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Isoniazid in Treatment of the Chronic Schizophrenic Patient

In order to determine the usefulness of isoniazid in the treatment of the chronic schizo-

phrenic patient, the present investigation was undertaken.

Sixty chronic schizophrenic patients of comparable age, and duration and severity of illness were randomly assigned to two groups, one of which received isoniazid for 90 days and the other received a placebo for the same period. Subjects of the experimental group were randomly assigned to two groups, one of which received 50 mg. of isoniazid t.i.d., and the other 100 mg. t.i.d. Ward procedure was identical for all patients. The behavior of all subjects was rated with a modification of the Gardner Behavior Chart before, at weekly intervals was rated with a modification of the Gardner Behavior Chart before, at weekly intervals during, at the termination of treatment, and two months after cessation of treatment by three independent observers—the ward charge nurse, the ward charge aide, and the chief of hospital industries. Studies on the isoniazid group included C. B. C., BUN, urinalysis, evaluation of liver function, and electroencephalograms before, during, and after treatment. Eosinophile counts were taken, and psychiatric and neurological examinations were performed on all subjects before, during, and after treatment. Psychological studies consisted of select subtests of the Wechsler-Rellevie Adult Intelligence Scale Form. of the Wechsler-Bellevue Adult Intelligence Scale Form 1, Rorschach Psychodiagnostics, Human Figure Drawing, and a newly devised test which considers an individual's conceptualization of the internal body organization. (Authors' Abstr.)

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Effect of Amobarbital (Amytal) and Affect on Conceptual Thinking in Schizophrenia, Depression

 Schizophrenic patients show impairment in conceptual thinking relative to depressive and neurotic patients. In view of the wide overlap in scores among the groups, it is doubtful whether measures of conceptual thinking can be used as reliable diagnostic indices.

2. Conceptual thinking in schizophrenia is resistant to change, so that neither affective stimuli nor drugs alone can modify it. Further impairment occurs only when the two are presented simultaneously. Under the conditions of this experiment it appears that in schizo-phrenia the effects of the drugs on conceptual thinking depend specifically on the presence of affective stimuli.

3. Conceptual thinking in depression is relatively adequate in quality under neutral testing conditions, but is easily impaired by affective stimuli or drugs. The impairment seems

related to the increased prominence of affective preoccupations.

4. The thinking of neurotic patients appears constricted in neutral situations. The introduction of affective stimuli does not impair their conceptual thinking. Drugs apparently lessen their constriction and facilitate conceptual thinking in neutral situations, but disrupt their thinking in affective situations. (Authors' Abstr.)

Incidence of Idiopathic Convulsions in Later Life

Data are presented to reemphasize that the onset of convulsions in later life is not presumptive evidence of organic brain disease and that the incidence of such phenomena in persons of more mature years without demonstrable pathology is by no means uncommon. (Author's Abstr.)

Succinylcholine Chloride in Electroshock Therapy

Electrocardiographic tracings and blood pressure recordings were taken on 215 patients

undergoing electroshock therapy.

Electrocardiographic arrhythmias were revealed by 2.6 to 8.7 per cent. of patients prior to treatment. Electroshock without drug therapy was followed by cardiac arrhythmias in 32.5 per cent. of patients; moderate tachycardia was initially induced, to be supplanted by bradycardia. Nodal rhythms, sinus tachycardias, and ventricular extrasystoles were the commonest arrhythmias observed. The systolic blood pressure increased sharply immediately after the electroshock and was associated with the tachycardia; patients who developed a bradycardia frequently had an associated decrease in blood pressure below control values. These secondary changes appear to be a function of the aortic depressor reflex.

Thiopental (Pentothal) sodium induced a transient hypotension with little effect on pulse rate, although 16.1 to 17.5 per cent. of patients developed arrhythmias. After electroshock the blood pressure and pulse rate were transiently elevated, to be replaced at times with bradycardia and hypotension; 34 2 per cent. of patients had abnormal cardiac rhythms.

Succinylcholine chloride administration appeared to induce a mild increase in pulse rate and systolic and diastolic blood pressure. An incidence of 10.5 to 21.5 per cent. of cardiac arrhythmias was recorded. After electroshock a fairly marked rise in blood pressure and pulse rate occurred. This was followed in some patients by a marked fall in blood pressure associated with a bradycardia. An increased incidence of postshock cardiac arrhythmias was recorded in the patients treated with succinylcholine. Pretreatment with thiopental, and particularly with adequate amounts of atropine, reduced this incidence below that of patients receiving no drugs. On this basis, it is concluded that most of these arrhythmias are of vagal

Since adequate pretreatment atropinization largely prevented postshock reflex brady-cardia, hypotension, and abnormal cardiac rhythms, this measure is recommended. While the authors formerly prescribed 0.4 to 0.6 mg. twice that amount appears to be required for

adequate prophylaxis.

Blood oxygenation and circulation, as noted by skin and fingernail color and capillary-refill time, remained excellent in all patients treated with thiopental sodium and succinylcholine chloride. This is in contrast to the condition in patients treated with unmodified electroshock, who frequently show a very intense cyanosis. In the entire series of patients treated with succinylcholine chloride, detrimental effects on cardiac status were not observed in any patient after treatment. The mortality rate was zero.

The authors feel very strongly that physicians using hypnotic and muscle-relaxant drugs should have adequate knowledge of the principles of resuscitation. Cooperation between the members of the psychiatric and the anesthetic departments is of benefit to the patient.

(Authors' Abstr.)

#### Electric Shock Treatment and the Menstrual Cycle

Introduction of electroconvulsive therapy into a menstrual cycle either shortened the menstrual cycle or unduly lengthened the cycle, thus causing temporary amenorrhea.

The averages of the first cycle during shock treatment increased but little up to the 10th treatment, when a sudden rise to a higher level occurred.

The averages of all menstrual cycles during ECT were significantly related to the number

of treatments given.

The effect of a series of shock treatments was cumulative. Increasing numbers of shock treatments caused increasing delay in resumption of menstruation after treatment.

The amenorrhea-producing properties of ECT were enhanced by combined subcoma or

coma insulin treatment.

The data were intrepreted as indicating that either diminution or increase of pituitary gonadotropic function may occur during ECT, the prevalent mode of action being diminution. (Author's Abstr.)

# Serial Administration of the "Amytal Test" for Brain Disease

Thirty-four patients were given the amobarbital test ("Amytal test") for brain disease serially at different stages of their illness.

A method of quantifying the test data is proposed. It was found that the results of the test paralleled improvement or deterioration of brain function as indicated by other methods of study.

The serial use of the amobarbital procedure should be of particular value in the study of patients with brain disease, with changes in behavior and in conditions in which the alterations of brain function are poorly understood, as after electric shock treatment.

It is concluded that the test is a valid method of indicating a present degree of alteration of brain function, change from a previous level of functioning, and of prognosticating the subsequent coursé. (Authors' Abstr.)

## Chlorpromazine

Chlorpromazine is a new phenothiazine derivative related to certain antihistaminic agents. It has pronounced effects on the central nervous system. In animals, it produces a type of depression which increases progressively with the dose, has strong antiemetic properties, inhibits the secretion of gastric juice, and produces hypothermia.

In man it potentiates the effects of cerebral depressants, lowers the blood pressure, and accelerates heart action. It produces motor retardation, somnolence, and weakness. Allergic reactions occur infrequently. Reversible impairment of liver function may be observed if the drug is used in large doses over extended periods of time.

The lethargy resulting from the drug in contrast to other sedatives is characterized by clarity of consciousness and retained responsiveness, which has been demonstrated by experimental psychological methods. Chlorpromazine, at any dosage, does not produce emotional disinhibition but selectively inhibits drive, which makes it unique among the more powerful

In this study chlorpromazine was not used in combination with other sedatives. Doses vary considerably with the individual subject and range from 50 to 800 mg, per day. Prolonged administration requires nursing and medical supervision.

Seventy-one psychiatric patients, ranging in age from 18 to 82 years, were treated over a four-month period. The drug has proved to be of unique value in the symptomatic control of most types of severe psychomotor excitement. Impressive therapeutic results were obtained in acute and chronic manic-depressive patients in the manic phase. Attacks are significantly shortened. Relapses are less frequent than with E.C.T.

Selective inhibition therapy with chlorpromazine is compared with two other standard treatments for manic conditions, i.e. E.C.T. and prolonged sleep. Little is known of the exact mode of action of the drug. A possible mechanism involving acetylcholine metabolism has been considered, and, on the basis of clinical evidence available, the reticular activating system in the brain stem is proposed as the site of action.

(Authors' Abstr.)

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The Form and Structure of the Human Claustrum

The claustrum is divisible macroscopically into a dorsal (compact) and a ventral (fragmented) part, the latter composed of small islands of grey matter whose rostral prolongation forms the claustrum parvum. The dorsal and ventral claustrum are closely similar histologically and are considered to form a homogeneous structure. The claustrum extends beyond the

traditional limits of the insula.

The region between lateral border of putamen and insular cortex is constituted by a complex fibro-cellular reticulum, the central part of which represents the macroscopic dorsal claustrum. The claustral reticulum is interwoven with the fibers of the external and extreme capsules. The external capsule exchanges fibers with the putamen, the extreme capsule with the insular cortex. The origin and termination of these fibers could not be determined.

The claustral formation contains fusiform, ovoid, triangular and polygonal cells. The synaptic relationships of the cells to one another and to neighboring cell-masses could not be ascertained. The dorsal claustrum is not joined to neighboring structures by cellular bridges. Grey islands of the ventral claustrum adjoin the amygdaloid complex and temporal cortex. The cells scattered between the claustral islands and the amygdala and cortex could not be definitely allocated to one or other formation.

Human Thalamus. An Anatomical, Developmental and Pathological Study

With the exception of the anlage for the geniculate bodies, the mantle layer of the thalamus shows uniform cell distribution up to the period somewhere between 65 and 104 mm. C-R length; whereas the cell groupings in the other parts of the diencephalon were observed much earlier—in embryos of 17 mm. C-R length. The probable reason for the late differentiation of the thalamus may lie in its more recent acquirement in the phylogenetic scale.

The question of the derivation of some of the thalamic nuclei is a difficult one.

From the epithalamic mantle layer there develop habenular nuclei and probably the nucleus parataenialis.

From the thalamic mantle layer there develop: the nuclei anterior medialis, ventralis and dorsalis; the nucleus medialis dorsalis; the nucleus lateralis dorsalis, nucleus lateralis posterior and nucleus pulvinaris; the nuclei ventralis anterior, ventralis lateralis and ventralis posterior; the intralaminar nuclei; some of the medial and midline nuclei. Of the last group, the derivation of the paraventricular nucleus is not certain. It may originate from the cells of the epithalamic mantle layer, or from those of the thalamic mantle layer, or even from both of these

The medial geniculate body and also the lateral dorsal geniculate body as a whole or in its largest part, are derived from the thalamic mantle layer. The ventral lateral geniculate body, as well as the nucleus reticularis, develop from the subthalamic mantle layer. It cannot be stated definitely whether the cells from the subthalamic anlage for the lateral geniculate body form only the ventral lateral geniculate body or also contribute to the formation of the dorsal lateral geniculate body.

The thalamic anlage for the medial geniculate body, and the thalamic and subthalamic anlage for the lateral geniculate bodies were first observed in an embryo of 29 mm. C-R length

(about 8½ weeks).

The anlage for the reticular nucleus is laid down in the mantle layer of the subthalamus in the first half of the second stage; after its dorsal migration this anlage becomes the reticular nucleus and as such was observed in an embryo of 65 mm. C-R length.

In a baby born at term, subdivision of the intralaminar complex into most of the separate

nuclei is possible. Of course, subdivision is aided greatly by topographic considerations.

Within the nucleus medialis dorsalis, the lateral mediocellular part and the medial magnocellular part may be observed.

The cells of the nucleus ventralis anterior are slightly larger than those of the nucleus ventralis lateralis, which in turn are slightly larger than those of the nucleus lateralis posterior;

however, it is impossible here to delineate them.

