242–8 (1949).]

A general comparison is made of pure alkaloids and synthetic curares, considering the parallelism between their curarizing action and the antagonism they exercise against the contraction caused by acetylcholine on the muscle of the frog.

VINCENT C. PETRILLO (Chem. Abstr.).

The Cerebrospinal Fluid in Some Cases of Heine Medin's Disease. Ferrando, Elias, Ringuelet, Maria L., and Dato, Alfredo Actis. [*Rev. asoc. bioquim. argentina*, **16**, *No.* 65, 20–31 (1949).]

In 92 cases of Heine Medin's disease the cerebrospinal fluid was nearly normal, with a tendency to increased content of albumin, glucose, and white corpuscles, and to decreased chloride. The globulin reaction was negative in 64 and weakly positive in 18 per cent. of cases. F. F. (Chem. Abstr.).

The Cerebrospinal Fluid in Rheumatoid Spondylitis. Boland, Edward W., Headley, Nathan E., and Hench, Philip S. (*Mayo Clinic, Rochester, Minn.*). [*Ann. Rheumatic Diseases*, **7**, 195–8 (1948).]

In 50 cases of rheumatoid spondylitis the concentration of spinal fluid sugar was normal in 70 per cent., slightly low in 12 per cent., and slightly high in 18 per

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cent. of the cases. An abnormal colloidal Au reaction was present in 1 per cent. of the cases. The protein concentration in the cerebrospinal fluid was increased in 42 per cent. of the cases, but there was no consistent relationship between blood and cerebrospinal fluid protein concentrations.

E. K. WEISBURGER (Chem. Abstr.).

The Pressure of the (Cerebrospinal) Fluid during Acetylcholine Shock. Alema, G., Mengoli, G., and Nobile, S. (Univ. Bologna, Italy). [*Boll. soc. ital. biol. sper.*, **24**, 904–7 (1948).]

The pressure of the cerebrospinal fluid of 30 persons reached a maximum 30 seconds after injection of 0·01 gm./kgm. acetylcholine (I). The maximum was mostly followed by a plateau of 1–2·5 minutes' duration. The return to normal pressure occurred in 2–15 minutes. The relation of these changes to those of the blood pressure (II) is discussed.

Arterial Pressure, Capillaries, and Photoplethysmogram in the Acetylcholine Shock. Alema, G., and Nobile, S. [*Ibid.*, 907–9.]

An initial decrease of (II) and pulse for a few seconds was followed in 18 of 30 persons with (I) shock by a high (II) crisis and an increase in differential pressure (III) and of the oscillometric index (IV). In 9 cases (II) was lowered, while (IV) remained unchanged, and (III) varied in all possible ways. The rest of the persons showed no change of (II), (III) or (IV). A contraction of the capillaries was seen in 13 persons. An increase of the curve of the photoplethysmogram was seen in 6 of 8 cases. It began 2–3 minutes after injection of (I) and lasted for 4–8 minutes. In 2 cases, in which (II) and (IV) did not vary, the curve decreased.

F. FROMM (Chem. Abstr.).

Multipie Sclerosis and Cerebrospinal Fluid Analyses. Krais, Wolfgang (Bad Cannstatt, Ger.). [*Deut. med. Wochschr.*, **74**, 1229–30 (1949).]

Cerebrospinal fluids (300 samples) of 273 patients in various stages of the disease were studied. Of these, 60 normal samples were drawn from severe and typical cases in the initial as well as advanced stages. The data as related to severity and duration of the diseases are given in 3 tables, but no specific conclusions are drawn.

D. L. NOETHER (Chem. Abstr.).

The Sugar and Calcium of Cerebrospinal Fluid in Koreans. UiSun, Lim. [*J. Korean Med. Assoc.*, **2**, *No.* 1, 46 (1949).]

The sugar content of cerebrospinal fluid was 31–111 mgm. per cent. in men, average 65·9, and 34–114 mgm. per cent. in women, average 66·8. The Ca content of spinal fluid was 3·2–12 mgm./100 c.c. in men, average 5·95, and 3·8–11·2 mgm./100 c.c. in women, average 6·22.

I. S. YUN (Chem. Abstr.).

Effect of Cholinesterase Inhibitors on the Toxicity of Procaine in Mice. Conway, A. C., Ting, K. S., and Coon, J. M. [*J. Pharmacol Exptl. Therap.*, **96**, 472–6 (1949).]

In mice, physostigmine and diisopropyl fluorphosphate had a significant protective effect, raising the LD50 of procaine 23 and 16 per cent. respectively. Neostigmine and "carbamic acid N, N-dimethyl-4-dimethylamino-3-isopropylphenyl ester methiodide" increased the susceptibility of mice to the toxic action of intravenous procaine, lowering the LD50 by 35 and 22 per cent. respectively. Methacholine had no significant effect on the toxicity of procaine. These results indicate that the reputed antiprocaine esterase activity of the cholinesterase inhibitors probably does not influence the toxicity of procaine in mice, and that other factors must be considered to explain the influence of these agents on procaine toxicity.

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

Mechanism of the Inhibition of Rat Brain Cholinesterase by Diisopropyl Fluorphosphate, Tetraethyl Pyrophosphate, and Eserine. Bain, James A. [*Proc. Soc. Exptl. Biol. Med.*, **72**, 9–13 (1949).]

The mechanism of inhibition of rat brain cholinesterase by the 3 most potent anticholinesterases, diisopropyl fluorphosphate, tetraethyl pyrophosphate, and

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eserine, was studied by a method which involves variations in enzyme concentration as well as inhibitor concentration. It was shown that the kinetics of eserine inhibition can be analysed by classical methods which ignore enzyme concentration, but the cases of the other 2 inhibitors may not be so treated. Inhibition by the fluoro- and pyrophosphate esters is irreversible, and depends on enzyme concentration and time of incubation of the enzyme with the inhibitor before addition of the substrate. The upper limit of cholinesterase concentration in rat brain is established to be 1×10^{-6} M if structural restrictions are not assumed.

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

The Action of Synthetic Thiamine on the Neuromuscular Excitability of Man. Torre, Michele. [*Acta Vitaminol.*, **2**, 33–4 (1948).]

Intravenous injection of 20–50 mgm. thiamine produced in men a quick diminution of muscular chronaxia of about 20-minutes duration. This strychnine-like effect is analogous to that observed by Chauchard in rabbits, guinea-pigs, and frogs (*cf. C. A.*, **36**, 2594[6]). F. FROMM (Chem. Abstr.).

Effect of Experimental Thiamine Deficiency on the Nervous System of the Rhesus Monkey. Rinehart, J. F., Friedman, M., and Greenberg, L. D. [*Arch. Path.*, **48**, 129–39 (1949).]

Bilateral symmetrical areas of degeneration in the corpus striatum and other parts of the brain, and weakness and ataxia, were seen in chronic thiamine deficiency in rhesus monkeys. Neither peripheral neuropathy nor degeneration of the cord was observed. M. L. C. BERNHEIM (Chem. Abstr.).

Vitamin E Deficiency, Dietary Fat, and Spinal Cord Lesions in the Rat. Luttrell, Charles N., and Mason, Karl E. (*Univ. of Rochester, Rochester, N.Y.*). [*Ann. N.Y. Acad. Sci.*, **52**, 113–20 (1949).]

