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Insulin Coma Therapy in Schizophrenia

1. Insulin coma therapy at the Pennsylvania Hospital produced an immediate improvement or remission in 67·7 per cent. of 780 patients treated between 1936 and 1951.

2. At least 334 patients, or 63·3 per cent. of all patients who originally improved, had a relapse; 44 per cent. of all these relapses occurred within 30 days, and 78 per cent. within 1 year of treatment. A second insulin course brought about an improvement or remission in 52 per cent. of 122 patients who had relapsed.

3. Factors associated with the most favorable prognosis include: age over 16, psychosis of less than 6 months' duration, with a clinical picture of paranoid, catatonic, or undifferentiated schizophrenia; and if during treatment the patient receives at least 30 to 60 coma hours and gains more than 30 pounds in weight.

4. The authors conclude that insulin coma therapy is effective in restoring the schizophrenic patient to his prepsychotic adjustment. This restoration to health is not accompanied by a permanent correction of the factors that predispose the patient to regress to schizophrenia.

(Authors' Abstr.)

The EEG Changes in Unilateral and Bilateral Frontal Lobotomy

1. In cases of unilateral and bilateral frontal lobotomy, temporal slow wave activity was found to be a prominent feature, though more transient than the dominant frontal slowing. This non-frontal slowing may be interpreted as the result of cerebral edema and hippocampal herniation from operative manipulation.

2. There is an apparent correlation between the degree of slow activity in the postoperative EEG and clinical improvement, in that slight or severe degrees of slowing were found to be more conspicuous in those cases that exhibited little clinical improvement. In contrast, moderate slowing was associated with moderate to marked clinical improvement.

3. The frontal slow wave activity, though decreasing in prominence, persists in the majority of cases for at least 3 years and possibly longer.

(Authors' Abstr.)

* A number of abstracts in this section are reproduced from *Chemical Abstracts*. To the Editors of this Journal we extend our grateful thanks.

The Effect of Adrenochrome and Niacin on the Electroencephalogram of Epileptics

1. Adrenochrome in dosages of 10 mgm. does not change the EEG of normal volunteers, but in 10, 25 and 50 mgm. doses increases the bilateral paroxysmal abnormalities in the EEG of epileptics, but has very little effect on the cortical focus itself.

2. Nicotinic acid given orally or intravenously in normal volunteers showed a slight shift in EEG frequency to the fast side; in epileptics the drug considerably decreases the bilateral diffuse paroxysmal abnormalities (except in true idiopathic epilepsy), but has very little influence on the focus itself.

3. The mode of action of the above-named drugs is discussed.

4. A tentative explanation is offered as to the genesis of the paroxysmal EEG disturbance in schizophrenia.

(Authors' Abstr.)

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"Protein Profile" in Multiple Sclerosis

Electrophoretic serum protein fractions of 43 patients with typical multiple sclerosis were studied. Simultaneous determinations of the cerebrospinal fluid total proteins, gamma globulins, and gamma globulin-total protein (G.G./T.P.) ratios were performed in 41 of these cases. The combined results of these protein changes are termed the "protein profile" of multiple sclerosis.

Of these 43 patients, 77 per cent. showed statistically a significant decrease in their electrophoretic serum albumin and A/G ratio values, concomitant with a significantly elevated alpha-2 and/or beta globulin fraction and a normal (or slightly elevated) gamma globulin value. Significantly elevated cerebrospinal fluid gamma globulin levels and/or (G.G./T.P.) ratios were found in 93 per cent. of the 41 patients studied. Of these 41 cases, 73 per cent. gave significant changes in both biological fluids or exhibited a positive "protein profile". Statistical analysis of both serum and cerebrospinal fluid data showed no overlap of the ranges of the normal and multiple sclerosis populations except for total protein, alpha-1, and gamma globulins.

For the purpose of following the clinical course of the disease over extended periods of time by means of serum electrophoretic patterns, a new graphic method, termed the "serogram", was devised. The average mean normal values (140 subjects) for each protein fraction is represented by a straight line. Deviations from this straight line are expressed as units of standard deviation (S.D.) for each fraction in grams per 100 ml. The reproducibility of the electrophoretic serum protein data for normal subjects if readily demonstrated by means of the "serogram". It therefore permits the rapid evaluation of serum protein changes during the clinical course of a disease either in individual cases or for the group as a whole.

In accordance with the slowly progressing course of multiple sclerosis, the serograms of the group show only a slight shift toward abnormal values on repeat studies after a time interval of one and a half to two years. However, marked accentuation of the "serogram" data was found in three patients whose clinical course deteriorated rapidly.

The patient material studied consisted of two groups: (1) 32 institutionalized patients, with an average disease duration of 22 years, and (2) 11 V.A. cases, with an average disease duration of 8 years. The characteristic serum protein pattern was found in 91 per cent. of the cases in Group 1, while only four patients of Group 2 showed this change. On the other hand, 90 per cent. of the patients in Group 1 disclosed the typical cerebrospinal fluid protein changes, as compared with 100 per cent. in the V.A. group. These findings indicate that the protein changes in the spinal fluid occur prior to those in the serum.

Studies are now in progress on the application of the "protein profile" to neurological disorders other than multiple sclerosis. It is thus hoped to obtain laboratory data useful in differentiating such diseases from multiple sclerosis, as well as in elucidating some of the etiological mechanisms of these neurological conditions.

(Authors' Abstr.)

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Changes in the EEG and in the Tendon Jerks Induced by Stimulation of the Fornix in Man

The human fornix was stimulated under light ether anesthesia and in the vicinity of the interventricular foramen; as a result, the electrical activity of the cortex showed an increased voltage and a reduced frequency in the homolateral frontal areas. Augmentation of the stimulus intensity or of its total duration caused a more marked slowing and, at the same time, a similar though less marked response could be visualized on the convexity of the whole ipsilateral hemisphere or even over the contralateral side. In a single case studied under local anesthesia, a comparable electroencephalographic effect was observed and, simultaneously, the patient looked and felt somnolent. Bilateral cingulectomy does not abolish these results but, after prefrontal lobotomy, no slowing appears in the isolated frontal regions.