No definite marked changes have been observed in the relative size of the thalamic nuclei in different developmental periods with the exception of the subthalamic component of the

The growth and maturation of the nerve cells progress very slowly throughout intra-uterine life, and they are not complete even in babies born at term. According to Scammon ('23), the weight of the brain of an infant of two years has doubled and at 15 years of age, has tripled, that at birth. Increase in the size of the nerve elements as well as an increase of the mesenchymal structures combine to account for this.

Merely from a consideration of the time of the appearance of the separate cell collections, during their development and, from their further transformation during the course of intrauterine life, some suggestion of the functional differences of the thalamic nuclei may be obtained. Thus, the earlier demarcation of the nucleus ventralis posterior suggests a function different from that of the other ventrolateral nuclei.

A late differentiation of certain nuclei, occurring all at the same time, may signify also their functional relationship. This may be true of the anterior nuclei, as well as of the nucleus lateralis dorsalis, the lateralis posterior and the pulvinaris. (Author's Abstr.)

The Histochemical Localization of Cholinesterases in the Central Nervous System of the Rat

1. A histochemical survey of the rat brain for specific and non-specific ChE activity has been conducted,

2. The chief sites of non-specific ChE found included the cytoplasm of fibrous astrocytes and other gliocytes, the walls of capillaries, the smooth muscle fibers of the larger blood

vessels and, in relatively low concentration, the cytoplasm of certain neurons.

3. Specific ChE activity was concentrated at the perikaryon membranes and along the axons and dendrites of numerous groups of neurons. In general, motoneurons exhibited high activity, whereas in neurons synapsing with motoneurons, directly or via internuncials, concentrations appeared to vary. The neurons of different correlation centers likewise exhibited extremes of high and low activity. The enzyme was present in low concentrations or absent in primary sensory neurons; most secondary afferent neurons exhibited moderate activity, and tertiary afferent neurons generally showed high or moderate activity.

4. Physiological implications of the present findings are discussed. (Author's Abstr.)

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A Clinical Evaluation of Mesantoin in Epilepsy

Mesantoin therapy, given to 40 patients with convulsive states of long duration and inadequately controlled by other therapy, effected considerable improvement. Thirty-seven per cent. were free of attacks for periods of three to 18 months, and 40 per cent. had a considerable reduction in frequency of attacks; a total of 77 per cent. were improved. On the other hand, 18 per cent. had no or only slight reduction in frequency, and 5 per cent. were worse while under therapy.

Gum hypertrophy caused by dilantin disappeared in 2 persons when mesantoin was substituted for dilantin, as did a severe prolonged ataxia in one case.

Toxic reactions occurred in half but were mild in most and many disappeared despite continued therapy. The potential danger of agranulocytic anemia is evident here, for one patient succumbed, the fourth reported case of this complication.

The results were obtained by substituting Mesantoin for dilantin in combination with

other current therapy. No comparison of effectiveness in similar dose levels was attempted. In this drug we have another agent, which is most effectual in motor seizures, that must be imployed with full realization of its toxic potentialities. (Authors' Abstr.)

An Electroencephalographic Survey of Mentally-Ill Epileptic Veterans
1. A survey of 1,850 patients in a neuropsychiatric V.A. Hospital indicates that 84 (4.5 per cent.) have convulsive or related disorders, such as fainting spells, attacks of dizziness, etc. Of the 84 patients, 75 (89 per cent.) were referred because of major seizures, whereas 9

(11 per cent.) complained of symptoms other than major seizures.

2. Of the 75 patients with major seizures, 47 (63 per cent.) showed some degree of abnormality in the EEG (26 abnormal, 21 mildly abnormal). Of the 9 patients with symptoms other than major seizures, 3 (33 per cent.) showed evidence of abnormality in the EEG (1 abnormal,

2 mildly abnormal).

3. In this group of 84 patients, 35 (42 per cent.) were diagnosed clinically as epilepsy (28 idiopathic, 7 traumatic). The remaining 49 patients (58 per cent.) carried miscellaneous neuropsychiatric diagnoses, both functional and organic.

4. In the entire group of 84 patients, 50 (60 per cent.) presented some degree of abnormality in the EEG (27 abnormal, 23 mildly abnormal). Specific EEG abnormalities are presented in correlation with the clinical diagnoses in these 50 cases.

5. Of the 35 patients diagnosed as epilepsy, 27 (77 per cent.) had some degree of EEG abnormality (16 abnormal, 11 mildly abnormal). In the group of 49 patients with other neuropsychiatric disorders and epileptic manifestations, 23 (46 per cent.) presented evidence of abnormality in the EEG (11 abnormal, 12 mildly abnormal).

6. The incidence of schizophrenic patients with convulsive or related disorders was found to be 1.1 per cent. or twice as high as encountered in the general population. Out of 16 patients with this diagnosis, 12 (75 per cent.) were found to have major seizures. Seven of the 16 patients (44 per cent.) presented some degree of abnormality in the EEG (3 abnormal, 4 mildly abnormal).

7. Out of 30 patients followed in an in-patient seizure clinic, approximately 50 per cent. have shown some degree of improvement. Seven patients are at present on trial visit from (Author's Abstr.)

the hospital.

The Hyperventilating Type of Human Female

1. The hyperventilation syndrome is frequent in women, occurring in about 27 per cent. of the general female population.

It occurs about three times more frequently in women than in men.

3. The cause and core of the hyperventilation syndrome is anxiety. Usually only a part of this anxiety is "cathected" or bound by the hyperventilation habit. The part that is bound causes the variegated secondary physical symptoms described in the text of this report. The unbound fraction which, like the devil is certain to crop up sometime in the life of the hyperventilator, leads a peculiarly vicarious existence, causing sometimes mere annoyance and irritation to others, but at other times it has serious social consequences.

4. A good many hyperventilators constitute a serious problem to their families, to society in general, and to the medical profession. They are the innocent propagators and purveyors of neuroses and psychoses in others, of such social problems as alcoholism, adultery, and divorce, and of unscientific healing cults and systems and quackery in general. Because they can be annoying, the physician should not make the mistake of assigning them a nuisance

value.

5. Most female hyperventilators go untreated by psychiatrists, first, because of the tendency of the symptoms to mask themselves in a myriad of physical forms, and, secondly, because of their relatively strong ego, their aversion to having the label "neurotic" pinned on

them, and their propensity to project part of their anxiety on to the environment.

6. The hyperventilation syndrome of psychogenic origin is of three grades of severity, namely, mild, moderate, and severe. Thus far its cure is fundamentally psychotherapeutic. With a better attitude and a deeper understanding on the part of the medical profession, the prognosis of the hyperventilation syndrome can be influenced for the better even in the more severe cases.

7. In the past sixty years the medical profession and psychiatry have met and overcome the challenges of conversion hysteria in the female. Like the conversion hysterics the hyperventilators are more to be pitied than condemned. The hyperventilators constitute a new challenge to the medical profession. I am certain that we will accept the responsibility for their adequate care and that with sympathetic and intelligent handling we will help not only those afflicted with hyperventilation but society as well. (Author's Abstr.)

Schizoid

1. The following traits are characteristic of the schizoid personality, (a) Uncomfortable feelings of inadequacy, (b) A desire to withdraw from people, and (c) A tendency toward autistic and dereistic thinking. External behavior gives the appearance of different types because the affect may be dull or extremely excitable. However, it is almost always inappropriate. Sex life may be inactive or polymorphous and chaotic but hardly ever smooth-flowing.

2. This type of personality is more frequently found to be the one from which schizo-

phrenia develops than any other.

3. The schizoid personality is developed out of the interplay of hereditary, constitutional, and environmental factors. The hereditary factor is merely a predisposition which may be overcome by environmental influences. (Author's Abstr.)

#### **OCTOBER**

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Effects of ACTH on Mental Function

An attempt was made to determine if ACTH regularly produces striking, specific changes in mood and behavior, as has been reported by some observers. Special attention was directed toward controlling several factors which have complicated evaluation of previous studies. Among these variables are:

- 1. The presence of severe or chronic illness.
- The patient's previous personality patterns.
- 3. Current environmental stress.

4. Attitudes of the investigators.

A group of 11 young male soldiers only mildly ill with acute hepatitis was chosen for investigation and subdivided into control and treatment groups. The pattern of distribution was kept secret from all observers. Periodic psychiatric observations were made before,

was kept secret from all observers. Periodic psychiatric observations were made before, during, and after the administration of the drug (or placebo).

Psychiatric observations revealed no gross intellectual, affective, or behavioral changes; controls could not be differentiated from patients getting the drug. A battery of psychologic tests was administered during the base-line period and repeated during the course of the drug administration. The psychologic test results did not demonstrate any sharp distinctions between the two groups, either before or after the initiation of treatment. Over-all level of intelligence, patterns of frustration-aggression, and imaginative responses to projective tests remained largely unchanged for both groups. Such fluctuations in test scores and performance as were observed were minor in nature and occurred with equal frequency in the two groups. It is concluded that major psychologic changes need not invariably occur with the use of ACTH. It is believed that such changes are probably rare in patients who do not have

of ACTH. It is believed that such changes are probably rare in patients who do not have chronic, severe illness either physical or mental.

Although this is a small sample, the strikingly uniform lack of major psychologic changes suggests that the central pharmacologic action of ACTH on the central nervous system (as shown by EEG evidence) has no specific effect on mood and behavior when administered in the usual clinical dosages. It is further postulated that the variables which this study attempted to minimize are probably among the chief factors responsible for the production of mental changes when they occur.

The advantages of close co-operation between psychiatrists and other medical specialists n the evaluation of therapeutic drugs and problems of rehabilitation are discussed.

(Authors' Abstr.)

Intravenous Sodium Iodide in the Treatment of Advanced Senile Psychosis and Arteriosclerotic Cerebrovascular Disease

Sodium iodide in the treatment of advanced senile psychoses and arteriosclerotic cerebrovascular disease resulted in no improvement in this series of 15 patients in the dosages given and in the number of treatments given. The 2 deaths in the authors' series made them hesitate to continue the treatments further by either enlarging the dosage of iodides or extending the number of treatments beyond ten. The fact that no improvement was noted in any of the 15 patients treated makes them doubt the efficacy of the use of sodium iodide in advanced senile or arteriosclerotic psychoses. (Authors' Abstr.)

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Effects of Small Lesions in Sensory Cortex in Trained Monkeys

1. Small lesions were made in the sensory cortex (areas 3, 1 and 2) of two Macaca mulatta and seven Macaca nemestrina monkeys. The latter were trained for tests of discrimination by palpation, dexterity and motor power.

2. The immediate and remote effects of the lesions are stated in quantitative terms by

means of these tests. In all cases substantial, and in some complete, recovery was measured

and recorded.

3. The results of the present study are compared and contrasted with previous work on the motor cortex (area 4). Lesions in either the motor or the sensory areas cause loss of motor power and dexterity. Those in areas 3, 1 and 2 do not cause inability to make movements but may cause initially unawareness of movements made and arrest of a limb in an unusual position. In all cases of post-central gyrus lesion a loss of tactile sensation occurs and before recovery this defect is compensated for by the greater use of visual cues.

4. Histological examination of the brains by the Marchi method showed very extensive fibre connections from areas 3, 1 and 2 into area 4 with the thalamus, but few fibres entering

area 5. Descending fibres into the spinal cord were found and counted.

5. A correlation of function and anatomical data indicates that a most intimate connection exists between areas 3, 1 and 2 and area 4, and that these cortical areas form a unit essentially linked with the thalamus and spinal cord, but sending few fibres into areas more (Authors' Abstr.) anterior and posterior.

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Traumatic Epilepsy after Closed Head Injury

Two thousand cases of closed head injury were studied from the war-time records of the Military Hospital for Head Injuries, Oxford.

Five hundred of these were a relatively unselected group and the incidence of post-

traumatic epilepsy was 6 per cent.

One hundred and ninety cases of traumatic epilepsy were considered in some detail. Focal seizures developed earlier than did general seizures.

Cases with a long post-traumatic amnesia (P.T.A.) had a higher incidence of epilepsy, and the fits developed after a longer time-lag than occurred in cases with a short P.T.A.

Constitutional factors appeared to be relatively unimportant.

The possible significance of the varying interval at which fits develop is discussed from the point of view of the aetiological factors concerned in traumatic epilepsy.

(Author's Abstr.)