The central nervous effects of vitamin E (I)-deficiency on rats (Ringsted, *C. A.*, **29**, 5492[3]) were confirmed. Rats on a (I)-deficient diet containing lard, through which air at 100° had been bubbled for 12 or 24 hours, exhibited a delay in the onset and an amelioration in the intensity of the neurologic symptoms, as compared with rats receiving fresh lard. The oxidized lard appeared to be toxic to (I)-deficient rats, as shown by a higher death rate.

MARSHALL E. DEUTSCH (Chem. Abstr.).

Influence of Nicotinic Acid and Riboflavin on the Threshold of Excitation of the Cerebral Cortex. Savini, R. (*Univ. Perugia, Italy*). [*Boll. soc. ital. biol. sper.*, **24**, 822–3 (1948).]

The threshold for the electric stimulation of the cerebral cortex of dogs was reduced to one-third by intravenous injections of 150 mgm. nicotinic acid. Subsequent or previous intravenous injections of riboflavin (I) had little influence. Injection of 5 mgm. (I) into the spinal fluid caused an epileptic attack.

F. FROMM (Chem. Abstr.).

Effect of Chronic Vitamin E Deficiency on the Nervous System in the Rat. Malamud, N., Nelson, Marjorie M., and Evans, Herbert M. (*Langley Porter Clinic, San Francisco*). [*Ann. N.Y. Acad. Sci.*, **52**, 136–8 (1949).]

Histological studies on female rats kept on a vitamin E-deficient diet for 400–500 days, and a male rat kept on the diet 250 days, showed neural lesions chiefly restricted to the fibers of the dorsal columns and resembling the lesion in tabes dorsalis of man. In all the females advanced changes were observed; the male showed minimal pathology. MARSHALL E. DEUTSCH (Chem. Abstr.).

Occurrence of Histamine in Nerves. Werle, Eugen, and Weicken, Gertrud. [*Biochem. Z.*, **319**, 457–62 (1949).]

Histamine is found (probably in the nerve fibrils) in human or animal nerve tissues. In peripheral nerves it is present in amounts of 2–50 γ/gm., while in the brain it is found in much smaller amounts (0·3 γ/gm.). Its function is unknown.

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On sectioning of a nerve the content increases about 100 per cent., and then gradually falls, in about 5 days, to below the original value.

S. MORGULIS (Chem. Abstr.).

Influence of Histamine on Nerve Block due to Antihistaminics. Barany, Ernst H., and Nordqvist, Percy. [*Nature*, **164**, 701 (1949).]

The sheath of a nerve was removed for a distance of about 7 mm., and a solution of 0·25 per cent. pyribenzamine (I) in frog's Ringer solution was applied. Conduction was tested with short bursts of stimuli at 50 seconds from a thyratron device. The nerve was blocked after 4 minutes, but the block could be removed in 3 minutes by washing with frog's Ringer solution to which had been added 0·25 per cent. (I) and 0·6 per cent. histamine-2HCl (II). To show prevention of block two nerve-muscle preparations from the same frog were used. The sheaths of the nerve were left intact. Nerve A was placed in 0·3 per cent. procaine-HCl (III) in frog's Ringer solution; nerve B was placed in 0·3 per cent. (III) containing 0·4 per cent. (II) in frog's Ringer solution. Nerve A was blocked after 18 minutes, whereas nerve B was still conducting after 100 minutes.

BERNARD WOLNAK (Chem. Abstr.).

The Role of Acetaldehyde in Manifestations Related to the Disturbances of the Metabolism of Ethyl Alcohol. Lecoq, Raoul. [*Compt. rend.*, **229**, 852–4 (1949).]

The injection of 20 ml. of an isotonic EtOH solution (25 per cent.) into a rabbit (2 kgm.), previously fed 0·5 gm. of tetraethylthiuram disulfide (T.T.D.), causes profound intoxication with muscular paralysis and depressed respiration. Death usually ensues in several minutes. The injection of EtOH in the absence of T.T.D. results only in intoxication of 10-minute duration. The simultaneous injection of EtOH with 15 mgm. of nicotinamide (I) and 25 mgm. adenine (II) after the ingestion of T.T.D. does not prevent intoxication, but affords the rabbit complete recovery in about 25 minutes. If (I) plus (II) mixture is injected 30 minutes before the injection of EtOH, the rabbit is protected from all toxic reactions. When 5 ml. of an isotonic solution of ACH (5 per cent.), with or without the mixture, is administered by intravenous injection, the rabbit recovers from the toxic response, which is different from the previously described intoxication, in about 35 minutes. The intermediary substances produced in the *in vitro* oxidation of EtOH are toxic in rabbits. Small amounts of (I) and (II) act as coenzymes in the rapid *in vitro* oxidation of these toxic substances, with the exception of AcH.

CARL ALPER (Chem. Abstr.).

Chemical Changes in the Brain in Some Pathological Processes. Promyslov, M. Sh. (*Inst. Obshchei i Eksptl. Patol., Akad. Med. Nauk S.S.S.R.*). [*Doklady Akad. Nauk. S.S.S.R.*, **69**, 235–6 (1949); *cf. C. A.*, **43**, 7122*b*.]

The lipide content of dry rabbit brain declines in diphtheria by some 10 per cent.; the lipoid N content increases about 1 per cent. The ratio of protein N to total N of the brain decreases; the higher the protein decomposition coefficient, the lower is the percentage of protein N.

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

Allergic Encephalitis Following Injection of Dialyzate of Brain Tissue. Hottle, Geo. A., Nedzel, Gleb A., Wright, John T., and Bell, J. Frederick (*Natl. Inst. of Health, Bethesda, Md.*). [*Proc. Soc. Exptl. Biol. Med.*, **72**, 289–91 (1949).]

The dialyzate (through cellophane tubing) of benzene-ether-extracted rabbit and bovine brain tissues is capable of causing signs and lesions of allergic encephalitis in guinea-pigs. The material recovered in the dialysate is free of protein, is biuret-negative in high concentration, and presumably contains only substances of low molecule weight.

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

Studies on Lipides in the Nervous System, with Special Reference to Quantitative Chemical Determination and Topical Distribution. Brante, Gunnar. [*Acta Physiol. Scand.*, **18**, *Suppl.* 63, 189 + *xxiv pp.* (1949).]