Similar stimulations caused an increase of the homo- and contralateral knee and ankle jerks.

The significance of these results is briefly discussed.

(Authors' Abstr.)

Clinical Correlates of the Spike-wave Complex

Out of 2,000 consecutive EEGs of neurologic patients, 121 (or 114 patients) had spike-wave complexes. Clinically, the spike-wave complex is practically diagnostic of epileptic phenomena. Spike-wave complexes are divided into the "classical" type, which correlates best but not exclusively with petit mal epilepsy; other generalized spike-wave dysrhythmias of which the multiple spike-wave corresponds most closely to grand mal epilepsy; and focal spike-wave, in which group focal seizures are more frequently found. Known etiologic factors and positive neurologic signs are rare in the "classical" spike-wave group and common in the focal spike-waves. Activation techniques are important in eliciting spike-wave complexes.

(Author's Abstr.)

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Cerebral Metabolism of Glutamic Acid in Multiple Sclerosis

The cerebral metabolism of 19 normal subjects and 32 patients with multiple sclerosis has been studied by the Kety-Schmidt technique with special reference to the cerebral metabolism of glutamic acid and its amide glutamine.

Measurements of cerebral metabolic rates for oxygen, CO_2, glucose, pyruvic acid, and lactic acid have also been made. Amidation of glutamic acid to its amide glutamine was found in 15 of 19 normal subjects. Failure of amidation occurred in 27 out of 32 with multiple sclerosis.

Intravenous administration of sodium succinate reversed the defect in the direction of amidation or utilization in half of the patients with multiple sclerosis. It is suggested that the failure of glutamic amidation in patients with multiple sclerosis may reflect a failure of one mechanism for elimination of ammonia from the brain.

(Authors' Abstr.)

Nature and Extent of the Biochemical Lesion in Human Epileptogenic Cerebral Cortex

The cases are presented as an apparent confirmation clinically of results obtained *in vitro* with glutamine and asparagine on epileptogenic brain tissue. The doses are admittedly large, but are diluted after administration. They must penetrate both the blood-brain barrier and the nerve-cell membrane barrier in sufficient concentration to be effective. The two compounds have no apparent effect *in vitro* or *in vivo* on normal nervous tissue function so that they are not "drugs" in the usual sense of the word. They are naturally occurring compounds which are normally consumed in the diet and normally present in body fluids and tissues of man. They are the first compounds administered to seizure patients with promising results, which are based upon an indication derived from metabolic studies on human epileptogenic brain.

(Author's Abstr.)

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Psychosomatic Study of 46 Young Men with Coronary Artery Disease

Psychiatric interviews, a detailed social inventory, and a battery of psychological tests were carried out upon a group of 46 young men with coronary artery disease and upon 49 healthy control subjects. All these men had already been studied carefully and data concerning medical history, anthropological measurements, and blood chemistry were available. After consolidating the information gathered by various means, the two groups were compared in terms of personality factors and also in other ways, including family incidence of cardiovascular disease, history of stress and strain, somatotype, and blood lipid levels.

The coronary patients had tended to work harder, under more stress and strain, although this was not necessarily physically strenuous work. Only a few more of the coronary patients than controls showed a consistent tendency toward compulsive striving, ascetic self-discipline, and great need to "get to the top" in their chosen work. When the two groups were compared in terms of specific personality traits, the differences were very slight. The coronary group showed less tendency to introspection than did the controls and more difficulty in handling their aggressive tendencies. The similarities between the groups were more striking, however, than were the differences, and their findings, in the main, did not confirm previous observations.

The authors found no convincing evidence that the personality differences exhibited by the coronary patients, as compared to the control subjects, could be implicated as significant factors in the genesis of coronary artery atherosclerosis. The effect of personality factors and emotional conflicts upon individuals with already diseased coronary arteries is important, but was not the primary topic of their investigation and was not discussed in detail.

The data suggested to them that the major factors in the genesis of atherosclerosis included maleness, body build, and some intrinsic metabolic fault, probably inherited.

(Authors' Abstr.)

Glutathione Metabolism in Men under Psychological Stress

Blood reduced glutathione concentration is significantly diminished 5–10 hours after such psychological stresses as jumping from a 34-foot tower while in harness, parachute jumping, and participation in night-infiltration exercises, but not after extremely severe, purely physical activity. The exact nature of the psychological stress capable of evoking this metabolic response is unknown. It is postulated that severe psychological stress operating over long periods may produce irreversible depression of the blood glutathione level and its associated metabolic dysfunctions.

(Authors' Abstr.)

Effects of Cortisone on Psychiatric Patients

Studies on 16 subjects were made to determine whether behavioral changes occur as a result of cortisone therapy. All subjects were treated exactly alike, except that half the group were given tablets containing cortisone and half were given placebo. A battery of psychiatric and psychological tests was administered: two forms of interview; part of the Wechsler-Bellevue Adult Intelligence Scale; the Rorschach test; part of the Thematic Apperception test; the Level of Aspiration Board; and an incomplete sentence test. Tests were administered to subjects before medication, after 30 days of medication, and after a follow-up period of no medication. Selected tests were also administered between 72 and 120 hours after the onset of medication. No one in the hospital other than the physician assigning medication knew which subjects actually received cortisone. Dosage was decreased from 300 mg. on the first day and to 75 mg. on the fifth day, and remained constant thereafter until the thirtieth day.

Differences between the group receiving cortisone and the group receiving only a placebo in test behavior were minimal. Clinical judgments of five observers tended to discriminate between the groups more accurately than did the tests. Certain methodological difficulties are pointed out and suggestions made for future investigations.

Although the results are limited by the small number of subjects and the wide range of individual differences in the group, they tentatively conclude that behavioral changes following the administration of cortisone do not occur in easily detectable form nor in a manner which is uniform from individual to individual.

(Authors' Abstr.)

1. Biochemistry, Physiology, Pathology, etc.

Polysaccharide Metabolism in Brain Tissue with Various Kinds of Stimuli of the Central Nervous System. Khaĭkina, B. I., et al. [*Doklady Akad. Nauk. S.S.S.R.*, **96**, 347 (1954).]