## Frontal Lobe Wounds Causing Disinhibition

Six cases of penetrating brain wound are described in which disinhibition appeared after involvement of the frontal lobes. It has been shown that disinhibition is a separate disturbance of function which need not necessarily be associated with other disturbances described as part of the frontal lobe syndrome. In most cases the patients are aware of the change in their personality due to the disinhibition, but can only exert minimal control over the new behaviour pattern

Disinhibition can appear when only one frontal lobe is involved, without any obvious anatomical correlation with any special site within the pre-frontal area, though, as has been pointed out, the extent of frontal lobe injury was severe in all these cases.

Disinhibition can coexist with a variety of affective experience and can occur without any associated intellectual impairment. Much destruction of frontal lobe tissue appears to be possible without producing intellectual loss in the conceptual sense.

The relation between the appearance of disinhibition and the pre-traumatic personality is described in full, and reasons are given to explain why disinhibition only occurs significantly in certain cases and involves different aspects of the personality in different people.

(Author's Abstr.)

Studies of the Connexions of the Fornix System

The connexions of the fornix system have been studied experimentally in the rat, rabbit and monkey by the method of retrograde cell degeneration. No cellular degeneration was found in the cells of the hippocampus after complete division of the fimbria or fornix.

These observations were consistent in animals of all ages and after survival periods varying from seven days to 10 months.

It is suggested that the absence of retrograde degeneration in the cells may be due to the rich system of recurrent collaterals derived from the proximal ends of the axons of the hippocampal pyramids.

Extensive fibre degeneration of the alveus occurs in the rat following lesions of the fornix system. From the distribution of this degeneration it appears that field CA<sub>1</sub> of the hippocampus

is related to the dorsal fornix and the other fields to the fimbria.

Division of the fimbria results in complete atrophy or shrinkage of all the cells of the ipsilateral medial septal nucleus and partial degeneration of the nucleus of the diagonal band. Additional involvement of the dorsal fornix or stria terminalis in the rat did not affect the degree or distribution of this degeneration.

No retrograde degeneration was found in the nuclei of the pre-optic and hypothalamic

Extensive destruction of the entorhinal cortex and amygdaloid nuclei was not accompanied by any degeneration in the septal nuclei.

Division of the stria terminalis did not lead to any cellular change in the amygdaloid ei.

(Authors' Abstr.) nuclei.

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2. Initial symptoms were focal or Jacksonian seizures in 37 per cent. of cases, hydro-

cephalus in 31.5 per cent., and physical and mental retardation in 31.5 per cent.

- 3. Sixty-three per cent. of the entire group had verified major seizures sometime during their illness. Such seizures were focal or Jacksonian in 75 per cent. of cases.
- 4. Eighty per cent. of the 15 patients studied by standard psychometric technics were found to be mentally retarded or defective.
  - 5. Forty-two per cent. of patients in this series were hydrocephalic.
- 6. It has been postulated that the high incidence of focal or Jacksonian seizures in patients with agenesis of the corpus callosum may be due to deficient neopallial commissural fibre systems which inhibit the spread of the seizure to the opposite hemisphere.

Standardization of Face-Hand Test

(Author's Abstr.)

A standardization of the face-hand test is presented. A positive face-hand test is designated as one in which errors persist after the tenth trial. Four classes of positive face-hand tests are recorded. A one-plus face-hand test consists of extinction only with touch stimuli. A two-plus response is characterized by extinction with pinprick and rubbing stimuli as well as with touch stimuli. A three-plus response consists of extinction and displacement with touch, rubbing, and pinprick stimuli. A four-plus response has all the characteristics of a three-plus response and in addition at least one of the following features: (a) exosomesthesia; (b) allesthesia; (c) perseveration of responses; (d) occurrence of errors even while the subject observes application of the stimuli. Three-plus and four-plus responses invariably indicate disease of the brain in subjects over the age of six years. One-plus and two-plus responses occur in patients with brain disease but are also manifested by a small number of normal adults and patients with psychogenic disorders. Patients with a four-plus response show the severest mental changes but the converse is not true. There is no correlation between the severity of the mental changes and the type of positive face-hand test manifested. Usefulness of this classification in the study of patients clinically and in experimental work is suggested.

(Authors' Abstr.)

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Observations on Organic Brain Damage and Clinical Improvement Following Protracted Insulin Coma

A study of eight cases of chronic schizophrenics who developed protracted coma during insulin shock therapy is reported. Five of the eight patients showed a marked improvement after protracted coma, and three remained unimproved. The improvement consisted of loss of tension and hostility. Patients became friendly, affable, relaxed and interested in the environment. In spite of the return of delusional systems, the improved patients were able to function on a higher level than previously. In four of the five improved patients, improvement was preceded by severe organic brain deficit of varied duration. The organic deficit was demonstrated through clinical observation, a battery of psychological tests and electro-encephalograms. Improvement is attributed to the organic brain damage which results in disruption of associative pathways not unlike the disruption in lobotomy. (Author's Abstr.)

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The Failure of Succinate to Alter the Metabolism of Ethyl Alcohol in Dogs and Rabbits

Measures Between Inpatient and Outpatient Care for Alcoholics. Sjöhagen, A.

1. Castex and his co-workers have reported that intravenous administration of succinate will rapidly alleviate alcoholic depression and concurrently reduce the concentration of alcohol in the blood. Because of the practical and theoretical importance of such a finding the authors have investigated the same problem.

In their experiments neither single, repeated, nor continuous intravenous injections of succinate changed the rate of disappearance of alcohol from the blood of rabbits or dogs (the first stage of the metabolism of alcohol). No effect on the second stage of alcohol metabolism following the injection of succinate could be demonstrated by determinations of the blood concentrations of acetaldehyde, pyruvic acid or glucose.

3. It is suggested that incomplete distribution of alcohol in the body may account for (Authors' Abstr.) the results obtained by Castex and his associates.

Alcohol Breath Tests and Breath Deodorization by Chlorophyll Derivatives

1. The ingestion of 100 mg. of chlorophyllin is without effect on the concentration of alcohol occurring in the blood and the breath after the consumption of whisky.

2. The chewing of chlorophyllin-containing gum is without effect on the alcohol content of the breath following the consumption of beer.

 Chlorophyllin does not interfere with the alcohol breath test.
 The breath odor after drinking alcoholic beverages is due primarily to the presence of highly aromatic substances characteristic of each beverage. The reported deodorization of beer breath with chlorophyllin suggests that this substance neutralizes some of the characteristic aromatic substances present. (Authors' Abstr.)

Relation of Blood Acetaldehyde Level to Clinical Symptoms in the Disulfiram-Alcohol Reaction Following the intake of about 50 ml. of absolute alcohol, the proportion of acetaldehyde in the blood of human subjects increases, and this is to some extent dependent on the dose of

alcohol. Values between 0.590 and 1.700 mg. per 100 ml. of acetaldehyde were found.

With preceding administration of disulfiram (tetraethylthiuram disulfide) a higher acetaldehyde concentration is found in the blood after intake of alcohol. In subjects showing a clinical disulfiram-alcohol reaction, values between 0.639 and 2.510 mg. per 100 ml. of acetaldehyde were found in arterial blood.

Following the intake of alcohol only, the acetaldehyde concentration may reach values of the same order of magnitude as those seen in disulfiram-alcohol reactions but alcohol alone does not produce any signs of the reaction.

The proportion of acetaldehyde in the blood rises with increasing dosage of disulfiram

but only up to about 4.5 g. of the compound during the 3 days preceding the test.

The grade of clinical reaction becomes more pronounced with increasing dosage of disulfiram but a medium reaction is released after the administration of a total of 1.5 to 2.0 g. during 3 days. (Author's Abstr.)

Effect of Alcohol on Respiration Before and After Treatment with Disulfiram

Study of ventilation in the course of the disulfiram-alcohol reaction has substantially confirmed previous investigations. Alcohol alone may either increase or reduce ventilation, whereas increased ventilations with a reduced carbon dioxide content in the expired air is regularly found in the course of the disulfiram-alcohol reaction. Inhalation of oxygen brings about a reduction of ventilation but produces no subjective improvement

(Author's Abstr.)

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#### 1. Biochemistry, Physiology, Pathology, etc.

Nucleic Acids of the Cells of the Central Nervous System in X-ray Treated Animals. Poggiali, Adriano. [Sistema Nervoso, 4, 547 (1952).]

In x-ray irradiated rabbits (100-900 r in one dose, or increasing doses by 100 r, on the

head) a decrease of the cytoplasmic ribonucleic acid and a slight decrease also of the thymonucleic acid of nuclei, were observed. Other morphological observations are described. C. SCANDURA (Chem. Abstr.)

Histochemical Detection of Tigroid Matter in Nerve Cells. Shabadash, A. L. [Doklady Akad. Nauk. S.S.S.R., 91, 405 (1953).]

The method depends on the presence of ribonucleic acid in the tigroid matter and is performed by selective binding by this acid of basic dye in buffers with pH 4·2-4·5. Methylene blue is the selected dye which gives clean differentiation from other structures of the neurons of the brain or the spinal cord; for the brain pH 4·5 is best, for the spinal-cord specimens 4·3. Acetate, citrate, or phosphate buffers can be used, the latter being somewhat better. After the methylene blue treatment and rinsing, the specimen is fixed with 6 per cent. NH<sub>4</sub> molybdate.

G. M. Kosolapoff (Chem. Abstr.)

Biochemical Studies on the Action of the Nerve. VII. Histochemical Determination of Choline-sterase. Okinaka, Shigeo, et al. [Igaku to Seibutsugaku (Med. and Biol.), 26, 221 (1953).] The distribution of acetylcholinesterase in the central nervous system, as determined by the method of Koelle, is given with a photograph reproducing the histogram.

M. NAKAMURA (Chem. Abstr.)

Transmission and Functional Action in Peripheral Nerves of Rats in Avitaminosis B<sub>1</sub>. Casella, C., and De Caro, L. G. [Arch. sci. biol. (Italy), 37, 229 (1953).]

The speed of transmission and amplitude of functional action of the sciatic nerve of rats

have been tested. No difference has been noted between rats suffering from avitaminosis B and control animals. Prolonged stimulation of muscles affected by tetanus causes no signs of increased fatigue of the peripheral nerves in animals suffering from avitaminosis. Probably the peripheral nerves, even in a state of advanced avitaminosis, contain enough vitamin E to continue their function. The vitamin B<sub>1</sub> level in the peripheral nervous system in animals suffering from avitaminosis B<sub>1</sub> decreases slower than in other tissues.

FRANK W. DANN (Chem. Abstr.)

Rates of Glycolysis in Human Red Cells in Relation to Energy Requirements for Cation Transport.

Bernstein, Ralph E. [Nature, 172, 911 (1953).]

Red blood cells separated from white cells utilized glucose at the rate of 1·18 millimoles/l. red cells/hr. at 37° (range of 18 samples, 0·9-1·35). White cells account for 25 per cent of the glucose utilization of standardized whole blood. Calculations from the transport data of Solomon and of Raker, et al. (C.A. 44, 10101a) indicate that the ion transport necessary to maintain the steady state requires a maximum of 1/3 of the free energy available from glycolysis. Incubation for 3 hours at 37° with glucose is sufficient to restore to normal levels the K lost and Na gained during storage at 4-8° for 1-3 days.

ROBERT B. DEAN (Chem. Abstr.)

Effects of Adrenalectomy and replacement Therapy on Brain Circulation, Oxygen Consumption, and the Electrocorticogram. Bergen, John R., et al. [Am. J. Physiol., 175, 327 (1953).]

A comparison of the relative rate of blood flow through heads of normal and adrenalectomized salt-maintained rats indicates that adrenalectomy decreases the flow. The decreased blood flow can be restored to normal in 2 hours with adrenal cortical extract,  $\Delta^5$ -pregnenolone. or cortisone but not with deoxycorticosterone. The circulatory slowing results in a marked, reduction of O consumption by the tissues. Restoration of O consumption is aided by adrenal cortical extract and  $\Delta^s$ -pregnenolone but not by deoxycorticosterone. The reduction in brain O consumption following adrenalectomy is accompanied by reduction of the electrocorticogram frequency. Restoration of the frequency is produced by the same steroids that restore blood flow and O consumption.