$CHCl_3$ extracts prepared from the residue of alcohol-ether extracts from tissue contain contaminants which seriously interfere with the determination of inositol,

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amino acids, and total lipides. There is evidence for the occurrence in the nervous system of lipides (not sphingomyelin) whose P is difficult to release with KOH, and of phosphatides containing more that 1 molecule glycerol per 1 atom P. Hydrolysis with saturated aqueous $Ba(OH)_2$ liberates all lipide choline. The effect of autolysis or of formalin preservation on the lipides of nervous tissue is discussed. The axon and nerve-cell cytoplasm contain chiefly lecithin and phosphatidyl ethanolamine (1·1 percent. of fresh tissue); also a few tenths of 1 per cent. gangliosides and possibly minute amounts of cholesterol. However, cholesterol and cerebrosides predominate in the myelin sheath, which also contains phosphatidyl serine, sphingophospholipides and a trace of lecithin, but generally no neutral fat or cholesteryl esters. The molecule ratios between the first 6 lipide groups are 8:4:2:2:2:1. These studies revealed further that no significant differences exist in the lipides of different regions of the brain cortex, and in general the lipides are the same in comparison, but higher in concentration than in the grey nerves. The nerves of the lobster differ from the unmyelinated vertrebrate nerves, in that the phospholipide is made up largely (80 per cent.) of a lecithin-like substance and practically no cerebrosides. The white matter of the cord is definitely richer in lipides than that of the brain. Interesting diagrams are given to illustrate the changes in over-all lipide content as well as in the comparison of the lipide material of the brain and cord of the rat at different stages of development from 7 to 70 days after birth. Neither acute lack of choline or thiamine nor relative lack of vitamin A or pantothenic acid during early development alter the lipide formation in the rat. The lipide complex of glioma and meningioma is similar in comparison, but much less than in ordinary grey matter. The most striking change in lipides during Wallerian degeneration is the big decrease in sphingomyelins and simultaneous increase in phospholipide resistant to KOH (choline-free). Lecithins are lost later in the degenerative process. Esterification of cholesterol sets in only after leucocytic infiltration, when a rapid removal of lipides also occurs. Diffuse sclerosis and encephalitis are accompanied by loss of lipides chiefly characteristic of the myelin sheath. The appendix describes all the analytical procedures, and includes 201 references.

S. MORGULIS (Chem. Abstr.).

Synthesis of and Decomposition of Polysaccharides in the Brain. Palladin, A. V. [*Fiziol. Zhur. S.S.S.R.*, **35**, 596–603 (1949).]

Phosphorylase is able to act on the polysaccharides formed in the brain tissue by the action of brain amylase. The system polysaccharides-glucose 1-phosphate-dextrin may be represented by an equilibrium triangle on the basis of *in vitro* enzymic studies using brain macerates of rabbits, rats, cats, and cows.

G. M. K. (Chem. Abstr.).

The Development of Muscle-Chemistry: A Lesson in Neurophysiology. Muralt, Alexander v. (*Hallerianum, Bern, Switz.*). [*Biochim. et Biophys. Acta*, **4**, 126–9 (1950) (*in English*).]

A review with 30 references. G. G. (Chem. Abstr.).

Lipides of Normal Brain. Johnson, A. C., McNabb, A. R., and Rossiter, R. J. [*Biochem. J.*, **43**, 573–7 (1948).]

By use of micro-methods, the concentrations of free and total cholesterol, cerebroside, total phospholipide, monoaminophosphatide and lecithin were determined (and from these the concentrations of ester cholesterol, sphingomyelin and cephalin were calculated), in whole brain of guinea-pigs, cats, and rabbits, and in white and grey matter from the brain of cat, dog, beaver and man. The concentrations (in mgm./100 gm. of fresh tissue) were in all cases greater in white than in grey matter. As a percentage of "essential lipides," the concentrations of cerebroside, total cholesterol, and sphingomyelin were greater in white matter, and lecithin and cephalin in grey matter. The results are compared with those of other workers on the same and other species. B. A. (Chem. Abstr.).

Phosphorylation of D-Glucosamine by Brain Extracts. Harpur, R. P., and Quastel, J. H. [*Nature*, **164**, 693–4 (1949).]

D-Glucosamine (I) is phosphorylated at the expense of adenosinetriphosphate (II) in the presence of extracts of acetone-dried brain; (I) also produced an inhibi-

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tion of the rate of acetylcholine (III) synthesis in these extracts. Beef brains were obtained within 30 minutes of the death of the animals, the grey matter removed and ground in ice-cold acetone. After filtering, the resulting powder was stored in a vacuum desiccator in the cold. Extracts of the resulting powder were made with water, centrifuged, and the opalescent centrifugate was used for phosphorylation studies with the Warburg manometer. Rates of gas output by glucose (IV), fructose (V), and (I) in the presence of 0·002 M (II) were determined. With low concentrations of (IV), where the (II) concentration is in no way limiting, the gas output in the first 15 minutes approaches the theoretical value for the conversion of (IV) to hexose diphosphate. The maximum velocity of phosphorylation takes place with a lower concentration of (IV) that that of (V), while the speed of phosphorylation of (I) is appreciably less than that of (V). Kinetic studies indicate that the affinity of (I) to the enzyme involved is of the same order as that of fructose. Experiments with mixtures of the hexoses and (I) at appropriate concentrations indicate that no addition of the rates of phosphorylation occurs, and the results are consistent with a competition of all 4 substrates for the enzyme involved. The inhibition by (I) of hexose phosphorylation by (II) might be explained by a competition, not for a common ezyme, but for the (II) itself. This explanation is made unlikely by the finding that N-acetyl-(I), which is not phosphorylated, exercises a large inhibitory action on the rates of phosphorylation of (I) and of (V).

BERNARD WOLNAK (Chem. Abstr.).

Oligophrenia Phenylpyruvica. I. Microbiological Determination of L- and D-Phenylalanine and of Phenyllactic Acid. Prescott, Blanche A., Borek, Ernest, Brecher, Arthur, and Waelsh, Heinrich (N.Y. State Psychiat. Inst., New York, N.Y.). [*J. Biol. Chem.*, **181**, 273–9 (1949).]

In a synthetic medium, free of phenylalanine (I), no visible growth is obtained with *L. arabinosus* during the first 40 –44 hours. Addition of L-(I) or L-, D, or DL-phenyllactic acid (II) up to 8 γ/ml. gave an equal growth response. Phenylpyruvic was also able to replace L-(I), while D-(I) gave no growth and DL-(I) gave only half of the normal growth. Combined L-(I) and D- and L-(II) were determined microbiologically after phenylpyruvic acid was removed by heating with 0·3 parts 6 N HCl in a closed tube at 105° for 15 hours. The L-(I) and the (II) were separated by extraction with Et_2O or $CHCl_3$ and then determined. Any D-(I) present together with L-(I) in the watery layer was easily determined by deamination with $NaNO_2$ and conversion to (II). Plasma of patients with oligophrenia phenylpyruvica contained no D-(I), but 34·5 mgm. per cent. of L-(I) compared to 0·95 mgm. per cent. found in normal persons. B. L. (Chem. Abstr.).

The Effects of Drugs on the Electrical Activity of the Brain. Toman, James E. P., and Davis, Jean P. (Univ. of Utah, Salt Lake City). [*J. Pharmacol. Exptl. Therap.*, **97**, *No.* 4, *Pt.* 11, *Pharmacol. Revs.*, 425–92 (1949).]

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

Inhibitory Effect of Muscle Adenylic Acid on Anaerobic Glycolysis of Brain. Greenberg, G. Robert (Western Reserve Univ., Cleveland, O.). [*J. Biol. Chem.*, **181**, 781–8 (1949).]

Anaerobic glycolysis by homogenates of mouse brain or of Me_2CO-powder of swine brain was inhibited by adenosine-5-phosphoric acid (I) and, still more, by inosine-5-phosphoric acid. Adenosine (II), (II)-3-phosphoric acid or (II) triphosphate failed to produce this inhibition. When the initial inhibition due to (I) was low, the inhibition tended to disappear with time, but a marked initial inhibition usually increased with time. The inhibition due to (I) was rapidly overcome by addition of $4·1 \times 10^{-3}$ M hexose diphosphate. Possible reasons for these effects are discussed. MARSHALL E. DEUTSCH (Chem. Abstr.).