Experiments with rabbits showed that total glycogen in the brain increases after stimulation with pervitin or cardiazol; the bound fraction of glycogen rises similarly. Pervitin increases the activity (synthetic) of phosphorylase which synthesizes polysaccharides, but the hydrolytic activity is raised but slightly. Prolonged administration of pervitin, however, lowers the brain glycogen.

G. M. Kosolapoff (Chem. Abstr.)

Manifestation of Pyruvic Acid Accumulation in the Nervous System. Dobrovolskaĭa-Zavadskaĭa, N. [*Ann. Méd.* (*Paris*), **54**, 525 (1953).]

Pyruvic acid renders the vascular wall more permeable, which causes transudation into the perivascular spaces with compression of the vessels. The accumulation of pyruvic acid is frequently the consequence of a vitamin B_1 deficiency. Pyruvic acid plays a role in polyneuritis, parkinsonism, multiple sclerosis, cerebral arteriosclerosis, and various other nervous disturbances.

A. E. Meyer (Chem. Abstr.)

A Second Case in the Same Family of Congenital Familial Cerebral Lipoidosis Resembling Amaurotic Family Idiocy. Brown, N. J., et al. [*Arch. Disease Childhood*, **29**, 48 (1954).]

The formalin-preserved brain of this 7-week-old infant contained a cholesterol concentration nearly 4 times that of a similarly treated brain from a control.

Kathryn Knowlton (Chem. Abstr.)

Substance P in the Human Brain. Zetler, Gerhard and Schlosser, Lucie. [*Naturwissenschaften*, **41**, 46 (1954).]

Previous work on cow brain was continued. The substance P (1) content of 22 different parts of the human brain is given; individuals were from 22 to 82 years old; analysis was made 14–42 hours after death. In units per g. moist weight the (1) content varies from 1·6 in the corpus callosum to 247·6 in the ala cinerea and 698·8 in the substantia nigra. Compared with the choline acetylase content of the same areas in dog brain it seems that, particularly in the mesencephalon area, the two show opposite tendencies; high (1) content is likely to have low acetylase value.

B. J. C. van der Hoeven (Chem. Abstr.)

Potassium Content of Cerebrospinal Fluid. Siegrist, H., and Meyer, H. H. [*Klin. Wochschr.*, **32**, 549 (1954).]

In 138 specimens the K concentration ranged from 6·22 to 23·05 mg. per cent., with a mean of 12·84 mg. per cent. No relation could be found between K content and neurologic or psychiatric disorders. Meteorological influences on the K concentration were discussed.

ERICH HEFTMANN (Chem. Abstr.)

Effects of Vigorous Physical Exercise on Cerebral Circulation and Metabolism. Scheinberg P., et al. [*Am. J. Med.*, **16**, 549 (1954).]

Exercise produced a decrease in cerebral vascular resistance (I) blood CO_2 (II), and pH, an increase in cerebral O consumption (III), and no significant alteration in arterial glucose. No correlation could be made between (II) and pH, and the alterations in cerebral circulatory or metabolic functions. A close correlation was found for (I) and (III).

JOSEPH HARRIS (Chem. Abstr.)

The Permeability of Brain Slices to Citrate. Coxon, R. V. [*Congr. intern. biochim., Résumés communs., 2e Congr., Paris*, 1952, 32–3.]

Experiments on the oxidation of pyruvate in various preparations of pigeon brain were done. In the case of slices of brain, most of the citrate formed remained within the slices and very little diffused into the surrounding medium. When citrate was added to the medium, only a little diffused into the slices. The significance of these findings is considered.

W. C. TOBIE (Chem. Abstr.)

Brain Lecithin. Klenk, E., et al. [*Hoppe-Seylers Z. physiol. Chem.*, **292**, 241 (1953).]

Lecithin (I) obtained from human brains showed only traces of choline-containing acetal phosphatides when purified by chromatography. Oleyl-stearyl-lecithin, $C_{44}H_{86}O_8N$P.H_2O, $(x)\ ^{20}_{D}+5·36°$ purified by the $CdCl_2$ addition compound, refluxed 1 hour with 4 per cent. HCl–MeOH, the Me esters extracted with petroleum ether, fractionally distilled *in vacuo*, then recrystallized from Me_2CO gave 30 per cent. C_{16}, 10 per cent. C_{18}, and 1·5 per cent. C_{20} saturated, and 3 per cent. C_{16}, 46 per cent. C_{18}, 8·5 per cent. C_{20}, and 0·6–4·3 per cent. C_{22} unsaturated esters calculated as the fatty acids.

DAVID STEFANYE (Chem. Abstr.)

Antagonistic Action of Cholinolytic and Anticholinesterase Compounds on the Activity of the Higher Nervous System in Man and Animals. Mikhel'son, M. Ya., et al. [*Byull. Eksptl. Biol. i Med.*, **37**, *No. 2*, 7–12 (1954).]

In dogs with preestablished conditioned reflexes, intramuscular injection of 1–5 mg. per kg. of pentaphen (Parpanit) abolished the conditioned reflexes. Simultaneous injection of 0·03 mg. per kg. of prophysostigmine (proserine) abolished the effects of pentaphen and the conditioned reflexes were normal. In white rats, atropine or scopolamine (1 to 5 mg. per kg.) also seriously interfered with preestablished conditioned reflexes, and prophysostigmine prevented the interference by either atropine or scopolamine. Intramuscular injection of 3 to 5 mg. per kg. of pentaphen in man induced serious psychic disturbances which were prevented by the simultaneous administration of prophysostigmine (0·02 mg. per kg.). The fact that atropine-like compounds can compete with acetylcholine in choline-accepting systems, inducing alterations in psychic activity, indicates importance of these systems in the functions of the brain. Physostigmine and prophysostigmine prevent the destruction of acetylcholine and thereby increase its effects. The importance of cholinergetic systems in the function of the brain is thus indicated.

J. A. S. (Chem. Abstr.)

Synthesis of Adenosinetriphosphate in Slices of Brain Cortex. Acs, G., et al. [*Kisérletes Orvostudomány*, **5**, 466 (1953); *Ukrain. Biokhim. Zhur.*, **25**, 17 (1953).]