E. D. WALTER (Chem. Abstr.)

Migrainoid Headaches. Donahue, Hugh C. [Arch. Ophthalmol., 44, 285 (1950).]

The pathological and biochemical aspects of headaches from histamine, muscle ischemia, hypoglycemia, and vascular changes are discussed and reviewed

W. C. Tobie (Chem. Abstr.)

Lesions of the Central Nervous System of the Guinea Pig in Hypervitaminosis A. Brusa, A.

and Testa, F. [Intern. Z. Vitaminforsch., 25, 55 (1943).]

Hypervitaminosis A of the guinea pig was accompanied by severe damage to the cerebral ex, cerebellum, thalamus, and mesencephalon.

JOSEPH S. HEPBURN (Chem. Abstr.) cortex, cerebellum, thalamus, and mesencephalon.

Chromatography of Free Amino Acids in Normal Human Spinal Fluid. Kamali, D., and Porcellati, G. [Boll. soc. ital. biol. sper., 28, 1275 (1952).]

Three amino acids were always present: glycine, alanine, and valine.

M. Elliott (Chem. Abstr.)

Bioelectric Cerebral Activity in Man during Vitamin B<sub>1</sub> Deficiency. Rottger, Ernesto, et al. [Semana méd. (Buenos Aires), 1953, (11), 382.]

A special wave rhythm appears when the vitamin B<sub>1</sub> level drops to a point that renal excretion is abolished. The wave coincides with the cardiac diastole

A. E. MEYER (Chem. Abstr.)

Phosphoaminolipides of Nervous Tissue of Premature Infants. Blancher, G., and Vaux-Saint-Cyr, C. [Compt. rend. soc. biol., 147, 266 (1953).]

Compared to values for the adult brain, the fatty acids of the phosphoaminolipides of the premature infant brain were less unsaturated and were especially lower in hexaenic acids. L. E. GILSON (Chem. Abstr.)

Chemical Changes in Rabbit Brain during Anoxia, Albaum, Harry G., et al. [Am. J. Physiol., **174**, 408 (1953).

Changes in metabolite concentrations of various portions of the rabbit brain were determined during progressive stages of anoxia and correlated with electric measurements of function. Disappearance of function and the inexcitability of all measurable elements during anoxia were associated with a moderate decrease of adenosinetriphosphate (ATP), phosphoanoxia were associated with a moderate decrease of adenosine approximate (ALL), prospective creatine, and glycogen. Disappearance of ATP was more rapid than that of phosphocreatine. Urethan controls had a higher level of ATP than the unanesthetized animals. The different regions of the forebrain showed no differences in ATP level or in depletion under anoxia.

E. D. Walter (Chem. Abstr.)

Nature of Sympathetico-adrenal Discharge under Conditions of Excitation of Central Autonomic

Structures. Redgate, E. S., and Gellhorn, E. [Am. J. Physiol., 174, 475 (1953).] The action of asphyxia and stimulation of the hypothalamus on the liberation of noradrenaline and adrenaline was studied in cats. Asphyxia leads to a liberation of adrenaline while excitation of the hypothalamus causes the appearance of either noradrenaline or adrenaline in the blood.

E. D. WALTER (Chem. Abstr.)

The Influence of Excitation of the Central Nervous System on Some Aspects of Metabolism in the Cerebral Hemispheres of Animals. Vladimirov, G. E. [Doklady Mezhdunarod. Fiziol. Kongr., Montreal, 19, 33 (1953).]

Excitation of the central nervous system by camphor intensifies glycolytic processes. Lactic acid (I) content in brain increases. Strychnine raises (I) in the blood but not in the brain. During excitation, brain pyruvic acid and (I) increased but neither adenosinetriphosphate (II) nor phosphocreatine (III) changed. Inorganic P rose from 15·3 to 19·9 mg. per cent. after stimulation for 25 seconds. The specific activity of various P fractions was determined after injection of P<sup>32</sup>. Relative specific activities of (II) and (III) rose slowly. Phospholipides were relatively inert, their specific activity being 3 per cent. within 4 hours and 10 per cent. after 24 hours. Deoxyribonucleotides had an even slower turnover; that of ribonucleotides was somewhat faster, while phosphoproteins had the most rapid turnover rate. The NH<sub>a</sub> content of brain rose during the first 15 seconds of stimulation, after 60 seconds returned to normal levels, and after 120 seconds dropped below the normal level.

HERMAN I. CHINN (Chem. Abstr.)

Characterization Test of Epileptiform State Phases by Means of the Transhemation Reaction. Blyumenfel'd, L. A., et al. [Doklady Akad. Nauk S.S.S.R., 92, 189 (1953).]
The rate of the transhemation reaction reflects the phases of the epileptic state. Pre-

convulsion state reduces the rate of transhemation, a change that becomes evident immediately upon introduction of camphor. The retardation is then replaced with a constantly increasing rate of transhemation. If the convulsions are feeble, the latter phase is not apparent. The postconvulsive state is characterized by gradual retardation of transhemation. The experiments were run on rabbits, and the transhemation reaction was run as described earlier.

G. M. Kosolapoff (Chem. Abstr.)

Brain Metabolism in Excitation and Inhibition of Central Nervous Activity. Palladin, A. V. [Doklady Mezhdunarod. Fiziol. Kongr., Montreal, 19, 129 (1953).]

Central nervous excitation was produced in rabbits by a single injection of pervitin (I) or of cardiazole (II). The animals were sacrificed by decapitation 4 hours after injection, the brain was frozen in liquid air and analyzed for ribonucleic acid (III), deoxyribonucleic acid (IV), lactic acid (V), free and bound polysaccharide (VI), amylase, phosphorylase, adenosine-triphosphate (VII), and phospholipides. With (I), there was little change in the nucleic acid concentrations in the brain; the rate of metabolism of (III) was unchanged and of (IV) fell slightly; the preformed (V) was less than normal and less than that observed after (II). Anaerobic glycolysis was greater with (I) than with (II) or in the normal state. During the first hour after (I), (VII) fell, but returned to normal within 2 hours and rose still further after 4 hours. With (II), (VII) remained normal for the first 2 hours and then fell slightly. The relative specific activity of (VII) was above normal during the first 2 hours after (I), but remained subnormal with (II). Prolonged excitation leading to convulsions lowered (IV) and (VI) with a concomitant increase in the activity of the enzymes destroying these substances.

Rats were stimulated with 25-40 v. and examined 30 minutes later. Chronic excitation lowered the activity of deoxyribonuclease (VIII) and decreased the amount of P<sup>3a</sup> incorporated into (III). In embryonic development (IV) was low in the 20-22 day embryo but rose towards the 28-29th day. Changes in the activity of (VIII) coincided with the appearance of new nervous functions. In other experiments, rats were kept awake for 2-3 days with a rotating drum which turned for 30 seconds every 5 minutes. During this period of insomnia, (VII) decreased and inorganic P increased. Glycolytic activity decreased. To inhibit central activity, medinal was used in doses adequate to produce sleep of 18-20 hours daily for 4-6 days. (VIII) activity increased considerably. (III) and (IV) changed only slightly. It was concluded that during sleep synthetic processes predominated. H. I. CHINN (Chem. Abstr.)

The Effect of a Cholesterol-free Brain Fraction Against Diet-induced Atherosclerosis. Jones, R. J., et al. [Circulation Research 1, 530-3 (1953).]

The feeding of a lipide-poor and virtually cholesterol-free residue of mammalian brain

mitigated the hypercholesteremia and atherosclerosis in cholesterol-fed chicks. This effect could be sustained for at least 5 weeks. The degree of reduction in hypercholesteremia was roughly proportional to the dose of brain extract (given as 5, 10, and 15 g./100 g. diet). The probable mechanism depends upon the capacity of oral cerebrosides to convert a large proportion of fecal sterols into unabsorbable coprosterol, thus rendering intestinal cholesterol unavailable.

Theresa McKee (Chem. Abstr.)

Phosphorus Metabolism in the Brain upon Stimulation of the Higher Nervous Activity. Palladin,

A. V., and Rybina, A. A. [Doklady Akad. Nauk. S.S.S.R., 91, 903 (1953).] The technique of labelled atoms was employed in the demonstration of the fact that pervitin and cardiazole produce a different reaction in the process of brain metabolism in respect to phosphates, particularly adenosinetriphosphate (ATP). Rabbits were given either of the 2 drugs (7-8 mg./kg., or 50-70 mg./kg. respectively) and the rapidly excised brain tissue was frozen in liquid air. When pervitin is used as the brain stimulant, within 1 hour there is observed a decline of ATP content in the brain, after this its content rises to normal within 2 hours, then continues to rise up to 4 hours reaching above normal levels. The inorganic phosphate shows a precisely reversed order of changes. When cardiazole was used as the stimulant, the brain content of ATP was supernormal in the 1st hour then dropped and remained subnormal after 2 or even 4 hours. The inorganic phosphate content gave a reverse order. If labelled phosphate was introduced simultaneously with the drugs (P<sup>33</sup>-phosphate in unspecified form) the radioactivity of the brain ATP gave the following picture: with pervitin the radioactivity of brain ATP rises over the 1st 4 hours; with cardiazole the activity is subnormal without much change over the duration of experiments. Thus, pervitin promotes the metabolic exchange in ATP and cardiazole does not.

G. M. Kosolapoff (Chem. Abstr.)

A New Concept of Organization of the Central Emetic Mechanism: Recent Studies on the Sites of Action of Apomorphine, Copper Sulfate, and Cardiac Glycosides. Wang, S. C., and Borison, Herbert L. [Gastroenterology, 22, 1 (1952).]

Experiments on 150 dogs indicated that apomorphine induces vomiting solely through a central action. However, this action is on receptors located in the chemoreceptor trigger zone and is not directly on the vomiting center per se. The site of emetic action was determined by the fact that trigger zone ablation resulted in total refractoriness to apomorphine without any change in responsiveness to oral CuSO<sub>4</sub> and that gastrointestinal denervation did not reduce the sensitivity to oral apomorphine. Experiments with CuSO<sub>4</sub> performed on 154 dogs revealed that this substance can induce emesis through 2 different actions: (a) reflex vomiting, due to gastrointestinal irritation, occurs after a short latent period of approximately 15 minutes following effective oral doses; (b) central vomiting due to excitation of the chemoreceptor trigger zone by circulating Cu, is elicited after intravenous injection and also follows large oral doses administered after gastrointestinal denervation. These results constitute the basis for a proposal of a functional procedure to ascertain the localization of the sites of action of other emetic agents. Experiments on digitalis emesis are presented to illustrate the suggested procedure. Trigger zone ablation sharply reduces the incidence of emesis following both intravenous and oral doses of scillaren C and lanatoside C, particularly of the latter. However, vomiting after a longer latency is still elicitable with elevated doses of digitalis glycoside in some of the operated animals. The emetic response to digitalis is not impaired either by gastrointestinal denervation or by cardiac denervation. It is concluded that digitalis has an important central (chemoreceptor trigger zone) component of action but that it also acts peripherally at a receptor site, yet unknown, which lies outside of the gastrointestinal tract. RUTH BERGGREN (Chem. Abstr.)

Hypothalamic Influences on Hydrochloric Acid Secretion of the Stomach. Porter, R. W., et al.

[Surgery, 33, 875 (1953).]
Stimulation experiments in the monkey reveal dual hypothalamic influences increasing the secretion of gastric HCl. The first originates in the anterior hypothalamus, is conducted through the vagus nerve, and is blocked only by vagotomy. The peak of its response is prompt. The second, whose peak response is later, arises in the posterior hypothalamus, is conducted humorally through the pituitary-adrenal system, and is blocked only by adrenalectomy.

The increase in gastric HCl induced by administration of insulin exhibits features of the responses to both anterior and posterior hypothalamic stimulation.

RUTH BERGGREN (Chem. Abstr.)

Phosphoproteins and Cerebral Metabolism. Engel'gardt, V. A., and Lisovskaya, N. P. [Doklady Mezhdunarod. Fiziol. Kongr., Montreal, 19, 209 (1953).]