Chemical Studies of Peripheral Nerve During Wallerian Degeneration. Johnson, A. C., McNabb, A. R., and Rossiter, R. J. (Univ., Western Ontario, London, Can.). [*Biochem. J.*, **45**, 500–8 (1949); *cf. C. A.*, **44**, 213*d*.]

The concentration of cholesterol esters, sphingomyelin, cephalin, essential lipide, myelin lipide, and total lipide was determined in degenerating cat sciatic nerves

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4-96 days after sectioning. The wet weight of the sectioned nerve increased temporarily (maximum in 4 days), but returned to normal after 64 days. The total lipide decreased steadily. The neutral fat decreased rapidly to a minimum (4–8 days), and returned to normal in 32 days. Myelin lipides (cerebroside, sphingomyelin, free cholesterol), unchanged at first, decrease rapidly between 8–32 days. The same is true for free cholesterol, but cholesterol esters, absent in control nerves, increased, reaching a maximum by the sixteenth day. Essentially the same changes were observed with regard to total lipides and sphingomyelin. Cephalin decreased more rapidly and lecithin less rapidly than the sphingomyelin.

S. MORGULIS (Chem. Abstr.).

Action of Potassium Ions on Brain Metabolism. *Dixon, K. C.* (*Univ. of Cambridge, Engl.*). [*J. Physiol.* (*London*), **110**, 86–97 (1949).]

Inhibition of anaerobic glycolysis (I), measured manometrically with slices of rabbit cerebral cortex in glucose-bicarbonate Ringer solution, began at concentrations of 20 milliequiv./1 of added K ions (in isotonic solution). Concentrations of 40 milliequivs./1 K^+ produced 75 per cent. inhibition of (I) in less than 10 minutes. Aerobic glycolysis was stimulated equally rapidly by addition of 30–50 milliequivs./1 K^+.

MORRIS ROCKSTEIN (Chem. Abstr.).

The Accumulation of Glycogen in the "Glycogen Body" of the Nerve Cord of the Developing Chick. *Doyle, W. L., and Watterson, R. L.* (*Univ. of Chicago*). [*J. Morphol.*, **85**, 391–403 (1949).]

The spinal cords of chick embryos were fixed in EtOH and then extracted with MeOH-$CHCl_3$ to remove cerebrosides (*cf.* Kerr, *C. A.*, **31**, 424[6]).

The glycogen was determined in these dry samples by the method of Good *et al.* (*C. A.*, **27**, 3496). Segments 26–29 of the chick nerve cord contained approximately 0·012 mgm. (3·2 per cent. average) of glycogen on the 10th day of incubation. This increased rapidly to 0·373 mgm. (15·7 per cent.) on the 14th day, and then at a slower rate to about 2·8 mgm. (34·4 per cent.) on hatching at 20·5 days. The value rose to 2·95 mgm. (34·5 per cent.) by 20·7 days, 3·75 mgm. (37·8 per cent) at 21·5 days, and 4·48 mgm. (42·5 per cent.) at 24·5 days. Most of the glycogen was in the glycogen body, which contained 56 per cent. of dry-lipide-free glycogen the 14th day of incubation and 76 per cent. at 21·5 days. The glycogen of the glycogen body represented approximately 5–10 per cent. of the total body glycogen from the 15th day of incubation to hatching. Unlike liver glycogen, the former was not depleted at hatching or after starvation for 24 hours after hatching. Segments of spinal cord not containing the glycogen body contained 0–2 per cent. of glycogen by dry weight.

E. K. WEISBURGER (Chem. Abstr.).

The Nature of the Golgi Apparatus. I. Parallelism Between Intercellular Myelin Figures and Golgi Apparatus in Somatic Cell. *Palade, George E., and Claude, Albert* (*Rockefeller Inst., New York, N.Y.*). [*J. Morphol.*, **85**, 35–70 (1949).]

Intracellular myelin figures were produced in a variety of fresh vertebrate somatic cells by adding ethanol in concentrations of 40–55 per cent. Isotonic solutions of sucrose appeared to delay formation of the myelin figures, while an increase in temperature or desiccation accelerated their formation. The myelin figures formed from lipide inclusions, and duplicated in morphology and topography the Golgi apparatus of corresponding cells.

II. Identification of the Golgi Apparatus with a Complex of Myelin Figures. [*Ibid.*, 71–111.]

Myelin figures were induced in cells by immersing thin discs of liver pulp in fixatives commonly used for the demonstration of the Golgi apparatus or in tissue homogenates between pH 5·8 and 5. Experiments with emulsions of phospholipide emulsions in saline solutions indicated that the droplets formed myelin figures and concentrated basic dyes. The Golgi apparatus is an artifact, namely a myelin figure or a complex of myelin figures developed in the cell during fixation and the preparation of specimens.

E. K. WEISBURGER (Chem. Abstr.).

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Loss of Potassium from Frog Nerves in Anoxia and other Conditions. *Fenn, Wallace O., and Gerschman, Rebeca (Univ. of Rochester, Rochester, N.Y.).* [*J. Gen. Physiol.*, **33**, 195–203 (1950).]

The sciatic nerves from frogs in Ringer's solution lose about 23 per cent. more K in solutions equilibrated with N as compared to solutions equilibrated with O, and apparently they tend to regain K when, after a period of anoxia, they are again oxygenated. Tying off the free ends of the nerve piece seems to increase the K loss. Likewise the K loss is increased by the addition of acetylcholine to the solution. Equilibration with 20 per cent. CO_2 in O increases the K loss in Ringer's solution, but decreases it if the nerves are in frog blood.

S. MORGULIS (Chem. Abstr.).

Muscle and Muscular Contraction. *Weber, Hans H. (Tubingen, Ger.).* [*Fiat Rev. German Sci.* (1939–46), *Physiology, Pt. III* (1948), 1–42.] *Neuromuscular Conduction of Impulse.* *Mercker, H. (Gottingen, Ger.).* [*Ibid.*, 45–50.] *Acetylcholine.* *Lullies, H. (Homburg, Ger.).* [*Ibid.*, 51–92.] *Peripheral Nerve and Impulse Conduction.* *Lullies, H. (Homburg, Ger.).* [*Ibid.*, 93–143.] *Electrophysiology.* *Schaefer, Hans (Bad-Nauheim, Ger.).* [*Ibid.*, 145–67.] *Conditioned Reflexes.* *Hoffmann, Paul (Freiburg i Br., Ger.).* [*Ibid.*, 169–83.] *Central Nervous System.* *Bethe, A., and Frank, E.* [*Ibid.*, 185–94.] *Electroencephalography.* *Kornmuller, A. E. (Gottingen, Ger.).* [*Ibid.*, 195–216.]

Reviews with many references. G. G. (Chem. Abstr.).

Breakdown of the Oxidized Forms of Coenzymes (I) and (II) by an Enzyme from the Central Nervous System. *McIlwain, H., and Rodnight, R. (Maudsley Hosp., London.)* [*Biochem. J.*, **45**, 337–42 (1949); *cf. C. A.*, **43**, 9105*d*.]