The cortex of *in vivo* frozen rat brains contains 1·0–1·5 mg. adenosinetriphosphate (I) per g. fresh tissue. Slices of brain cortex prepared from the decapitated animal contain only 0·2–0·3 mg./g. (duration of necessary operations 5–10 min.). If the slices are shaken in a mixture of 95 per cent. O_2 and 5 per cent. CO_2 in glucose (II)-containing saline, a resynthesis of (I) takes place. In rat brain cortex slices the content of (I) rises to 0·6–0·8 mg./g., in those of guinea pig to 1·0 mg./g. In presence of (II) this value is maintained for at least 40 minutes. The slices lose up to 50 per cent. of their nucleotides, adenine and ribose appearing in the supernate. The loss is more than can be accounted for by the injury of surface layers. The *in vitro* resynthesis of (I) requires O and (II). Of all substrates tested (II) is the only one which results in the resynthesis of 0·6–0·8 mg./g. (I) In presence of succinate, pyruvate, malate, glutamate, and aspartate, O consumption is raised as well as in presence of (II), yet the (I) level is only 50 per cent. of that obtained by (II). This is regarded as a biochemical proof of the fact that (II) is the only adequate substrate for brain cortex. It is concluded that instead of the rate of respiration the (I) content of slices should be used as a reliable indicator of their

physiological condition. When glutamate is given to the slices with glucose, the content of (I) is less than in absence of glutamate. The effect depends on the concentration of glutamate, 0·01 M causing a 50 per cent. depression of (I) content. From determination of the rate of glutamine formation it is concluded that the latter process uses up the high-energy phosphate to such an extent that a decrease of (I) results.

F. B. STRAUB (Chem. Abstr.)

The Role of the Reactive Groups of Proteins in the Functioning of the Nervous System. Kochtoyanz, Ch. [*Congr. intern. biochim., Résumés communs, 2e Congr., Paris*, 1952, 436–7.]

If the SH groups of the proteins of the pneumogastric nerve are blocked, the action of the heart and of the skeletal (voluntary) muscles is impeded. The action of acetylcholine on the heart is also inhibited. Liberation of the SH groups restores the former activity. In voluntary muscle fatigued by prolonged stimulation of the nerve, cysteine causes the abolition of fatigue and restores nerve function. Urea has the same action by freeing SH groups of the proteins. If an isolated cervical superior sympathetic ganglion is perfused with a $CdCl_2$ solution, stimulation of the preganglionic nerve no longer produces contraction of the nictitating membrane, probably since the Cd blocks the SH groups. Subsequent perfusion with a cysteine solution restores nerve activity by permitting the liberation of the acetylcholine. Blocking the SH groups of the innervation of the small intestine reduces the secretion of digestive enzymes.

W. C. TOBIE (Chem. Abstr.)

Note on the Free Amino-acid Content of Rat Brain. Ansell, G. B., and Richter, D. [*Biochem. J.*, **57**, 70 (1954).]

In addition to the usual amino-acid pool of tissues, the brain tissue contains a small group of compounds (glutamine, glutamic acid, and γ-aminobutyric acid) in relatively high concentration with a special function. The glutamic acid apparently occupies a central position in the metabolism of the brain and has the unique ability to undergo oxidation, amidation, transamination, and decarboxylation. The decrease by about 2·6 mg. per cent. in the free amino N of the rat brain in pentothal anesthesia is ascribed chiefly to a fall in the glutamic acid level. Nine amino compounds appear in paper chromatograms of deproteinized extracts of rat brain.

S. MORGULIS (Chem. Abstr.)

Substance P in the Central Nervous System of the Cow. Zetler, G., and Schlosser, Lucie. [*Naturwissenschaften*, **40**, 559 (1953).]

Results are reported on analysis of 11 regions of the cow brain for substance P (the method of Pernow is used). The ala cinerea has the highest concentration 486·4 Pernow units per g.

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

Central Nervous Function and Changes in Brain Metabolite Concentration. III. Glycogen in the Normal Behavior of Mice. Chance, M. R. A. [*J. Exptl. Biol.*, **30**, 468–74 (1953).]

Increases in glycogen content of the brain occur after a jump, a fall, or after aggressive behavior in a fight. No increase was found during sleep, after running or walking, or after defensive behavior in a fight.

LAWRENCE P. MILLER (Chem. Abstr.)

Ammonia and Glutamine in the Brain at Increased Oxygen Pressure. Gershenovich, Z. S., and Krichevskaya, A. A. [*Doklady Akad. Nauk. S.S.S.R.*, **95**, 837 (1954).]

White rats were subjected to pressure-chamber experiments under 4 and 6 atmospheres of pure O, the experiments being run until the end of convulsion periods, after which the animals were decapitated and the brains immediately frozen in liquid air and analyzed for NH_3, glutamic acid, and glutamine. Increased O pressure increases the NH_3 content of the brain (shown graphically), even in the preconvulsion stage, while the convulsive stage does not necessarily signify a still higher NH_3 content. Almost complete disappearance of glutamine from brain tissue is noted previous to the convulsions. The amount of free glutamic acid, on the other hand, rises, especially in the convulsive stage.

G. M. KOSOLAPOFF (Chem. Abstr.)

Function of Glutamic Acid in Nerve Tissue. Weil-Malherbe, H. [*Naturwissenschaften*, **40**, 545 (1953).]

A lecture dealing with the NH_3 content of nerves, enzymic reactions of glutamic acid in nerve tissue, glutamic acid as energy source, its effect in hypoglycemic coma, and psychological effects.

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

Oxygen Consumption of the Brain at Various Ages of the Albino Rat. Weill, J. D., and Mandel, P. [*Compt. rend. soc. biol.*, **147**, 1818 (1953).]

The O consumption is low for the first 14 days after birth, then rapidly increases nearly to the adult level in the next few days.

L. E. GILSON (Chem. Abstr.)

Cerebrospinal Fluid of Normal and Vitamin A-deficient Swine as Determined by Lumbar-puncture Method. Sorensen, D. K., et al. [*Am. J. Vet. Research*, **15**, 258–60 (1954).]