The specific activity of P<sup>32</sup> in cerebral tissue was fractionated into inorganic (I) and

protein P (II). Incubation of washed slices at 37° with P<sup>32</sup> increased the specific activity of (I) about 2.5 times that at 0°. Similar treatment increased the specific activity of (II) more than 10 fold. Incubation of tissue with glucose plus NaCN, dinitrophenol, or NaN<sub>3</sub> decreased markedly the specific activity of (II) without affecting appreciably that of (I). The metabolic importance of (II) is discussed in the light of these findings.

HERMAN I. CHINN (Chem. Abstr.)

A Nerve-inhibiting factor in Brain and Spine. Florey, Ernst. [Naturwissenschaften, 40, 295

Brains and spinal cord of animals (horse, cow, cat, rabbit, guinea pig, rat, mouse) contain a substance which in dilution down to 10<sup>-6</sup> will give an inhibitory effect on peripheral nerves of crawfish (Cambarus clarkii and Palinurus argus). It inactivates the nervous automat centers of the heart, slows down the transmittal of impulses to the claws, and cuts out the spontaneous intestinal activity. The factor is stable in boiling water, dialyzable water and HCl-EtOH soluble, insoluble in EtOH, PrOH, BuOH, Me<sub>2</sub>CO, Et<sub>2</sub>O, CHCl<sub>3</sub> and C<sub>6</sub>H<sub>6</sub>; it is active only at pH less than 7. Tests on guinea pig and rabbit ileum indicate that aqueous brain and spine extracts (boiling water) have a contracting effect in normal Tyrode solution; probably the B. J. C. VAN DER HOEVEN (Chem. Abstr.) same factor is involved.

Phosphocreatine Changes in the Brain Tissues of Rats. Tseitlin, L. A. [Biokhimiya, 18, 311 (1953.)

An intense hydrolytic splitting of phosphocreatine occurs in dialyzed extracts of brain tissues, optimum for which is pH 6·0-7·1. The formation of phosphocreatine in the brain tissues by means of esterification with the adenyl system proceeds slowly in the absence as well as in the presence of fluorides. Attempts to determine whether the formation of phosphocreatine proceeded by means of transfer of the phosphate fraction of phospho-amino acids to the creatine met with no success. B. S. LEVINE (Chem. Abstr.)

Incorporation of Labeled Phosphate into the Lipides of Brain Dispersion. Dawson, R. M. C. [Biochem. J., 55, 507 (1953).]

Phospholipide P present in adult brain tissue is in a state of dynamic equilibrium with the inorganic phosphate in the cerebral cells. Incorporation of labeled phosphate into the brain lipides is associated with oxidative phosphorylation, optimum incorporation requiring oxidizable substrate, O, phosphate acceptor, Mg ions, and cytochrome c. The incorporation process is greatly accelerated by the presence of F ions. The incorporation is inhibited by hypertonic mediums or by a low concentration of Ca ions and glucose. Inhibitors which uncouple oxidative phosphorylation also uncouple the respiration from the incorporation of labeled phosphate into the lipides of a guinea-pig brain dispersion. The mechanism is believed to include an esterification of P32 into high-energy phosphate compounds which then phos-S. Morgulis (Chem. Abstr.) phorylate phospholipide precursors.

Exchange of Albumin Between Plasma and Cerebrospinal Fluid. Fishman, Robert A., and Halla, Roman J. [Am. J. Physiol., 175, 96 (1953).]

The exchange of I<sup>13</sup>-tagged albumin, administered intravenously, between plasma and cisternal fluid was studied in normal dogs. The appearance time of iodoalbumin in cisternal fluid was less than 40 minutes. The equilibrium time, representing the mixing of the spinal fluid albumin with the plasma albumin pool, occurred about 20 hours after injection. The appearance turnover times of the albumin in plasma and cisternal fluid were 6.3 and 8.0 days average turnover times of the albumin in plasma and cisternal fluid were 6.3 and 8.0 days, respectively. The delayed appearance and equilibrium times and turnover rate may be functions of the blood-cerebrospinal fluid barrier, E. D. WALTER (Chem. Abstr.)

Phenylpyruvic Acid Oligophrenia. Stadler, H. E., and Dryer, Robert L. [Arch. Pediat., 70, 298 (1953).]

In a case of this disease in a child 11 months old, the urine contained 0.12 g. phenylpyruvic acid per 100 cc. Of the qualitative tests for this acid, the formation of a fleeting green color with FeCl<sub>3</sub> was found preferable to the formation of a yellow precipitate with 2,4-dinitrophenylhydrazine or the production of a mahogany color with alkali picrate, since the latter tests are not specific. Since creatinine reacts with alkali picrate in the same manner, creatinine must first be removed from the urine by treatment with Lloyd's reagent. Glucose also gives the 2,4-dinitro-phenylhydrazine reaction. JOSEPH S. HEPBURN (Chem. Abstr.)

Effects of Insulin on Melanoma and Brain Metabolism. Woods, Mark, et al. [Biochim. et Biophys. Acta, 12, 329 (1953).]

Normal mouse brain and melanoma slices showed similar  $Q_{CO_2}^{O_2}$  values. But whereas addition of Mg and PhOH increased the  $Q_{CO_2}^{N_2}$  of brain, it slightly inhibited the  $Q_{CO_2}^{N_2}$  of

melanoma. And insulin (I) increased the  $Q_{CO_2}^{N_2}$  of melanoma, but not of brain. Crystallized Zn-(I) freed of hyperglycemic factor was as effective as regular Zn-(I) in raising the  $Q_{CO_2}^{N_2}$  of melanoma; the factor, freed of (I) had no appreciable effect. The relative concentrations of Zn and (I) influenced critically the extent of increase of  $Q_{CO_2}^{N_2}$ . Under aerobic conditions, (I) increased the respiratory quotient,  $Q_{CO_3}^{O_2}$ , and absolute Pasteur effect of melanoma.  $Q_{O_2}$  (respiration) never increased, but sometimes decreased. The  $Q_{CO_2}^{N_2}$  of tumor slices of melanoma-bearing mice exposed to temperatures of 35 of 40° was lower than that of slices from mice exposed to temperatures around 20°. (I) caused an increase in the  $Q_{CO_2}^{N_2}$  of the former slices to a value about that of the latter slices (whose  $Q_{CO_2}^{N_2}$  was affected by (I) only slightly). Prolonged exposure to high temperatures resulted in inhibition of tumor growth and further decline in  $Q_{CO_2}^{N_2}$ .

Action of Some Glycosides on the Central Nervous System. Alibrandi, G., et al. [Atti soc. lombarda sci. med. biol., 8, 146 (1953).]

Local application on the motor area of the dog brain showed that g- and k-strophanthin and thevetin had a high convulsive effect. Gitoxin had little activity; digitoxin, gitalin, and deoxycorticosterone glucoside had none. The effect of strychnine was slightly enhanced by gitoxin, not influenced by gitalin and digitoxin, and impaired by deoxycorticosterone glucoside.

A. E. Meyer (Chem. Abstr.)

Effect of Sodium Dehydrocholate on the oxygen uptake of Liver and Cerebral Cortex Slices of fed and starved rats. Schanker, L. S., and Eisenbrandt, L. L. [J. Pharmacol. Exptl. Therap., 109, 367 (1953).]

Na dehydrocholate (I), 0.00047 M in a medium containing glucose, depressed the O uptake of cerebral cortex slices of fed and starved rats. This depression did not occur in a

Na dehydrocholate (I), 0.00047 M in a medium containing glucose, depressed the O uptake of cerebral cortex slices of fed and starved rats. This depression did not occur in a glucose-free medium. Starvation had no effect on the O uptake of the brain slices. In a glucose-free medium (I) depressed the O uptake of liver slices from fed rats but not liver from starved rats. With glucose added to the medium this depression did not occur with liver from either fed or starved rats.

L. E. Gilson (Chem. Abstr.)

Nucleases in the Cerebrospinal Fluid. (1) Ribonuclease in Normal, Neurologically Normal, and in Pathological Cerebrospinal Fluids. Kovacs, Ernest. [Can. J. Med. Sci., 31, 437 (1953).]

Ribonuclease (RNA-ase) was studied in 800 cerebrospinal fluid samples by the uranyl acetate precipitation technique followed by total acid-soluble P determinations before and after incubation. Normal and neurologically normal cerebrospinal fluids showed low RNA-ase activity, less than 20 per cent. of the substrate being depolymerized in 24 hours. A few specimens showing high values were encountered; I specimen each in acute nasopharyngitis, 25 per cent.; infectious mononucleosis, 28 per cent.; and myositis, 30 per cent. Meningitis cerebrospinal fluids showed a wide range of RNA-ase activity, 0-50 per cent. Poliomyelitis specimens showed uniformly the highest values, 15-52 per cent. This high RNA-ase activity in the case of poliomyelitis paralleled chronologically the chromatolysis of the motoneurons and is of special significance.

A. E. Teeri (Chem. Abstr.)

Brain Biochemistry in Relation to Experimental Epilepsy. The Effect of Experimental Epilepsy upon Oxidation-reduction Processes of the Brain. Kudryavtseva, A. I., and Kudryavtseva, N. G. [Ukrain. biokhim. zhur., 22, 435 (1950).]

Young rabbits were killed 10 minutes, 2 hours, and 24 hours after epileptic seizure caused by an electric current. Ascorbic acid (I) was determined by the method of Birch et al., glutathione (II) by the method of Kvenzel and Vahkold, and catalase (III) by the method of Bach and Zubkova. Alternating domestic current of stepped-up voltage caused 4 to 8 seizures. After 30-40 minutes the biochemical changes were back to normal. No major epileptic seizures were invoked since the central nervous system (CNS) of the animal was never fully exhausted. Results: The H<sub>2</sub>O content of the CNS of rabbits in experimental epilepsy, caused by electroshock, fluctuated within the normal range; (I), (II), and (III) increased sharply, pointing to increased oxidation processes in the animal brain. Increased contents of (I), (II), and (III) were observed not only directly after the seizure, but also after 2 hours and 24 hours. Conclusions: The dry residue contents of different parts of the rabbit brain in experimental epilepsy fluctuate within the normal; (III) activity in the cerebral hemispheres is increased; total and reduced (II) contents in the cerebral hemispheres are considerably increased, whereas oxidized (II) is decreased. After the experimental seizure (I) increases in the hemispheres and brain stem The following values were found. Normals: average dry residue in percentage: cerebral hemispheres 20·7, cerebellum 23·0, brain stem 26·8; (III) in mg. of H<sub>2</sub>O<sub>2</sub>/g. of tissue: cerebellum 105·6; (I) in mg. percentage: cerebral hemispheres 19·0, cerebellum 22·9, brain

stem 13.6; (II): cerebral hemispheres, total 1.20, reduced 0.71, oxidized 0.29. Experimental epilepsy: after 10 minutes: average dry residue in percentage: cerebral hemispheres 20·60 per cent., cerebellum 22·99, brain stem 26·98; (III) in mg. H<sub>2</sub>O<sub>2</sub> per g. of tissue: 188·1 in cerebral hemispheres; (I) in mg. percentage: cerebral hemispheres 22·35, cerebellum 26·43, brain stem 14·98; (II) total in cerebral hemispheres 1·65, reduced 1·48, oxidized 0·17; after 2 hours: average dry residue: cerebral hemispheres 20·20, cerebellum 23·41, brain stem 26·07; (III) 170.8 in cerebral hemispheres; (I) cerebral hemispheres 23.48, cerebellum 29.13, brain til) 170-3 in Cetebral hemispheres, (1) Cetebral hemispheres 23-48, Cetebral 129-13, brain stem 16-32; (II): 1-72, 1-53, 0-18, respectively; after 24 hours: average dry residue: cerebral hemispheres 20-60, cerebellum 23-39, brain stem 26-52; (III) 172-2; (I) cerebral hemispheres 22-44, cerebellum 26-27, brain stem 15-58. (II): 1-57, 1-45, 0-12, respectively.

CLAYTON F. HOLOWAY (Chem. Abstr.)

Mechanism of Action of Chemical Substances at Nerve Endings and the Part Played by Peripheral Ganglia. Burn, J. H. [Acta Physiol. Scand., 29, 40 (1953).]