Preparations from the mammalian central nervous system rapidly inactivate coenzymes (I) and (II), but the latter is inactivated at a slower rate (70–85 per cent. of former). The degrading enzyme acts only on oxidized forms, acting upon a bond at an ionized quaternary N atom. The inactivation of either coenzyme is accompanied by liberation of nicotinamide. The enzyme acts on a nicotinamide nucleotide (not a nucleoside), but not on various nicotinamide derivatives. The enzyme does not affect dihydrocoenzymes (I) and (II), nor do they affect the enzyme action on the coenzymes (I) and (II). S. MORGULIS (Chem. Abstr.).

Electrical Phenomena in Nerve. *(I) Squid Giant Axon.* *Shanes, Abraham M.* [*J. Gen. Physiol.*, **33**, 57–73 (1949).]

The effects of veratrine, yohimbine, cocaine, procaine and D.D.T. have been studied. The suggestion is offered that the effects can be explained as being associated with changes in K concentration at the fiber surface, regulated by a labile permeability and metabolism.

(II) Crab Nerve. [*Ibid.*, 75–102.]

Similar studies on the effect of veratrine, iodoacetate, cocaine, procaine, D.D.T. and KCl on the resting and action potentials of the leg nerve. The results are discussed from the same viewpoint suggested above.

S. MORGULIS (Chem. Abstr.).

The Mechanism of Arterial Hypertension after Potassium Injections into the Nerve Centers. *Cicardo, V. H.* [*Arch. intern. pharmacodynamie*, **80**, 199–208 (1949).]

The hypertension which follows intracisternal injection of KCl into dogs is prevented by the destruction of the spinal cord and vagi of adrenalectomized and hypophysectomized dogs, or by ergotamine in hypophysectomized dogs. Thus the sympathetic centers, the adrenals and the hypophysis are causative factors. Repeated injections of KCl cause gradually less hypertensive effect. KCl is much more effective than electric stimulation.

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

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Recent Studies of Cerebral Blood Flow and Cerebral Metabolism in Man. Schmidt, Carl F., and Kety, Seymour S. [*Trans. Assoc. Am. Physicians*, **60**, 52–8 (1947).]

In schizophrenia the cerebral metabolism (measured by O_2 consumption) was normal, was not influenced by small doses of pentothal or amytal, and tended to decrease following convulsions produced by electric shock or metrazole. Cerebral metabolism was normal in severe hypertension, but tended to decrease in subjects with brain tumor, and in diabetic coma.

JOSEPH S. HEPBURN (Chem. Abstr.).

Problems of Diffusion of Small Amounts of Substance within the Human Body. Heinz, Erich. [*Biochem. Z.*, **319**, 482–92 (1949).]

A mathematical treatment of the subject. S. MORGULIS (Chem. Abstr.).

Effect of 2-Methylnaphthoquinone on the Action Potential of Nerve and Muscle. Torda, Clara, and Wolff, Harold G. [*Am. J. Physiol.*, **158**, 465–9 (1949).]

In the presence of low concentrations of 2-methylnaphthoquinone the latency and the threshold increased, and the amplitude of the action potential of nerve and muscle dectreased. The muscle function on direct stimulation was not significantly impaired. Since the naphthoquinone, in the concentrations used, inhibits only the choline acetylase, the dysfunction observed suggests that acetylcholine is necessary to maintain an optimal function of nerve. E. D. WALTER (Chem. Abstr.).

Effect of Carbon Dioxide on Brain Glucose, Lactate, Pyruvate, and Phosphates. Bain, James A., and Klein, J. Raymond. [*Am. J. Physiol.*, **158**, 478–84 (1949); *cf. C. A.*, **43**, 9202*g*.]

The brains of normal and convulsing cats subjected to conditions designed to alter the CO_2-bicarbonate-carbonic acid system were analyzed after freezing with liquid air. In normal animals, breathing 10 to 30 per cent. CO_2 mixtures resulted in a lowering of lactate and pyruvate levels and had little effect on glucose or phosphate concentrations. In convulsed animals these conditions markedly limited the expected rise in lactate, pyruvate and inorganic phosphate, and prevented the fall in high-energy phosphates. There was a rise in brain glucose, but little effect on brain to plasma glucose ratios. The results are discussed with relation to possible mechanisms and the effects of CO_2 on the central nervous systems.

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

Potassium and Neuromuscular Transmission. Hajdu, S. (Istvan), and McDowall, R. J. S. [*Nature*, **163**, 841 (1949).]

The denervated rat diaphragm muscle preparations are more sensitive to K ion than the normal preparation stimulated through its nerve. No response to an electric stimulus is observed in a functionally denervated (curare or lack of glucose) muscle if treated with K ion (0·08 per cent. in Kreb's solution), following addition of the *functional denervator*. The same observation has been made on muscle with its nerve cut. Acetylcholine response remains. However, if the K ion addition precedes the functional denervator addition, then muscle response is *nil* (inexcitable by either electric or acetylcholine stimulus).

CHARLES FARMILO (Chem. Abstr.).

The Influence of the Central Nervous System on the Rest Nitrogen and the Proteins of the Blood. Fluch, Max, and Grief, Stefan. [*Z. ges. exptl. Med.*, **113**, 549–52 (1944).]

The central nervous system was stimulated by suboccipital introduction of air into the ventricules of the brain. The rest N dropped fron 20 to 40 mgm. per cent. to a minimum of 10–25 mgm. per cent. after 7–24 hours and returned to normal in 48–60 hours. The total protein (normal 7–8 gm. per cent.) and the globulin fraction (normal 3–4 gm. per cent.) rose 0·5–2 gm. per cent. in 1·5 hours, then dropped 2–4 gm. per cent. to a minimum in 7–24 hours, and returned to normal in 48–60 hours. However, in some experiments the drop to a minimum did not occur. The albumin fraction exhibited minor variations.

J. H. WEISBURGER (Chem. Abstr.).

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Iron Content of the Brain Tissue. (I) Ultrafilterable and Non-Ultrafilterable Forms of Iron in Grey and White Matter of the Large Hemispheres of Dog Brain. Dushechkina, O. Ya. [*Fiziol. Zhur. S.S.S.R.*, **35**, 284–92 (1949).]

The ultrafilterable fraction of Fe is 16 per cent. in the grey matter and 25·5 per cent. in the white matter. Average total Fe per 100 gm. raw tissue is 0·993 mgm. in grey matter and 9·44 mgm. in white matter; for dry weight these are 5·776 and 3·188 respectively. Determinations were made colorimetrically with CNS^- method; sample fusion was done with $BaCO_3$ in quartz crucibles, as Pt gave a yellowish color which interfered with the determinations.

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

Sulfur Metabolism in the Central Nervous System. Mitolo, Michele, Ruccia, Domenico, Romano, Franco, Mattia, Luisa De, and Salvatore, Addolorata. [*Boll. soc. ital. biol. sper.*, **24**, 1113–15 (1948); *Atti e relaz. accad. Pugliese sci.* (1948); *cf. C. A.*, **44**, 6849.]

Fresh central nervous system of albino rats, guinea-pigs and rabbits respectively contained on the average in mgm. per 100 gm.: total S, 195, 281, 275; inorganic S and thioconjugated S, 8, 18, 8; neutral S, 46, 144, 50; lipide S, 50, 24, 23. Administration of strychnine reduced the total S. in all 3 species by 10–20 per cent., but in the rat this reduction was highest in the protein S fraction; in the other 2 species, in the non-protein fraction. Application of ethylurethan caused an increase of total S by 21–42 per cent. in all 3 species. This increase was more marked in the protein S fraction, also in the neutral S fraction of the rat and the guinea-pig, and in the lipide S fraction of the rabbit.