An increase in cerebrospinal-fluid pressure up to 220 mm. was observed in pigs which were deficient in vitamin A, against 80–145 (av. 109·5) mm. in normal pigs. The lumbar-puncture method can be used to detect the onset of vitamin A deficiency.

RUDOLPH SEIDEN (Chem. Abstr.)

The Histochemistry of Cholinesterase Activity in the Nervous System. Csillik, B., and Sásay, Gy. [*Acta Morphol. Acad. Sci. Hung.*, **4**, 103 (1954).]

In using a modified Nachlas-Seligman naphthyl acetate technique, stable cholinesterase (I) was localized in the cytoplasm of autonomic and sensory ganglion cells, in postganglionic fibers, in motor end plates, and in tactile corpuscles. Labile (I) was localized in the larger sensory ganglion cells, peripheral myelin sheaths, and in the intercellular substance of the gray matter. Glial, Schwann, and connective tissue cells gave negative reactions.

JOHN F. LHOTKA (Chem. Abstr.)

Brain Acetylcholinesterase Activities in Rabbits Exhibiting Three Behavioral Patterns Following the Intracarotid Injection of Diisopropyl Fluorophosphate. Aprison, M. H. et al. [*Am. J. Physiol.*, **177**, 175 (1954).]

The injection of the same dose (0·1 mg. kg.) of diisopropyl fluorophosphate (DFP) into the right common carotid artery of rabbits resulted in 3 different behavioral states. The animals usually circled to the left, some however, turned to the right, and a few retained their normal behavior. Forced circling whether to the right or left is associated with an asymmetric reduction of acetylcholinesterase activity on the 2 sides of the brain. In animals that circle to the left, the right frontal cortex and right caudate nucleus were primarily involved, while in animals which turn to the right the frontal cortex on both sides of the brain as well as the right caudate nucleus are implicated. The fall of acetylcholinesterase from 90 to 54 per cent. of normal in the left frontal cortex was associated with a change in behavior, namely a reversal in direction of circling from the left to right.

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

Cholinesterase Activity and Electroencephalograms During Circling Induced by the Intracarotid Injection of Diisopropyl Fluorophosphate (DFP). Harwood, C. Theresa. [*Am. J. Physiol.*, **177**, 171 (1954).]

The cholinesterase content prior to and subsequent to (DFP) injections was determined in the cerebral cortex, caudate nucleus, thalamus, midbrain, cerebellum, and medulla of the rabbit brain. Electric potentials were recorded from the motor and limbic cortical areas, caudate nuclei, and thalami. The caudate nucleus shows the greatest depletion of enzyme following the administration of (DFP). However, the potentials recorded from the sub-cortical structures do not exhibit changes that can explain the adversive syndrome observed in rabbits following the intracarotid administration of (DFP). The ratio of mecholyl to acetylcholine hydrolyzing power of the enzyme is consistent. Since mecholyl and acetyl-choline are diagnostic substrates for the identification of the true or type-E Enzyme, the data show that only the true enzyme is utilized in the hydrolysis of these substrates.

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

Cerebral Arteriography in Chronic Carbon Disulfide Poisoning. Cesaro, Angelo Nunziante and Luccarelli, Saverio. [*Folia Med.* (*Naples*), **37**, 264 (1954).]

Various changes in the arterial pattern and appearance are described. The circulation is slowed down. Carbon disulfide poisoning causes essentially a syndrome of cerebral arterio-sclerosis.

A. E. MEYER (Chem. Abstr.)

Phosphoproteins and the Processes of Metabolism in the Brain. Lisovskaya, N. P. [*Doklady Akad. Nauk. S.S.S.R.*, **95**, 1033 (1954).]

Experiments with rats with the aid of P_{32} showed the following: (1) Phosphoproteins (I) are a real fraction of proteins in the rat brain which are characterized by specific metabolism. (2) The rate of their transformation greatly exceeds that of other P compounds, including nucleic acids. Their metabolism depends on oxidative processes in the cells and all blocking agents (NaCN, narcotics) hinder the (I) metabolism. The metabolism is connected with oxidative phosphorylation; in the presence of dinitrophenol the (I) metabolism declines. Although glucose can serve as the substrate whose oxidation is tied in with (1) metabolism, glutamic acid cannot so serve.

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

Respiration and Hexokinase Activity on Rat-brain Homogenates in the Presence of Substances of Probable Keto Steroid Nature Extracted from Nervous Tissue. Marmori, M., et al. [*Enzymologia*, **16**, 117 (1953).]

Neuroketone, a lipide solution extract from nervous tissue, inhibits the respiration and hexokinase activity of rat-brain homogenates.

ERICH HIRSCHBERG (Chem. Abstr.)

Arterial Hypertension Provoked by Excitation of the Cerebral Cortex. Cicardo, V. H. [*Rev. soc. argentina biol.*, **29**, 242 (1953).]

Monopolar electric stimulation of the cerebral cortex by means of a thin electrode passed through a trepanation of the skull of curarized, nonanesthetized dogs produced marked arterial hypertension when applied to motor and premotor areas. This is attributed to stimulation of the sympathico-adrenal system with resulting liberation of adrenaline from the adrenal medulla and noradrenaline from the sympathetic nerve endings. Barbiturates prevent completely the rise in blood pressure, sympathicolytics (hydergin, priscol) partially or totally prevent it, and hydantoinates diminish but do not abolish it.

L. E. GILSON (Chem. Abstr.)

Neuraminic Acid in Cerebral Tissue of the White Rat. Chatagnon, C., and Chatagnon, P. [*Compt. rend. soc. biol.*, **147**, 1992 (1953).]

Neuraminic acid is present in rat cerebral tissue in approximately the same proportion as in human and ox brains. It is also present in the mucin of the salivary glands and in the mucoprotein of the rat urine.

L. E. GILSON (Chem. Abstr.)

Aldolases of the Brain. Palladin, A. V., and Polyakova, N. M. [*Ukrain. Biokhim. Zhur.*, **21**, 341 (1949).]