The increased sensitivity towards acetylcholine of the denervated sphincter iridis is apparently due to a loss of cholinesterase. It was also found that the denervated nictitating apparently due to a loss of cholinesterase. It was also found that the denervated nictitating membrane is hypersensitive to noradrenaline because there is less amine oxidase available to destroy it. The same holds true for adrenaline since hypersensitivity to noradrenaline is closely correlated with hypersensitivity to adrenaline. From the effects on the normal and denervated nictitating membranes (studied in the spinal cat) sympathomimetic amines fall into 3 distinct groups. First, the simplest amine, phenylethylamine (also derivs. with CH<sub>3</sub> group attached to  $\alpha$ -C or OH group in p-position in the ring) and tyramine act by competing for the enzyme, while phenylisopropylamine or its N-methyl derivs. inhibit the enzyme at the sympathetic nerve endings. The second group have an OH attached to the  $\beta$ -C of the side chain and act both by inhibiting or competing with the enzyme and by combining with the recentors both by inhibiting or competing with the enzyme and by combining with the receptors. Ephedrine acts partly on the nictitating membrane and partly by inhibiting amine oxidase. The third group of sympathomimetic amines, which all contain 2 OH groups in the 3,4 positions in the ring, do not compete for the enzyme but may suppress the release of transmitter. S. Morgulis (Chem. Abstr.)

Action of Succinylcholine and Curare on the Muscle Spindles. Granit, Ragnar, et al. [Acta Physiol. Scand., 29, 86 (1953).]

The quaternary ammonium base (succinylcholine iodide) has a transient blocking effect on neuromuscular transmission. It is a powerful and selective activator of muscle spindles leaving the Golgi organs intact. Even after the large and small fiber motor end-plates are blocked by curare, succinylcholine can still activate the spindles.

S. Morgulis (Chem. Abstr.)

The Structure of Brain Sphingosine. Kiss, József, and Bánfi, Dezsö. [Magyar Kém. Fólyóirat, **59,** 232 (1953).]

Natural sphingosine was converted by ozonolysis into  $\alpha$ ,  $\gamma$ -dihydrozy- $\beta$  aminobutyrolactone. The latter was then converted into threoninol or into a related compound of known configuration. Aminotetrose was isolated in form of its dinitrophenyl osazone among the decomposition products of the ozonolysis of diacetylsphingosine. Aminotetronic acid obtained at the ozonolysis of triacetylsphingosine was separated in a crystallized form as its well defined lactone HCl. ISTVÁN FINÁLY (Chem. Abstr.)

Influence of Citrate and Choline Citrate on the Anaerobic Synthesis of Acetylcholine. Fuchs, U., and Keiss, H. [Klin. Wochschr., 31, 951 (1953).]

Choline acetylase from brain extract produces the same amount of acetylcholine from citrate as from acetate. Choline citrate is as effective as choline and citrate. Citrate is not only a source of acetate but also binds the Ca++ ions, which activate cholinesterase.

ERICH HEFTMANN (Chem. Abstr.)

Pentoses in the Blood, Urine, and Spinal Fluid in Patients with Head and Facial Injuries. Masturzo, M., and Negro, L. [Boll. soc. ital. biol. sper., 29, 255 (1953).]

Normal persons showed in 46 per cent. presence of pentoses in the blood with an average of 1.38 mg. in 100 cc. and a maximum of 4.5 mg. In 18 cases of head injuries, 67 per cent. had pentose in the blood with an average of 2.63 and a maximum of 9.5 mg. Pentoses were found in the urine of the controls in 84.6 per cent. with an average of 6.01 and a maximum of 15 mg. The patients showed pentoses in the urine in 94.5 per cent. with an average of 8.63 mg. and a maximum of 17.5 mg. The spinal fluid of the injured persons gave mostly lower, but in a few cases higher, values than the blood. A. E. MEYER (Chem. Abstr.)

Adrenal Cortical Function in Chronic Schizophrenia (Stress, Adrenaline Test, Adrenocorticotropic

Hormone Test). Faurbye, Arid, et al. [Acta Endocrinol., 8, 215 (1951).]
In schizophrenics and normal controls the adrenal function has been investigated by means of (1) stress, (2) adrenaline test, (3) adrenocorticotropic hormone (ACTH) test. The ACTH test and the adrenaline test gave uniform and clear responses in all normal controls, but in schizophrenics the responses were uneven and there was a far greater individual variation than in the normals. It is concluded that there is a slight relative adrenal cortex insufficiency

in the chronic schizophrenic, but it is uncertain whether this insufficiency is an original constitutional trait which facilitates the manifestation of schizophrenia or whether it arises simultaneously with the disease as a result of a provoking stress, secondary to the psychosis caused by inactivity, or as part of a compled metabolic disturbance which is the cause of the psychosis or accompanies it. E. P. HALPERN (Chem. Abstr.)

Allergy to Estrone in Cases of Migraine, de Wit, J. C. [Acta Endocrinol., 5, 173 (1950).]

An investigation was made in 70 cases of migraine, and it was found that in 42 cases (60) per cent.) the attacks were related to the menses. Of these, 39 (93 per cent.) had an allergic reaction to estradiol benzoate (in oil) and estrone (in oil and water). Eleven women of this group had an attack of migraine together with the allergic reaction. In 28 cases where there was no relation between the onset of the attacks and menstruation, there was no allergic reaction to the estrogens. E. P. HALPERN (Chem. Abstr.)

Epilepsy and Endocrine glands. II. Influence of Cortisone on Predisposition to Experimental Reflex Epilepsy in the Dog. Pasolini, F. [Boll. soc. ital. biol. sper., 28, 298 (1952).]

Althqugh deoxycorticosterone acetate inhibits Anantea epilepsy in dogs, cortisone

increases it, possibly by increased water retention. There is biological antagonism between the 2 compounds.

M. Elliott (Chem. Abstr.)

The Effect of Electric Shock on the Adrenals of the Rabbit. Pekkarinen, A., et al. [Acta Endocrinol., 10, 167 (1952).]

Electric shock given to 9 rabbits on 10 successive days increased the size of the adrenals, decreased the concentration of adrenaline and of cholesterol, while the ascorbic acid remained unchanged. The response of individual animals showed considerable variation.

H. B. COLLIER (Chem. Abstr.)

Mode of Action of Acetylcholine. Mode of Action of Biologically Active Substances. Zupančič, A. O. [Acta Physiol. Scand., 29, 63 (1953).]

It is assumed that the receptive protein is identical with (ChE) (cholinesterase) which combines with free ester mols. (ACh) released from the inactive form existing in the tissues. This results in stimulation with subsequent hydrolysis to inactive compounds while the (ChE) is ready to react with more (ACh). A distinction is made between the receptive (R) (ChE) which is essential for (ACh) action, and barrier (ChE) of the interstitial fluid which interferes with the (ACh). The stimulating effect of stable choline esters indicates that this must be produced by combination with (RChE) and not by a process of hydrolysis. In the leech muscle it was found that the (ChE) of the interstitial fluid is of the nonspecific type, whereas the muscle enzyme proper is acetylcholinesterase and is roughly 10 times more active. The potentiating influence of eserine is attributed to this distribution, and this view is supported by the observation on the frog sartorius muscle with negligible interstitial fluid (ChE) activity which cannot be markedly sensitized to (ACh) action by eserine. The hypothesis that cell receptors excitable by (ACh) are identical with (RChE) is extended to other biologically active substances and it is assumed that these produce their specific effects by acting on the enzyme which inactivates them. Thus, the cell receptors for adrenaline are thought to be identical with monamine oxidase (MO). Ephedrine (a methylated amine) is known to be an (MO) inhibitor; progesterone, which prevents the stimulating action of adrenaline on the rabbit uterus, strongly inhibits (MO) in vitro. Similarly, cell receptors for histamine would be expected to be identical with tissue diamine oxidase (DO), and many antihistaminic drugs (antistine, benadryl) were found to be powerful inhibitors of (DO). Likewise, the rat uterus, which is very poor in (DO), is not stimulated by histamine. According to the hypothesis, CO<sub>2</sub>-sensitive structures would be identical with carbonic anhydrase (CA). Cyanide is a reversible inhibitor of (CA) and also stimulator of chemoreceptors. Lobeline is regarded as the most potent stimulator of chemoreceptors and is a strong inhibitor of (CA) in vitro. Nicotine, also a strong stimulator of chemoreceptors in low concentrations, probably acts on (ChE), and in spite of its close pharmacological similarity to lobeline, does not inhibit (CA).

S. Morgulis (Chem. Abstr.)

Reducing Properties of Muscle Tissues and Cerebral Hemispheres under Various Functional Conditions of the Organism. Lakhno, E. V., and Chagovets, R. V. [Doklady Akad. Nauk. S.S.S.R., 91, 133 (1953).]

Tissues of rabbits were examined as to their reducing properties (with methylene blue as the reagent). A single stimulation of muscle through the skin over 1 hour led to considerable decline of the reducing properties of the tissue and reduced activity of dehydrogenases of glutamic, hydroxybutyric, lactic, and malic acids. Experimental training of the muscle leads to some increase of the reducing properties and enzymic activity. The study of the gray and white matter of front and mid-parts of the brain was made similarly. After 1-hour stimulation (induction current) the reducing properties of the gray matter and the white matter lying directly below the former were reduced by 20-40 per cent.; after a 2 hour rest the decline was somewhat normalized and was noted even after 17 hours' rest. Experimental training over 2 weeks led to a 56 per cent, increase in the reducing properties of the gray matter. Narcosis by barbiturates lowers the dehydrogenating properties of both gray and white matter (30-40 per cent. and 20-25 per cent., respectively). Electrical stimulation of narcotized animals led to a higher reducing ability of the hemisphere that was being stimulated (difference of some 30 per

cent.), indicating that under narcosis the effect of stimulation or irritation is more localized. Infiltration block of the spinal area of a rabbit with procaine while the animal was under narcosis, followed by electrical stimulation of the hind leg muscle for 1 hour, led to no detectable difference in the reducing properties of the 2 hemispheres.

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

Protein Analysis of the Cerebrospinal Fluid by Photoelectrical Interpretation of the Xanthoproteic Reaction. Duensing, F. [Med. Klin. (Berlin), 44, 740 (1949).]

The photoelectrical method used permits better discrimination between normal and

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

Silver Impregnation of Nerve Fibers. Peters, A. [Nature, 171, 613 (1953).]

Blocking of various end-groups of protein suggests that the Ag impregnation of nerve fibers is due chiefly to the combination of histidine groups with the metal and confirms the fibers is due chiefly to the combination of histidine groups with the metal and commins the recent work of Grassman and Kursch. Blocking of amine, carboxyl, sulfhydryl, and disulfide groups did not decrease the intensity of staining, aldehyde groupings are not present (negative Feulgen test) in alcohol-fixed material, and extraction of nucleic acids with trichloroacetic acid did not affect the impregnation, leaving the ring-containing amino acids, tryptophan, tyrosine, and histidine to be considered. Use of 2,4-dinitrofluorobenzene, which blocks tyrosine and histidine, greatly reduces staining. When the impregnation was carried out for 17 hours in AgNO<sub>2</sub> solution buffered over the range pH 4·0-9·0, it was found that very little Ag was taken up below pH 7; but above this value the amount increased rapidly to pH 9, suggesting the combination of Ag with the NH groups of histidine, which has a pK value of 6-7 (the the combination of Ag with the NH groups of histidine, which has a pK value of 6-7 (the pK of tyrosine is 10). Ag impregnation of smears of hemoglobin, fibrinogen, pepsin, and protamine showed a descending order of intensity of impregnation, paralleling their histidine, but not tyrosine, content. M. HETRICK (Chem. Abstr.)

Skin Changes and Prevention of Convulsions in Vitamin D<sub>2</sub>-hypervitaminosis in Young Albino Rats. Froehlich, Alfred. [Naunyn-Schmiedebergs Arch. exptl. Pathol. Pharmakol., 219, 512 (1953).]

The reduction of the convulsion-producing effect of acid fuchsin, alopecia, thickening of the epithelium of the head, and inhibition of growth of young rats by excess of vitamin  $D_a$  are interpreted as a consequence of decreased permeability of the tissues. The effect of theophylline which reestablishes the cramp effect is based on an increase of permeability. The formation of a "scull cap" in rats is caused by excretion of  $Ca_3(PO_a)_a$  in the surface of the destroyed skin, secondary to degeneration. Recovery is possible if the admiristration of the destroyed skin, secondary to degeneration. viosterol is interrupted at a proper time. A. E. MEYER (Chem. Abstr.)