F. Fromm (Chem. Abstr.).

Cocarboxylase as Catalyst of Intermediate Reactions in Nerve-Muscle Metabolism. Woker, G. [*Intern. Z. Vitaminforsch.*, **21**, 10–17 (1949).]

Cocarboxylase (thiamine pyrophosphate) combines with lecithin to form a salt which, by cleavage, gives rise to thiamine, choline pyrophosphate anhydride, and stearo-oleo-glycerophosphate. The last-mentioned compound reacts with free fatty acid to produce a glyceride and HPO_3. Choline pyrophosphate anhydride becomes by intramolecule rearrangement, first choline pyrophosphate, then its inner ester, lastly by hydrolysis, choline pyrophosphoric acid ester. Thiamine combines with pyruvic acid to form an inner half-acetal of thiamine pyruvate; this compound reacts with H_2O to form CO_2 and the thiamine ester of decarboxylated pyruvic acid (acetaldehyde ester of thiamine). Removal of 2 H atoms, e.g. by oxidation, converts this into acetyl thiamine, which may react with the choline pyrophosphoric acid ester to form acetylcholine and regenerate cocarboxylase. Cholinesterase converts acetylcholine into AcOH and choline, which is partially demethylated and then oxidized to sarcosine. Isourea and sarcosine condense to form creatine, which reacts with adenosine triphosphate to yield phosphocreatine (phosphagen). Also choline and pyruvic acid may condense to form a half-acetal which, by loss of CO_2, becomes acetaldehyde choline half-acetal; this, by oxidation and formation of H_2O, yields acetylcholine.

Joseph S. Hepburn (Chem. Abstr.).

Pyrophosphatase Activity of Brain Tissue. Gordon, J. J. [*Nature*, **164**, 579–80 (1949).]

Fresh rat brain was converted to a dry powder by the method of Fleischhacker (*C. A.*, **33**, 7825[1]). Suspensions were incubated with pyrophosphate, and the liberation of orthophosphate was determined colorimetrically. Maximum pyrophosphatase activity was seen in the range pH 6·8–7·4, at a substrate concentration of 0·0005 M, and in the presence of 0·02 M $MgCl_2$. The enzyme was destroyed by heating for 0·5 hour in boiling water, and was strongly inhibited by $CaCl_2$, $CuSO_4$, alloxan, and Na iodoacetate. The brain system appears to be similar to that reported in erythrocytes (Naganna and Menon, *C. A.*, **42**, 7354*i*), and both probably contain active thiol groups. Fred H. Snyder (Chem. Abstr.).

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Influence of Ingestion of Quinine Salts on the Electrical Activity of the Cerebral Cortex in Man. Gallouin, L., and Lemaire, R. [*Compt. rend. soc. biol.*, **143**, 436–7 (1949).]

Ingestion of 1–1·5 gm. of quinine sulfate causes an increase in the duration of the individual α-waves of the electroencephalogram, without change in frequency.
L. E. GILSON (Chem. Abstr.).

Site of Action in the Central Nervous System of a Bacterial Pyrogen. Chambers, W. W., Koenig, H., Koenig, R., and Windle, W. F. [*Am. J. Physiol.*, **159**, 209–16 (1949).]

The response to injection of purified pyrogenic extract of a *Pseudomonas* species was studied in cats and dogs, both intact and with central nervous system lesions. The febrile response to the pyrogen was mediated through the central nervous system, and the spinal cord needed to be in functional communication with one or more centers in the brain. E. D. WALTER (Chem. Abstr.).

Role of the Sympathetic Nervous System in the Metabolism of Adrenaline During Muscle Irritation under Various Conditions. Utevskii, A. M., and Butom, M. L. [*Biokhimiya*, **14**, 452–9 (1949); *cf. C. A.*, **42**, 8918*b*.]

Sympathetic nerve impulses in the frog cause the disappearance in muscle tissue of the reversibly oxidized form of adrenaline (dehydroadrenaline), and its reduction to adrenaline; bound adrenaline is also liberated in the process. These changes are unaffected by curare, but the effects are cancelled by ergotamine. Motor nerve impulses are without influence on the adrenaline-dehydroadrenaline systems and on bound adrenaline. H. PRIESTLEY (Chem. Abstr.).

Metabolism of Dogs During Intoxication from Agenized White Wheat Flour. Monahan, E. P., and Lalanne, G. G. [*Am. J. Physiol.*, **159**, 298–302 (1949).]

The metabolism of 6 dogs was studied to determine what changes occur in conjunction with intoxication from the ingestion of agenized white wheat flour. There was a large increase in serum acetylcholine and a striking decrease in serum cholinesterase activity during intoxication. These changes were progressive, being greatest toward the end of the period of intoxication. No impairment of kidney or liver function was detected. No consistent or biologically significant changes occurred in blood chemistry and urinary excretion products during the course of intoxication. E. D. WALTER (Chem. Abstr.).

Distribution of Certain Enzymes in the Brain of the Pigeon. Sinden, Jo Ann, and Scharrer, Ernst. [*Proc. Soc. Exptl. Biol. Med.*, **72**, 60–2 (1949).]

Results of histochemical tests for alkaline and acid phosphatase, phosphamidase and cholinesterase on various parts of the pigeon brain are described. There are marked differences in the enzyme contents of various structures of the brain.
L. E. GILSON (Chem. Abstr.).

Bifrontal Lobotomy for the Relief of Organic Pain. LeFever, Harry E. [*Ohio St. med. J.*, **45**, 128–130 (1949).]

Bifrontal lobotomy has been found successful as a surgical procedure for the relief of certain mental disorders. A major psychological result of the operation is an indifference to situations for which the patient was previously highly concerned. Hallucinations may continue, but the patient is no longer bothered by them. It became evident that the extreme pain associated with certain non-curable diseases might be diminished by bifrontal lobotomy. The first operation (for pain relief) was done in 1945 by Von Wagenen. The operation (unpublished) completely relieved a painful phantom arm that had resisted other treatments. Five further cases of operation for relief of organic and psychic pain are described. G. W. KNOX (Psychol. Abstr.).

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2. Pharmacology and Treatment.

Certain Actions of Curare on the Central Nervous System. *McCawley, E. L.* [*J. Pharmacol. Exptl. Therap.*, **97**, 129–39 (1949).]

In experimental animals purified curare, d-tubocurarine chloride and intocostrin can, with rapid intravenous injection and the absence of anesthetics or narcotics, induce central nervous system stimulation as shown by clonic convulsions and a typical spike discharge in the electroencephalogram. This action is prevented by central depressant drugs. Large doses of curare cause an irreversible depression of the central nervous system, which is unaffected by anticurare agents but is reversed temporarily by metrazole. When synaptic transmission is measured in a ventral root after stimulation of the dorsal root, curare produces a block of internuncial neurone activity and finally the two-neurone arc discharges disappear. L. E. GILSON (Chem. Abstr.).

Curare. Its Pharmacology and its Use as an Adjunct to Convulsive Shock Therapy. *Kuitert, John H.* [*Arch. Phys. Med.*, **26**, 99–104 (1945).]

Discussion with 22 references. E. K. WEISBURGER (Chem. Abstr.).