Enzymic preparations obtained from the brains of animals such as gophers, rats, rabbits, dogs, and horned animals have high aldolase activity. A higher activity was found for dog and horned-animal cerebellum and gray matter of the cerebral lobes than for white matter and medulla. Aldolase activity for the rabbit in earlier developmental stages was less than for mature animals. Brain homogenate (1:100) and a substrate of the Na salt of fructose-1,6-diphosphate (1) were used. The Brain homogenate (1·2 ml. containing 12 mg. tissue) was added to a reaction mixture composed of 3 ml. acetate buffer of pH 6·7, 0·5 ml. of the Na salt of (1), 0·5 ml. of 2 per cent. $NaHSO_3$, and 0·8 ml. of water, a total volume of 6 ml. The samples were incubated at 37° for 1 hour, and 2 ml. of 10 per cent. CCl_3COOH was then added, the control being a sample immediately fixed with CCl_3COOH. After preparation of the proteins, inorganic P and alkali-labile P were determined after 20 minutes hydrolysis at room temperature with 1N KOH. Inorganic P was determined according to the Fiske-SubbaRow method, and fructose according to Roe. Protein was determined by H_2SO_4 digestion of the homogenate followed by colorimetric Winkler determination.

CLAYTON F. HOLOWAY (Chem. Abstr.)

Effects of Corticotropin and Various Convulsion-inducing Agents on the P^{32} Content of Brain Phospholipides, Nucleoproteins, and Total Acid-soluble Phosphorus Compounds. Torda, Clara. [*Am. J. Physiol.*, **177**, 179 (1954).]

Adrenocorticotropic hormone (ACTH) given in a single intraperitoneal injection (3 mg./100 g. body wt.) increased the P^{32} content of the phospholipide fraction approximately by 31 per cent. in less than 15 minutes without significantly modifying the P^{32} contents of the other P-containing fractions. Convulsions induced by electroshock (1-minute duration) and pentylenetetrazole (5-minute duration) resulted in a decrease of the concentration of the radioactivity of brain phospholipides without a significant change in the P^{32} content of the other P-containing fractions. The results indicate that brain phospholipides are utilized during cerebral activity. During increased cerebral activity, including convulsions, a rapid breakdown of 1 of the constituents (probably a lecithin) of the brain phospholipides occurs. ACTH increases phospholipide synthesis.

E. D. WALTER (Chem. Abstr.)

Relation of Glutamic Acid Metabolism to Certain Members of the Krebs Cycle in Brain. Bessmann, Samuel P. [*Congr. intern. biochim., Résumés communs., 2e Congr., Paris*, 1952, 31.]

The transamination of γ-aminobutyric acid is discussed. The further metabolism of succinic semialdehyde is still undetermined. In addition concentrations (0·01 M) of glutamic acid normally found in the brain stimulate the oxidation of malate, fumarate, and succinate by brain homogenates. The reaction is a transamination between glutamate and oxalacetate.

W. C. TOBIE (Chem. Abstr.)

Labeling of Brain Phospholipides with Radioactive Phosphorus. Dawson, R. M. C. [*Biochem. J.*, **57**, 237 (1954).]

In guinea-pig brain dispersions actively incorporating P^{32} no appreciable incorporation was found in phosphatidylethanolamine, phosphatidylserine, or sphingomyelin, and the renewal of P in lecithin was also very slow. On the contrary, in actively respiring brain dispersions the renewal of diphosphoinositide P proceeds at an appreciable rate. But most of the incorporation of P^{32} into the lipides of a brain dispersion occurs in association with the synthesis of a material solution in fat solvents, probably acidic in nature and containing glycerophosphate as part of its molecule. This distribution of radioactivity between the labeled phospholipides of brain is remarkably similar to that found in liver slices.

S. MORGULIS (Chem. Abstr.)

Acetylcholine as a Transmitter Substance in Sympathetic Ganglia. Kewitz, H. [*Naunyn Schmiedebergs Arch. exptl. Pathol. Pharmakol.*, **222**, 323 (1954).]

From experiments with the perfused superior cervical ganglion of the cat, it is concluded that scopolamine, atropine, and trasentine H inhibit the nicotine-like action of acetylcholine in sympathetic ganglia as well as in the post-ganglionic end points of parasympathetic fibers. The transmitter action of the ganglia, however, is not impaired. This proves that acetylcholine is not necessary for the transmitter function. Procaine acts fundamentally like the parasympatholytic substances. Surface anesthetics such as pantocaine and procaineamide inhibit preferentially the transmitter action and slightly the acetylcholine excitation. Phenothiazine derivatives as phenergan, latibon, and megaphene have both inhibiting qualities. The inhibition of acetylcholine is stronger and lasts longer than the disturbance of transmission.

A. E. MEYER (Chem. Abstr.)

Differentiation Between Excitation by Acetylcholine and the Function of Transmission of Sympathetic Ganglia by Means of Perfusion Fluids of Varied Composition. Kewitz, Helmut and Reinert, Harald. [*Naunyn-Schmiedebergs Arch. exptl. Pathol. Pharmakol.*, **222**, 315 (1954).]

Lack of glucose or K in the perfusion fluid of isolated superior cervical ganglia of the cat causes a decrease in the sensitivity to acetylcholine (1). This does not interfere with the transmission of preganglionic electric impulses. With reference to excitation by (1) the perfusion fluid may contain meso-inositol in place of glucose. Phytin inhibits the (1) action completely and faster than lack of glucose. Ca ions produce strong spontaneous excitation; when this subsides the function of transmission is paralyzed and the (1) effect is reinforced and prolonged. Lack of Na causes abolition of both functions within a short time.

A. E. MEYER (Chem. Abstr.)

Potassium Content of cerebrospinal Fluid. Lowenthal, A. [*Compt. rend. soc. biol.*, **147**, 2059 (1953).]

Average values found were 12·2 mg. per cent. for normal men, 12·7 mg. per cent. for women, and somewhat lower values for young children.

L. E. GILSON (Chem. Abstr.)

2. Pharmacology and Treatment

The Effect of Carbon Dioxide on Cerebral Blood Flow, Spinal Fluid Pressure, and Brain Volume During Pentothal Sodium Anesthesia. Wilson, W. P., et al. [*Current Researches Anesthesia and Analgesia*, **32**, 268 (1953).]