Changes in the Distribution of Phosphorus Compounds in the Process of Synthesis of Acetylcholine in Extracts of Brain Tissue. Kometiani, P. A. [Soobshcheniya Aka. Nauk.
Gruzin. S.S.R., 12, No. 1, 17 (1951).]
In rabbit-brain tissue homogenates and in Me<sub>2</sub>CO-formed precipitations from brain

tissue the synthesis of acetylcholine leads to formation of a difficulty hydrolyzable P substance, which appears to be phosphorylcholine, which forms by phosphorylation of choline and not via acetylcholine. Cytochrome c does not stimulate formation of acetylcholine or phosphorylation of choline. G. M. Kosolapoff (Chem. Abstr.)

Histochemical Studies on the Changes of Brain Glycogen Caused by Starvation. Kumamoto, Tetsuzo. [Osaka Daigaku Igaku Zasshi, 5, 553 (1953).]

Ten male rabbits were starved from 6 to 27 days. As the starvation proceeded glycogen (1)

in liver and brain decreased. The rate of decrease in the liver was smaller than that in the brain. In the area postrema, cerebral ventricle, and central canal (I) remained even at the later stage of starvation. The decrease of (I) was quicker in the neocortex than in the archicortex

ITIRO TYUMA (Chem. Abstr.)

Change in Lipides of the Brain under the Influence of Bacillus perfringens. Poverennyl, A. M., et al. [Ukrain. Biokhim. Zhur., 25, 127 (1953).]

Male guinea pigs, 380-420 f., were given intramuscular injections of 0·1 ml. of 15 per cent. CaCl<sub>2</sub>, followed in 2 hours, by the same dose of toxin (lethal in 72 hours). The animals were killed 48 hours later, by introducing air into the heart cavity. The dried tissues, nerve, membranes and brain were extracted with ether, and the brain tissues were again extracted with hot, 96 per cent. EtOH. The lipide content of the brain tissues in the affected animals rose from 10.37 per cent. of the total (fresh) brain weight in the controls to 11.82 per cent. The to 0.2243 per cent. The ether-solution lipide P increased from 0.1345 to 0.1603 per cent. The alcohol solution fraction from 3.02 to 3.7 per cent.; alcohol solution lipide P, from 0.0559 to 0.059 per cent., and galactose, from 0.1107 to 0.1567 per cent. There was no change in the diamino phosphatides. The increase of P in the ether solution lipides might be due to phosphorylcholine, formed at the locus of infection, or in the blood, from the lecithin under the influence of the B. perfringens lecithinase. The great increase of cerebrosides could be considered as a specific reaction of the nervous tissue to the action of the toxin. The calcula-Boris Cutoff (Chem. Abstr.) tions were based on the fresh weight of the tissues.

Experimental Epilepsy Induced in the Rhesus Monkey by the Intracarotid Injection of Diiso-propyl-fluophosphate (DFP). Himwich, Harold. [E. Trans. Am. Neurol. Assoc., 76, 177 (1951).]

Intracarotid injection of diisopropyl fluophosphate (I) in rhesus monkeys produced 3 characteristic parts of a focal seizure: aura, fit, and postconvulsive hemiplegia, or one or two of these parts, depending on dosage used. (I) destroys cholinesterase, (II) and its neurological effects are therefore presumed to be related to the accumulation of acetylcholine in the brain. (II) concentration dropped more in the caudate nucleus of the injected side than in any other part of the brain in animals exhibiting forced circling after (I) injection.

MARION HORM PESKIN (Chem. Abstr.)

Metabolism in Slices of Brain Cortex. The Level of Adenosine Triphosphate and its Changes Under the Influence of Glutamic Acid. Ac, G., Balaz, R., and Straub, F. B. [Ukrain. Biokhim. Zhur., 25, No. 1, 17 (1953).]

Examination of brain-cortex slices prepared from guinea pig and rat specimens showed that immediate freezing of the head in liquid air leads to an adenosine triphosphate (ATP) that immediate freezing of the head in liquid air leads to an adenosine triphosphate (ATP) level of 1.5 mg./g.: during the customary 5-10 minutes delay in freezing necessitated by preparation of the slices, this level declined to 0.2-0.3 mg./g. Shaking the specimens at 38° in Krebs solution in the presence of glucose and a 95 per cent. 0<sub>3</sub>-5 per cent. CO<sub>3</sub> mixture led to an increase of ATP to 1 mg./g., which was maintained for 1 hour. Under anaerobic conditions, products of dephosphorylation of ATP appeared. If glucose was replaced by glucose 6-phosphate and fructose 1, 6-diphosphate, synthesis of ATP did not take place, possibly because of impermeability of the tissue cells to the phosphorylated substances. Succinic, malic, glutamic, lactic, and pyruvic acids also increased the rate of respiration of brain tissue, but the level of ATP achieved in their presence was only 50 per cent of that attained with glucose the level of ATP achieved in their presence was only 50 per cent. of that attained with glucose. NaF (0.01M) arrested synthesis of ATP; 2,4-(0.1N)<sub>2</sub>C<sub>4</sub>H<sub>3</sub>OH increased respiration and lowered the ATP level, possibly by repression of Pasteur effect. Simultaneous use of glucose and glutamic acid raised the ATP level only by 0.5 mg./l. if the glutamic acid concentration was 0.01M; a lower concentration led to decreased synthesis of ATP. Of the acids tested, only aspartic acid had a slight possible effect. The repression ATP formation with low levels of glutamic acid was found to be reversible upon addition of pure glucose. When glutamic acid was added to the system, the latter showed increased respiration. The decrease in ATP may be the result of oxidation of glutamic acid—a process energetically favored over glucose oxidation. Aerobic glycolysis caused by glutamic acid was feeble and slow. The glutamic acid consumed by the tissue appeared as glutamine, the concentration of which reached a maximum within 15 minutes and remained at this level indefinitely. G. M. K. (Chem. Abstr.)

Specificity of Pigeon Brain Acetocholine Esterase. Whittaker, V. P. [Biochem. J., 54, 660

(1953).]
The "true" cholinesterases of erythrocytes, brain, and cobra venom act not only on acetylcholine and some other esters but also on a wide range of noncholine esters. Of the noncholine aliphatic esters so far studied 3,3-dimethylbutyl acetate is most rapidly hydrolyzed. The phylogeny of the avian brain is discussed. The greater part of the forebrain represents a development of striatal tissue from which the mammalian basal ganglia are derived. The higher proportion of this striatal tissue in the avian forebrain accounts for its relatively higher cholinesterase content compared with the mammalian brain. However, this does not account for the high activity of the optic lobes, cerebellum, or the brain stem for which a low proportion of fiber tracts in the avian brain may be responsible. The uneven distribution of the acetylcholine-acetocholinesterase-choline acetylase system in various synaptic areas leads to the concept of cholinergic and noncholinergic type of synaptic transmission in the mammalian brain. It is suggested that the central nervous system of birds possesses a larger proportion of cholinergic synapses.

S. Morgulis (Chem. Abstr.)

The Proportion of Phosphatase Activity Demonstrable in the Brain by Histological Techniques. Pratt, O. E. [Biochem. J., 55, 140 (1953).]

The histological sites in brain, where adenosine triphosphate, adenosine 5-monophosphate, thiamine pyrophosphate, and glycerophosphate are hydrolyzed by acid and alkaline phosphatases, present characteristic differences. The preferential suppression of each reaction by suitable inhibitors and the difference in conditions required indicate that these are distinct enzymes. The histological study of phosphatase activity is made possible by precipitations of inorganic P at the site of its formation in the presence of Pb or Ca ions, producing colored compounds. The activities of acid and alkaline phosphatases, 5-nucleotidase, adenosinetriphosphatase, and thiamine pyrophosphatase are of the same order of magnitude in frozen, dried, paraffin-infiltrated brain tissue or in fresh tissue. The staining represents a high proportion of the tissue. Pyrophosphatase activity in the histological preparations was negligible, probably because of the high solubility of this enzyme in saline media.

S. Morgulis (Chem. Abstr.)

Changes in Oxygen Consumption and Radio-Iodine (Iodine<sup>181</sup>) Uptake Following Hypothalamic Lesions in the Albino Rat. Beattie, J., and Chambers, R. D. [Quart. J. Exptl. Physiol., 38, 75 (1953).]

Bilateral lesions in the caudal hypothalamus of albino rats designed to sever the efferent pathways from the hypothalamic nuclei bring about a transient in O consumption of about

7 per cent. 24 hours after infliction of the lesions followed by a fall of about 10 per cent. of the control value 72 hours after the operation. This low O consumption remains constant for as long as 13 days. (I)181 uptake by the thyroid gland over a period of 4 hours was not significantly different from that of a control group irrespective of the time after the lesions were inflicted. The histological structure of the thyroid gland 7 and 14 days after the lesions were made indicated that the thyrotropic hormone production was somewhat increased. The fall in O consumption was not related to body weight or body-temperature changes. It may be caused by the withdrawal of hypothalamic control of the rate of secretion of adrenaline.

RACHEL BROWN (Chem. Abstr.)

Changes in Blood Glucose Levels after Hypothalamic Lesions. Beattie, J., and Chambers, R. D. [Quart J. Exptl. Physiol., 38, 87 (1953).]

Section of the efferent hypothalamic pathways to the brain stem produces a fall in resting blood glucose level of about 38 per cent. below normal. Injection of a standard dose of insulin produced after 30 minutes the same fall in blood glucose concentration in rats with hypothalamic lesions as in normal animals.

RACHEL BROWN (Chem. Abstr.)

Cofactor and Metal Requirements of Brain Mitochondria. Christie, G. S., et al. [Proc. Roy. Soc., B141, 523 (1953).]

The survival of isolated brain mitochondria was measured by determination of the rates

of oxidation of substrates of the tricarboxylic acid cycle and the processes of oxidative phosphorylation. The survival time was short but was prolonged by addition of certain soluble factors: adenosine triphosphate, coenzyme (I) glutathione, Co, and a new factor. Co was relatively inactive in the absence of glutathione, and glutathione was inert in the absence of Co. The new factor resembled glutathione in this respect. Even in combination these 3 factors required the presence of adenosine triphosphate and coenzyme I for exertion of their full effect. Cu antagonized Co, but its inhibitory effect was abolished by increasing the concentration of Co. These coenzymes are ineffective unless added to the mitochondria at the start of incubation. They apparently contributed toward the preservation of the integrity of the mitochondrial particles. JOSEPH S. HEPBURN (Chem. Abstr.)

Hexokinase in Various Areas of the Brain and in Various Functional States. Palladin, A. V., and Polyakova, N. M. [Doklady Akad. Nauk. S.S.S.R., 91, 347 (1953.)]

In narcotic sleep there is observed a somewhat lowered activity of hexokinase along with a rather high level of carbohydrate metabolism in the brain, but the level of carbohydrate consumption is lowered. The greatest hexokinase activity in dog brain is found in the gray matter of the cerebrum, followed by cerebellum, medulla, the white matter of the cerebrum, and finally the spinal cord.

G. M. Kosolapoff (Chem. Abstr.)

Effect of Cerebral Cortex on Carbohydrate Metabolism in the Skin. Lavrov, A. P., et al. [Vestnik Venerol. i Dermatol., No. 3, 3-5 (1953).]

Sugar loading of a rabbit followed by narcosis (amytal) does not cause an increase of

sugar content in the skin and produces only a slight rise in blood sugar. On wakening the sugar G. M. Kosolapoff (Chem. Abstr.) values approach normal.

The Permeability of the hemato-encephalic Barrier to Trypan Blue, especially during Acute Oxygen Deficiency. Eich, Jakob and Woermers, Kurt. [Deut. Z. Nervenheilk, 164, 537 (1950); Chem. Zentr., 1951, (1) 2309.]