Narcosis of Dogs with Polamidone. *Berge, E., and Muller, H.* (*Justus Liebig Hochschule, Giessen, Ger.*). [*Tierärztl. Umschau*, **4**, 372–7 (1949).]

Polamidone is 2-dimethylamino-4,4-diphenyl-5-heptanone-HCl. A dose of 2 to 3 mgm. per kgm. body weight, injected intravenously within ½ to 1 minute, gives safe and long-lasting narcosis which is free of side reactions.
R. SEIDEN (Chem. Abstr.).

The Pressor and Depressor Effects of Certain Sympathomimetic Amines. *Wislicki, Leo.* [*Brit. J. Pharmacol.*, **4**, 304–7 (1949).]

Amphetamine (I) and its d-isomer (II) are equally potent in their effects on blood pressure of anesthetized or spinal cats. Ephedrine (III) differs from (I), (II), and methyl-(I) in that on repeated doses (III) does not cause a depressor response. The various amines are interchangeable in blocking the pressor effect; thus, methyl-(I) may give a depressor response when given after fair doses of (I), (II), or methyl-(I), none of these effects being influenced by atropine. The pressor effect of adrenaline persists independently of changes in the action of the other amines.
RICHARD F. RILEY (Chem. Abstr.).

Antisympathetic Action of Sympathomimetic Amines. *Åström, A.* [*Acta Physiol. Scand.*, **18**, 295–307 (1949).]

A group of sympathomimetic amines was investigated from the point of view of their ability to antagonize the inhibition produced by adrenaline, l-noradrenaline, or by electric stimulation of the mesenteric nerves. The experiments were made on isolated strips of rabbit intestine. The 14 amines were separated into 3 classes (adrenaline, ephedrine, and tyramine). The antisympathetic property of ephedrine or l-N-ethylephedrine is rather common to sympathomimetic amines, with the exception of such dihydroxyphenyl substitutes as adrenaline, arterenol and aleudrine. Whatever antisympathetic action has been observed with adrenaline or aleudrine is thought to result from some oxidation product of these substances. Ephedrine, both d- or l-, and benzedrine have practically the same effect on the intestine and have a similar antisympathetic action. It is generally believed that sympathomimetic amines act directly upon the cell, but it is also suggested the action may be through an inhibition of the amine oxidase. These experiments seem to support the interpretation that all the amines studied act directly upon the effector cells. S. MORGULIS (Chem. Abstr.).

Influence of Nicotinic Acid and Riboflavin on Metrazole Shock. *Calabro, Q., and Savini, R.* (*Univ. Perugia, Italy*). [*Boll. soc. ital. biol. sper.*, **24**, 823–4 (1948); *cf. preceding abstract.*]

A convulsion was caused in normal dogs by 0·8 c.c./5 kgm. of 10 per cent. metrazole (I). After injection of 90–150 mgm. nicotinic acid (II) and 5 mgm.

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riboflavin (III) the convulsion was produced by 0·2–0·3 c.c. (I) Injection of (II) and (III) into the spinal fluid made the shock by (I) more ent and let it last longer. F. FROMM (Chem. Abstr.).

The Effect of Hypophysectomy on Resistance to Narcotics. Soo, Chung Chang. [*J. Korean Med. Assoc.*, **1**, *No.* 1, 53 (1948).]

The resistance to $MgSO_4$ and chloral hydrate was decreased 24 hours after hypophysectomy. I. S. YUN (Chem. Abstr.).

Antiepileptics. Hazard, Rene, and Cheymol, Jean (*Faculté Med., Paris*). [*J. Pharm. Pharmacol.*, **2**, 1–9 (1950).]

A review (in French) of the chemotherapeutic agents. The relation between molecule constitution and pharmacological action is discussed.
S. W. GOLDSTEIN (Chem. Abstr.).

Effect of 3-(*o-Tcloxy*)-1,2-*Propanediol* (*Tolserol, Myanesin*) *on the Electrograms of Human Cortex and Subcortex. Spiegel, E. A., and Wycis, H. T.* (*Temple Univ. Med. School, Philadelphia, Pa.*). [*Proc. Soc. Exptl. Biol. Med.*, **72**, 446–8 (1949).]

Tracings and description. L. E. GILSON (Chem. Abstr.).

Effect of Various Concentrations of Alcohol on Sorptive Power of Cells of Sympathetic and Animal Nervous Systems. Romanov, S. N. (*Inst. Exptl. Med. Acad. Med. Sci. U.S.S.R.*). [*Doklady Akad. Nauk S.S.S.R.*, **69**, 473–6 (1949).]

In vitro experiments with dissected specimens of rabbit nervous system in neutral red solutions showed that the absorption of the dye has a minimum at 4 per cent. EtOH concentration, rises to a plateau at 10–14 per cent., and rises sharply up to 22 per cent.EtOH concentration in sympathetic ganglia. The sensory ganglia give a similar curve, displaced by 6 per cent. to the higher EtOH concentrations. Immersion for 5 minutes in 5 per cent. EtOH lowers absorption on subsequent immersions in higher concentrations, indicating a protective mechanism of the tissues. G. M. KOSOLAPOFF (Chem. Abstr.).

Blood Cholinesterase and Narcosis, with Special Reference to Sodium Pentothal. Brillanti, Felice (*Univ. Bologna, Italy*). [*Boll. soc. ital. biol. sper.*, **24**, 915–17 (1948).]

Cholinesterase (I) in the femoral blood of dogs first decreased in pentothal narcosis reached a minimum 15 minutes after the beginning of treatment and returned to normal or higher 15 minutes later. The increase of (I) to values above normal continued after discontinuation of narcosis. The changes of (I) are parallel to those seen in the same dogs in narcosis with $CHCl_3$, Et_2O, or evipal.
F. FROMM (Chem. Abstr.).

Electroencephalograms in Narcosis by Barbiturates. Colombati, S., and Alema, G. (*Univ. Bologna, Italy*). [*Boll. soc. ital. biol. sper.*, **24**, 903–4 (1948); *cf. A. Riv. neurol., Dec.*, 1947.]

The electroencephalogram of 14 patients in slight narcosis by 0·4–0·6 gm. narcovene S (Na salt of isopropylbromoallyl-N-methylmalonylurea) was similar to that in narcosis by Na pentothal (*cf.* Brazier and Finesinger, *C. A.*, **39**, 1466[4]).
F. FROMM (Chem. Abstr.).

The Pharmacological Action of 2-Phenylisopropylamine on the Nervous System. I. The Action of Cortical Excitability and Subordination Chronaxia of the Bulbopontinic Motor Neurones. Scarinci, V. (*Univ. Bologna, Italy*). [*Boll. soc. ital. biol. sper.*, **24**, 887–90 (1948).]

II. Action on the Variation of Subordination of Encephalic Nerves, Produced by Strychnine. [*Ibid.*, 890–2.]

See *C. A.*, **44**, 740*d*. F. FROMM (Chem. Abstr.).

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Synaptic Blocking Agents. (I) Technique of Assay of Products Active in Parkinsonism. Longo, V. G., and Bovet, D. [*Farm. sci. e tec.* (*Pavia*), **4**, 515–25 (1949).]