In 10 patients light thiopental anesthesia produced no significant decrease in cerebral blood flow but lowered cerebral metabolism and arterial-venous O difference. Inhalation of 7 per cent. CO_2 for 4–8 minutes increased cerebrospinal fluid pressure, cerebral blood flow, and brain volume.

KARL F. URBACH (Chem. Abstr.)

Re-evaluation of Metrazol in Experimental Barbiturate Poisoning. Bailey, Herbert A., et al. [*Current Researches Anesthesia and Analgesia*, **32**, 274 (1953).]

In experimental barbiturate poisoning of 17 dogs with pentobarbital, metrazol therapy under varying conditions appeared to contribute little to the survival of the animals and was found capable of severe blood pressure depression without increasing neuro-muscular excitability.

KARL F. URBACH (Chem. Abstr.)

The Evaluation of Pentylenetetrazole as a Barbiturate Antagonist. Fazekas, Joseph F., and Koppanyi, Theodore. [*Current Researches Anesthesia and Analgesia*, **33**, 58 (1954).]

The antagonistic activity of pentylenetetrazole against pentobarbital is demonstrated in mice receiving $L.D._{98}$ and higher doses of the barbiturate. The interpretation of their experimental data by Bailey *et al.* is criticized.

KARL F. URBACH (Chem. Abstr.)

The Distribution of Mescaline (Labeled with Radioactive Carbon^{14}) in the Animal Organism and its Association with the Proteins of the Liver. Block, Wolfram and Block, Katharine [*Congr. intern. biochim., Résumés communs., 2e Congr., Paris*, 1952, 429.]

Mice more closely resemble men in the rate of excretion of mescaline (1) in the urine than do other animals. In white mice to which (1) (labeled with C^{14}) was administered, the brain was always the least radioactive of the organs. The (1) was rather rapidly incorporated in the proteins of the liver. After separation from the proteins, (1) could be identified by chromatography and electrophoresis on paper, followed by conversion to the picrate.

W. C. Tobie (Chem. Abstr.)

Depression by Barbiturates of the Metabolism of Electrically Stimulated Cerebral Tissues. McIlwain, H. [*Congr. intern. biochim., Résumés communs., 2e Congr., Paris*, 1952, 440.]

Modifications of cerebral activity by barbiturates *in vivo* are discussed. It has been found possible to stimulate the metabolism of isolated cerebral tissues by electric methods (not described). Phenobarbital, butethal, and dial inhibit respiration of electrically stimulated sections of rat or guinea-pig cerebral cortex at concentrations (not stated) which have little or no effect on respiration in the absence of electric stimulation. These compounds also decreased the lactic acid which accumulated (with glucose as substrate) in reaction mixtures with stimulated tissue. This change occurs during narcosis *in vivo* and is the opposite of that induced by the drugs in unstimulated tissue *in vitro*. Chloral (and to some extent high concentrations of Mg. ions) had a similar action. Inhibition of stimulated tissue was promptly reversed on removing the drug.

W. C. Tobie (Chem. Abstr.)

Treatment of Parkinsonism and Other Disturbances of the Extrapyramidal Motor System. Luyendijk, L. [*Vorderingen Geneesk.*, 1945–48, 354 (1949); *Excerpta Med., Sect. VIII*, 3, 366 (1950).]

A discussion and review, including the pharmacological action of different compounds.

W. C. Tobie (Chem. Abstr.)

Cholinesterase Activity of the Nervous Tissue in Acute and Chronic Intoxication from Bulbocapnine. Pappalardo, Piero. [*Acta Neurol. (Naples)*, 7, 208 (1952).]

In rats intramuscularly injected with 30 mg. bulbocapnine/kg. the cholinesterase activity in the cerebellum (especially by repeated daily treatments), in the nuclei of the brain basis, in the encephalic trunk, and in the bone marrow was lower, but in the brain cortex and bulb (especially by repeated treatments in the same day) higher than in controls.

C. Scandura (Chem. Abstr.)

The Use of Correctives in the Prevention of Barbiturate Intoxication. Koppanyi, Theodore and Fazekas, Joseph F. [*Am. J. Med. Sci.*, **226**, 597 (1953).]

Pentylenetetrazole is clinically and pharmaceutically the most suitable analeptic to use in barbiturate preparations for preventing poisoning upon overdosage. A critical ratio has been established for combining pentylenetetrazole with phenobarbital Na at 3:2, and pentylenetetrazole with pentobarbital or secobarbital Na at 3:1.

Marion Horn Peskin (Chem. Abstr.)

The Actions of Barbiturates on the Contractions of Voluntary Muscle. Kraatz, Charles P., and Gluckman, Melvyn I. [*J. Pharmacol., Exptl. Therap.*, **111**, 120 (1954).]

Four types of effects on voluntary muscle function are evoked by relatively low concentrations of the barbiturates, the incidence and intensity of the effect varying with the barbiturates and with the test object (dog, rabbit, and frog preparations). The 4 types are: (*a*) Potentiation of the maximum twitch by a probable direct action on the fiber. The thiobarbiturates are more active in this respect and the relative potency of the compounds parallels their pharmacological potency generally and their protein-binding affinity. (*b*) A curare-like activity which augments the action of curare on artificially stimulated fast muscle. The oxybarbiturates regularly manifest this property; the thiobarbiturates do so only under special conditions. (*c*) A type of mild anticurare activity, characteristic only of the thiobarbiturates. (*d*) A protective action against curare demonstrable on naturally activited muscles of the neck and chest and limited to just a few of the compounds. Barbiturates in general appear able to penetrate muscle.

L. E. Gilson (Chem. Abstr.)

Histochemical Studies on the Brain Glycogen of Rabbits and its Changes During Insulin Hypoglycemia. Shimizu, Nobuo and Inoue, Gyozaburo. [*Med. J. Osaka Univ.*, 3, 337–43 (1952).]