An O deficiency of the brain was induced in 35 white rats weighing 90-180 g. and in

22 cats 5-10 weeks old by subjecting the animals to low-pressure treatment. During narcosis a 1-2 per cent. trypan blue solution was injected into the arterial vascular system of the brain. Examination of frozen sections of the brain revealed no differences between the animals which had been subjected to the low pressure treatment and the controls. Various conditions may account for the fact that even the brains of the controls appeared to be stained, although, actually none of the dye had passed the hematoencephalic barrier intravitally. The barrier remained impermeable even in cases of acute O<sub>2</sub> deficiency. It shows the same stability towards histamine in cases of CO poisoning. The hemato-encephalic barrier is damaged only by experimental conditions which affect the endothelium of the blood vessels of the brain. This can result, e.g. from injection of alcohol. Localization of the hematoencephalic barrier in the endothelium of the blood vessels of the brain is, therefore, assumed

M. G. Moore (Chem. Abstr.)

The Role of the Hypothalamus in the Control of Thyroid Function. Greer, Monte A. [J. Clin. Endocrinol. and Metabolism, 12, 1259 (1952).]

Apparently the pituitary gland of the rat secretes 2 thyrotropic factors, a "growth" factor and a "metabolic" factor. The maintenance of the size of the thyroid is evidently dependent on the presence of a normal functional pituitary-hypothalamus relationship. If the hypothalamus relationship. If the hypothalamus relationship. hypothalamus is destroyed by electrolytic lesions or is separated from the pituitary, the thyroid does not undergo hyperplasia when the animal is given thiouracil. However the thyroid is able to maintain an approximate normal (I) metabolism even when the influence of the hypothalamus has been removed. Both the growth factor and the metabolic factor seem to be regulated, at least in part, by the level of circulating thyroid hormone. Although the exact mechanism is unknown, it is possible that the hypothalamus may exert either a neural or a neurohumoral control over the growth factor. N. R. STEPHENSON (Chem. Abstr.)

Developmental Brain Metabolism. Effects of Cortisone, Anoxia, Fluoracetate, Radiation, Insulin, and other Inhibitors on the Embryo, Newborn, and Adult. Hicks, Samuel P. [Arch. Pathol., 55, 302 (1953).]

Enzyme inhibitors were given to newborn adult, and pregnant rats and mice, and the lesions in the nervous system were described. Newborn animals, which survived anoxia for long periods, showed almost no brain damage. Glycogen decreased in the heart and liver, and probably in the brain-stem neurons. Iodaocetate, given before the anoxia, caused death within 3 minutes, although controls in air showed no lesions after 24 hours. Fluoride and insulin were also, but somewhat less, effective. Chlormercuribenzoate, oxophenarsine-HCl and cortisone had no effect on anoxic survival. Insulin produced hypoglycemia and necrosis of the brain-stem neurons in newborn animals, but no convulsions. In pregnant animals, hypoglycemia did not selectively damage the fetuses, though the mother showed cerebral damage. Cortisone or corticotropin in newborn animals caused considerable necrosis of the neuroblasts in the outer cortical zones, and repeated doses late in pregnancy caused wide-spread damage. Cortisone, corticotropin, testosterone, and diethylstilbestrol caused occasional neuron necrosis in the striatum or cerebral cortex, also hyperchromicity of nuclei and cyto-plasm followed by some disintegration of nuclei and actual necrosis of oligodendroglia. These changes resemble those seen after heavy doses of ionizing radiation. The combination of chlormercuribenzoate, iodosobenzoate, porphyrindin, oxophenarsine-HCl and iodoacetate caused widespread necrosis of neuroblasts in the fetus, but the combination of the last 2 failed to produce selective damage. From these experiments it appears that the neurectoderm is very resistant to metabolic poisons. The neuroblast resists anoxia and hypoglycemia but is affected by sulfhydryl reagents, steroids, and fluoroacetate. The neonatal neuron is vulnerable to agents affecting glucose metabolism, but retains the sensitivity of the neuroblast to steroids and fluoroacetate. The adult neuron is not susceptible to the agents which injure the neuroblast. M. L. C. BERNHEIM (Chem. Abstr.)

The Role of Cholinesterase at the Myoneural Junction. Barnes, J. M., and Duff, Janet I. [Brit. J. Pharmacol., 8, 334 (1953).]

The response of the rat phrenic nerve-diaphragm to indirect stimulation underwent a succession of changes as its cholinesterase (I) was inhibited by diethyl p-nitrophenylphosphate (II). It was impossible to prevent the response to single stimuli even with high concentrations of (II), though the response to a tetanus failed. Both true and pseudo-(I) were present in rat diaphragm and they responded to inhibitors in the same way as does (I) of other tissues. Fasciculations and enhanced response to single stimuli took place while (I) activity was reduced 50-90 per cent. The power to sustain a tetanus disappeared when only 10 per cent. of the cholinesterase remained but reversal occurred on removing the inhibitor but before appreciable (I) had time to be released from inhibition.

RICHARD F. RILEY (Chem. Abstr.)

Carbon Dioxide and Cortical Spike Frequency. Gellhorn, E., and French, L. A. [Arch. intern. pharmacodynamie, 93, 427 (1953).]

In the cat brain, unilateral separation of the cortex from the underlying structures causes a reversal of the effects of hypercapnia, so that concentrations of 10-35 per cent. CO<sub>2</sub> reduce the frequency of topically induced strychnine spikes on the isolated side. This seems to be due to the elimination of the excitatory effect of CO<sub>2</sub> on the hypothalamus.

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

## 2. Pharmacology and Treatment

Action of Tetraethylthiuram Disulfide (Antabuse) on Glucose Metabolism. Maldonado, Adriana Tapia. [Tésis quím., Univ. Chile, 3, 135 (1951).]

Antabuse had no influence on the glycemic curve after glucose ingestion. The pyruvic acid in the blood showed normally a marked increase within 30 minutes after glucose ingestion with return to normal at the end of the 1st hour. This temporary peak was abolished and in a few instances reversed. The increase in blood aldehyde was delayed but the change was not statistically significant. A. E. MEYER (Chem. Abstr.)

Convulsive Threshold Values to Parenterally Injected Pentamethylenetetrazole in epileptic Monkeys. Chusid, Joseph G., et al. [J. Appl. Physiol., 6, 139 (1953).]

The convulsive threshold to the rapid intravenous injection of 10 per cent. metrazole (I) was 2.9-6.3 mg./kg. in 70 per cent. of 16 monkeys made epileptic by treatment with alumina cream. In control monkeys the threshold was 8.5-29 mg./kg. Intramuscular (I) injections of 8-28 mg./kg. produced motor convulsions, usually focal in onset, in all epileptic monkeys, while none of the controls convulsed with dosages of up to 44 mg./kg., and only 2 of 7 showed convulsions at 48 mg./kg. The convulsive response of 16 epileptic monkeys to 16 mg./kg. was similar whether administered subcutaneously or intramuscularly.

THERESA MCKEE (Chem. Abstr.)

Convulsive Thiobarbiturates. Richards, Richard K. [Current Researches Anesthesia & Analgesia, 30, 348 (1951).]
Sixteen 5,5 substituted thiobarbiturates were studied in mice, rabbits and monkeys.

Mixed sedative and convulsant activity of many of the compounds was observed in mice. In rabbits the convulsive properties became more pronounced. In monkeys almost all of the compounds produced sleep. Subconvulsive doses of most of the convulsant barbiturates protected mice against metrazole convulsions.

KARL F. URBACH (Chem. Abstr.)

Penetration of Procaine into the Brain and Convulsive State. Garattini, S., and Genovese, E. [Atti soc. lombarda sci. med. biol., 8, 17 (1953).]

Metrazole shock causes a higher concentration of procaine in the brain of guinea pigs after intravenous administration of the latter than occurs normally. Electroshock does not have this effect. In strychnine convulsions the effect varies with the severity of the shock.

A. E. MEYER (Chem. Abstr.)

Effect of Hexamethonium Bromide on the Cerebral Circulation in Hypertension. Dewar, H. A., et al. [Brit. Med. J. (II), 1017 (1953).]

In 6 patients in whom a mean drop of 30 per cent. in arterial pressure was induced with hexamethonium bromide, there was no significant change in mean cerebral blood flow. In 4 of these patients the rate of cerebral O utilization was measured and found to be unaltered by the treatment.

MARSHALL E. DEUTSCH (Chem. Abstr.)

Synergy between Phenobarbital and Benadryl as Anticonvulsants. Agolini, G., et al. [Atti soc. lombarda sci. med. biol., 8, 123 (1953).]

Small doses of benadryl enhance the phenobarbital preventive action against metrazole convulsions. High doses of phenobarbital improve the prevention of nicotine convulsions by benadryl.

A. E. MEYER (Chem. Abstr.)

Cerebral Sugar Metabolism During Narcosis. Fregni, R., et al. [Atti soc. lombarda sci. med. biol., 8, 135 (1953).]

Administration of deoxycorticosterone acetate or glucoside, ether, or barbiturates causes an increase of carbohydrates in the brain.

A. E. MEYER (Chem. Abstr.)

Convulsive Effect of Possible Metabolites of Isonicotinoy! Hydrazide and their Combinations.

Colizzi, C., and Garattini, S. [Atti soc. lombarda sci. med. biol., 8, 93 (1953).]

Na isonicotinate does not produce convulsion but the acid amide causes late convulsions

Na isonicotinate does not produce convulsion but the acid amide causes late convulsions when given in large doses. NH<sub>a</sub>Cl is convulsant in quantities which could be present if both N atoms of the isonicotinoyl hydrazide (I) were transformed into NH<sub>a</sub>. Hydrazine can give late convulsions but only at doses higher than can be produced from therapeutic doses of (I). The mechanism by which isonicotinic acid increases the convulsive power of hydrazine is not known.

A. E. Meyer (Chem. Abstr.)

Antagonistic Action of Some Pharmaceuticals towards Convulsions Produced by Isonicotinic Acid Hydrazide (Isoniazid). Cogni, G., and Mihich, E. [Boll. soc. ital. biol. sper., 29, 27 (1953).]

Convulsions following subcutaneous injections of isoniazid can be relieved by administration of luminal, i.e. delay in the appearance of convulsions and postponement of death. Convulsions after injection of isoniazid are probably due to transformation products of the original molecule. Dormison was very potent in preventing convulsions and death produced by isoniazid. Analogous results were obtained by the administration of p-aminohippuric acid alone and together with Na pyruvate. Pyruvic acid facilitates acetylation. Isoniazid combines with pyruvic acid to check acetylation. There is increased facility of elimination of sulfanilamide and p-aminohippuric acid after acetylation.

Frank W. Dann (Chem. Abstr.)

Substances Synergistic and Antagonistic to the Hypnotic Effect of Barbiturates. Colombo, O., and Rovati, V. [Boll. soc. ital. biol. sper., 29, 314 (1953).]

The hypnotic effect of pentothal in rats is markedly augmented by Nevanide (p-amino-N,

The hypnotic effect of pentothal in rats is markedly augmented by Nevanide (p-amino-N, N-diethylbenzamide), even at small doses, although this compound alone has hardly a hypnotic effect in this species. The dinitrile of succinic acid given 1 hour before, abolished pentothal sleep. Thiamine, adenosinetriphosphate, and prostigmine prevent sleep by the barbiturate.

A. E. Meyer (Chem. Abstr.)

Favorable Effect of a Low-Calcium Diet on a Periodic Psychosis. Speijer, N. [Ned. Tijdschr.

Geneesk., 3, 2424 (1949).]

In a patient with periodic psychosis, increased Ca in the blood was associated with the psychotic intervals. On a diet low in Ca, the frequency and severity of the psychotic phases diminished. Application of this observation to other cases is discussed.

W. C. TOBIE (Chem. Abstr.)

The Vitamin B<sub>1</sub> Treatment of Alcoholic Psychoses. Baldi, F. [Studi fac. med. senese, 16, 48 (1948).]

Pharmacology, physiology, and other aspects are discussed.

W. C. TOBIE (Chem. Abstr.)

Serum Cholinesterase After Electroconvulsive Treatment. Laganara, D., and Preziosa, I. [Ann. Bisceglie, 1, 140 (1948).

After electroshock treatment of 30 patients and after seizures in 10 epileptics, serum cholinesterase was greatly increased associated with an increase in acetylcholine. The significance of the increase is discussed.

W. C. Tobie (Chem. Abstr.)