Injections of 1 mgm./kgm. of nicotine tartrate into the ear vein produce dyspnoea, inability to remain upright, and body tremors which are accentuated in the extremities. The substance to be tested for ability to prevent these tremors is given intravenously 5 minutes preceding the nicotine. In another test nicotine is injected in increasing dosage up to temporary heart arrest (0·4 to 0·6 mgm./kgm.). and after one hour the test substance is injected, followed by the same dose of nicotine, which now must not produce any alterations in an electrocardiogram. Diparcol and parpanit show high activity lasting for about one hour. Trasentin, benzedrine, benadryl, and procaine, which have central nervous action beneficial in Parkinsonism, but not related to their spasmolytic, sympathomimetic, antihistaminic, or analgesic action, also show a moderate effect of shorter duration. Et_4NI has a fleeting effect at high dosage. Atropine and scopolamine have no effect, showing a difference in mode of action. Some N-substituted phenothiazine derivatives were tested; they were 3356 R.P. ($CH_2CHMeNEt_2$ derivative) (I), phenergan (II), and 3015 R.P. ($CH_2CH_2NMe_2$ derivative) (III). (I) was most active, providing some protection for 3 hours; (II) was active for one hour, and (III) had no activity. The results were in accord with clinical observations.

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

Efficacy of Peripheral-acting Drugs in the Treatment of Experimental Spasticity. Hajek, Norma P., and Hines, H. M. [*Arch. Phys. Med.*, **30**, 517–22 (1949).]

Rats were injected in one leg with sufficient tetanus toxin to produce shortening and rigidity in one limb, but not in the contralateral limb, which served as a control. Injection of curare or neostigmine produced some relaxation, but did not bring about sufficient elongation of the shortened muscle or prevent or lessen the atrophy and loss of strength. A 5 per cent. solution of NH_4Cl was given 3 times daily by gavage, without any effect on the spasticity, the atrophy and the loss of strength.

E. K. WEISBURGER (Chem. Abstr.).

Therapeutic Concentrations of Penicillin in the Cerebrospinal Fluid Following Parenteral Penicillin and Oral Caronamide. Boger, Wm. P., Baker, Richard M., and Wilson, Wm. W. [*Trans. Am. Neurol. Assoc.*, **73**, 105–7 (1948).]

Penicillin appeared in the cerebrospinal fluid of 18 of 23 patients with paresis after 5 days of treatment with 100,000 units penicillin every 3 hours intramuscularly, and of 20 of 25 patients receiving for 5 days the same injections + 3 gm. caronamide orally every 3 hours. Concentrations attained in the 2 groups were 0·019–0·052 and 0·052–2·5 units/c.c. respectively. Plasma concentrations of penicillin were also higher in the second group.

MARION HORN PESKIN (Chem. Abstr.).

Chemical Pharmacological Antagonism Between Picrotoxin and Barbiturates. Garcia, Wenceslao Tejeda. [*Rev. facultad farm. y bioquim., Univ. nacl. mayor San Marcos* (*Lima, Peru*), **10**, 282–92 (1948).]

The minimum lethal dose in rabbits is for phenobarbital 150 mgm. per kgm., pentobarbital 130 mgm., pentothal 80 mgm., for picrotoxin (I) 1·2 mgm. (I) counteracts the depressant effect of the barbiturates on respiration. The antidotic balance for one part (I) is 26·6 to 32 parts barbiturates. The dose of (I) given to save the life in barbiturate intoxication would be fatal in a normal animal. The antidotal effect appears between 2 and 24 hours.

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

Post-Stilbamidine Neuropathy, with Reference to Retention of the Drug in the Body. Sati, Mohammed Hamad. [*Ann. Trop. Med. Parasitol.*, **43**, 4–12 (1949).]

A number of kala-azar patients who had been treated with fresh solutions of stilbamidine (I) and had recovered were examined for neuropathy symptoms and urinary excretion of (I). Forty-one out of 45 such cases showed symptoms, chiefly related to neuropathy of the trigeminal, cervical, upper dorsal, 7th and 9th cranial nerves. Symptoms appeared in 1 to 13 months, usually 6 months, and

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disappeared in 2 years. Urinary analysis for fluorescent material (*cf.* Henry and Grindley, *C. A.*, **40**, 6185) showed the excretion of 13–146γ/100 c.c. of (I) in 31 cases showing neuropathy. This excretion was present as late as 3 years after cessation of therapy. The effects of light on the stored (I) and their relation to the neuropathy are discussed. CARTER D. JOHNSTON (Chem. Abstr.).

Effect of Acridine Compounds on the Respiration of the Brain of the Six-day Chick Embryo. O'Connor, R. J. [*Nature*, **163**, 405 (1949); *cf. C. A.*, **43**, 7135*g*; *Albert and Marshall, C. A.*, **42**, 7366*e*.]

Exposure of the isolated brain tissue to the acridine compound resulted, within 2 hours, in pycnosis (swelling and fusion of chromosome in dividing cells). The results were obtained by a micromanometric method and are interpolations from curves relating inhibition of O_2 consumption to concentration. The following acridines were studied: 9-amino-acridine-HCl (*C. A.* numbering), 9-amino-4-phenyl-10-methylacridinium bromide, 9-amino-10-methylacridinium bromide, 9-amino-3-trifluoromethyl-acridine-HCl.

CHARLES FARMILO (Chem. Abstr.).

Effect of Amphetamine on the Synaptic Transmission of Sympathetic Ganglia and Spinal Cord. Luco, J. V., Martorell, R., and Reid, A. [*J. Pharmacol. Exptl. Therap.*, **97**, 171–6 (1949); *cf. C. A.*, **42**, 7435*b*.]

In cats anesthetized with nembutal amphetamine (I) in small doses had a potentiating effect on the response of the sympathetic (stellate) ganglion, but in large doses it was depressant. Tachyphylaxis did not occur. The effect of (I) on the spinal reflex was studied in cats anesthetized with dial, and in decerebrate cats. With submaximal and maximal stimuli small doses of (I) potentiated the monosynaptic response and large doses depressed the response. The action of (I) is partially antagonized by barbiturates. L. E. GILSON (Chem. Abstr.).

Epilepsy Treatment with Citrullamon. Rauch, Hans Joachim, and Elsken, Bernhard. [*Arztl. Wochschr.*, **3**, 631–4 (1948).]

Citrullamon V, $C(O)CPh_2)NHC(O)N(CH_2)_3$– $CH(NH_2),CO_2H$, is prepared through the condensation of benzil with -amino-ureidovaleric acid. It does not have the hypnotic effects of luminal and is less toxic than sodium diphenylhydantoin.

W. T. SMITH, Jr. (Chem. Abstr.).

Modified Ultraviolet Spectrophotometric Method for Determination of Barbiturates. Gould, T. C., and Hine, C. H. [*J. Lab. Clin. Med.*, **34**, 1462–70 (1949).]

The barbiturates are directly extracted with Et_2O from as little as 1 ml. of serum in a semimicro continuous extraction apparatus. The solvent is evaporated and the residue is brought into solution as the Na salt by means of a borate buffer, pH 9·5. The optical d. of the solution is determined at 225, 240, and 265 mμ on a Beckman DU spectrophotometer, and the amount of drug is calculated by means of a standard curve prepared by a method which eliminates blank serum interference. This procedure gives recoveries ranging from 92–101 per cent. The formula for calculation by " base-line method " is described and its advantages discussed. Salicylates interfere, but sulfonamide compounds do not.

BERNARD KLEIN (Chem. Abstr.).

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