Histochemical examination of tissues from rabbits with insulin hypoglycemia showed severe loss of glycogen (1) in the cerebral cortex and striatum. A lesser change was noted in

the cerebellum. The neocortex had nearly complete loss of (1) from the 6 layers. The hippocampus is deprived of (1), while the dentate gyrus is affected only slightly. The nerve cells containing (1) are only slightly affected by hypoglycemia.

M. J. CARVER (Chem. Abstr.)

Influence of Narcosis Upon the Formation of Phosphopyruvic Acid in the Brain. Ivanenko E. Kh. [*Ukrain. Biokhim. Zhur.*, **21**, 350 (1949).]

Phosphopyruvic acid (1) was not found in the normal tissues of white mice, rats, or rabbits. An average of 24·6 mg. per cent. of phosphopyruvic acid P appeared in white-mouse brain under the influence of ether narcosis. The inorganic p decreased from 76·3 mg. per cent. to 58·4 or a 23·5 per cent. decrease with respect to the norm, in narcosis. Standard tests for (1) synthesis from lactate added to the brain tissue indicated: (*a*) that the tissue of rabbit and white-mouse brain, to which phosphate and lactate have been added, do not contain (1) in the absence of narcosis, (*b*) that (1)–P in the brain under the same conditions, with narcosis, is found in the amount of 14·–52 mg. per cent., (*c*) that general narcosis intensifies the (1) synthesis process from added lactate.

CLAYTON F. HOLOWAY (Chem. Abstr.)

Lysergic Acid Ethylamide (LAE), a New, Strong, Sedative, Psychotic Agent from Ergot. Solms, H. [*Schweiz. med. Wochschr.*, **83**, 356 (1953).]

The action of lysergic acid ethylamide (1) was studied on both healthy and mentally ill patients. From 0·5 to 0·75 mg. of (1) subcutaneously produces in the healthy human a schizophrenic-like condition of adynamia, indifference, and lack of will power with intensive depersonalization phenomena without sleep. Electroencephalograms show that the adynamia from (1) is completely different from barbiturate or physiological sleep.

HAROLD S. BAILEY (Chem. Abstr.)

A Biochemical and Pharmacological Suggestion About Certain Mental Disorders. Woolley, D. W., and Shaw, E. [*Proc. Natl. Acad. Sci. U.S.*, **40**, 228 (1954).]

A general discussion of the hypothesis that serotonin may play a role in mental processes and that the suppression of its action may result in a mental disorder.

J. D. TAYLOR (Chem. Abstr.)

Method for the Determination of the Effects of Drugs on the Pain Threshold of Human Subjects. Deneau, G. A., et al. [*Can. J. Med. Sci.*, **31**, 387 (1953).]

The method consists of inducing a sharp pain in the calf muscles by applying pressure with a sphygmomanometer cuff; the pressure required to induce pain is taken as a measure of the pain threshold. The normal threshold can be determined with an accuracy of ± 10 mm. Hg pressure. With placebos, a maximum increase of 4 per cent. over the normal pain threshold occurred one hour after administration. Acetylsalicylic acid produced an increase of approximately 20 per cent. at the same period; this was significantly greater than placebo effects. The effect of mild narcotic agents, given orally, upon the pain threshold was also measured. Codeine phosphate and pethidine-HCl both produced a significant increase in the pain threshold. The method permits the use of untrained human subjects and is sufficiently sensitive to measure the effects of the antipyretic nalgesics.

A. E. TEERI (Chem. Abstr.)

Methylpentynol as a Hypnotic for Old People. Simpson, Ronald G. [*Lancet*, **266**, 883 (1954).]

Methylparafynol (3-methylpentyne-3-ol) was an effective hypnotic without significant side effects in 61 of 94 patients 65 years and older.

BARBARA R. MURRAY (Chem. Abstr.)

Clinical Use of Reserpine in Geriatrics. Harris, Raymond. [*Ann. N.Y. Acad. Sci.*, **59**, 95 (1954).]

In a "double blind" study, the administration of reserpine to 26 elderly hypertensive patients, with an average age of 68 years, lowered the systolic blood pressure 8 per cent. and the diastolic blood pressure 11 per cent. and decreased the average heart rate. The sedative and tranquilizing effects of reserpine appeared to be of value in reducing the emotional and mental tensions of geriatric patients.

E. W. GRANT (Chem. Abstr.)

Human Pharmacology of Reserpine. Winsor, Travis. [*Ann. N.Y. Acad. Sci.*, **59**, 61 (1954).]

Reserpine (I) was administered to 65 patients representing various types of hypertension. Results indicated that (I) was a good hypotensive agent, being most effective in middle-aged patients with hypertension of a few years' duration, with severe diastolic elevations in their blood pressure and with moderate amounts of organic damage to organs. The action of (I) was increased by combining it with hydrazinophthalazine (II). In certain individuals, the addition of azamethonium to (I) and (II) was more effective than the combination of (I) and (II).

E. W. GRANT (Chem. Abstr.)

Clinical Usage of Rauwolfia Alkaloids, including Reserpine. Wilkins, Robert W. [*Ann. N.Y. Acad. Sci.*, **59**, 36 (1954).]

The most beneficial effects of Rauwolfia (I) and reserpine (II) are the decrease of neurotic symptoms in all patients and the lowering of blood pressure, particularly in the young, labile, neurotic hypertensives with tachycardia. (I) and (II) have a striking additive, if not synergistic, effect when given in combination with other hypotensive agents. Both (I) and (II) cause sedation, bradycardia, hypotension, nasal stuffiness, and weight gain. They can be taken apparently indefinitely and do not result in tolerance or addiction.

E. W. GRANT (Chem. Abstr.)

Pharmacology of Rauwolfia Alkaloids, including Reserpine. Plummer, Albert, J., et al. [*Ann. N.Y. Acad. Sci.*, **59**, 8 (1954).]

Reserpine possesses both the central nervous depressant and hypotensive actions of the root of *R. serpentina*. Its effects, including sedation, reduced emotional response, peripheral autonomic alterations, and circulatory changes, are caused by an alteration of sympathetic-parasympathetic balance by partial supression of sympathetic predominance at the hypothalamic level.

E. W. GRANT (Chem. Abstr.)