plus" or greater reaction were inoculated with 0·5, 1, 1·5 and 1·5 c.c. of a full-strength filtrate at four-day intervals. The greatest reactions were of a mild systemic type, and occurred after the third dose. One month after immunization three enrollees with plus-minus reactions, who were not immunized, in three different camps had meningococcic meningitis. After immunization of the remainder of the group no further cases occurred. Twenty-six cases of meningitis have occurred in these camps in the past two years. None have occurred in those immunized persons in the same groups in the seven winter months since inoculation. Prior to inoculation there were nine outbreaks of meningitis of one case each, and eleven outbreaks in which the number of cases varied from two to twelve. Only one case occurred in the period of from one month to one-and-a-half years since the immunizations were completed in those twenty camps. T. E. BURROWS.

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5. Pathology and Biochemistry.

Histopathologic Changes in the Brain in Experimental Hyperinsulinism. (*Arch. Neur. and Psychiat., vol. xxxix, p.* 467, *Mar.*, 1938.) *Weil, A., Liebert, E., and Heilbrunn, G.*

The authors found that in rabbits the injection of doses of 200–400 units of insulin was followed by severe damage to the cortical neurones. In those rabbits dying in a seizure there was liquefaction, vacuolation and homogenization of the ganglion cells. In those which survived some months there was marked shrinkage of the cytoplasm and nuclei. In both groups there was diminution in the number of neurones to a marked degree. The changes appear to be the result of intra-cellular anoxæmia.
G. W. T. H. FLEMING.

Lesions of the Brain following Fever Therapy. (*Journ. Amer. Med. Assoc., vol. cix, p.* 2116, *Dec.* 25, 1937.) *Hartman, F. W.*

Decreased oxygen saturation of the blood occurs constantly after fever therapy. Animals having a saturation below 65 volumes per cent. died. Factors producing this anoxæmia are alkalosis, accelerated blood-flow, increased temperature, and increased demand for oxygen by the tissues. The pathological changes resulting from fever therapy are typical of anoxæmia produced in other ways. Anoxæmia may be prevented by the administration of oxygen throughout the fever therapy, and carbon dioxide may be used to counteract the alkalosis and apnoea.
T. E. BURROWS.

Significance of Acetylcholinesterase as well as of Specific Receptors of the Acetylcholine-sensitive Contractile Substrates. (*Skand. Arch. Physiol., vol. lxxviii, pp.* 40–58, 1938.) *Kahlson, G., and Uvnas, B.*

The relation between the acetylcholinesterase and the sensitivity to acetylcholine is very complicated. Even in such perfect objects as the back muscle of the leech or the rectus muscle of the frog, as the experiments with ergotamine and quinine show, the extreme inhibition of the enzymic activity does not necessarily lead to an increased sensitivity to acetylcholine. In the smooth ring muscle of the frog stomach which shows typical acetylcholine contraction none of the powerful enzymic inhibitors augmented the sensitivity, but the weakly inhibiting ergotamine had such an effect. However, the authors do not suggest that there is no relation between the enzymic activity and acetylcholine sensitivity. It is pointed out that acetylcholine is only effective so long as there is a concentration gradient, and as soon as the inside and outside concentrations are equalized it becomes dynamically inactive. The reason that the gastric muscle responds so much more quickly than the rectus muscle or the leech muscle is the more rapid diffusion of the drug into it. In an

easily permeable substrate the inhibition of the enzyme will permit the attainment of a higher concentration, but only in the difficultly permeable muscles will there be an increased sensitivity. But this cannot explain why in muscle one enzyme inhibitor increases the sensitivity markedly, while another, even a stronger inhibitor, does not affect it. The acetylcholine sensitivity can apparently be influenced either by changes in the receptors or in the contractile elements themselves. The experiments with NaF, physostigmine or quinine indicate that the rise in sensitivity is determined by an enzyme-resistant choline-ester. It is further pointed out that it is difficult to understand why the increased sensitivity is caused by physostigmine during narcosis with chloralose or EtOH but not with ether.

S. MORGULIS (Chem. Abstr.).

Mechanism of the Biological Synthesis of Acetylcholine. (*Nature, vol. cxli, p.* 374, 1938.) *Mann, P. J. G., Tennenbaum, M., and Quastel, J. H.*

Stedman and Stedman (*C.A.*, xxxii, *p.* 2200) claim that $AcCH_2CO_2Na$ is involved in the formation of acetylcholine in the brain. It is here stated that more acetylcholine is formed at 18° without $AcCH_2CO_2Na$ than at 45° with it, using $CHCl_3$—extracted brain. It is suggested that the $AcCH_2CO_2Na$ assists in the breakdown of a complex precursor of acetylcholine, but that it is not directly involved in the synthesis of the latter. MARCELLE SCHUBERT (Chem. Abstr.).

The Mechanism of Acetylcholine Formation in the Brain in Vitro. (*Biochem. Journ., vol. xxxii, pp.* 243–61, 1938.) *Mann, P. J. G., Tennenbaum, M., and Quastel, J. H.*

Acetylcholine is present in fresh brain tissue in a combined form which is pharmacologically inactive. A method for the estimation of this precursor of acetylcholine is given. The breakdown of the precursor to give acetylcholine can be effected by shaking with chloroform or by treatment with acid. At room temperature pH 3·0 causes breakdown and at 37° a pH of 6·0–6·5 is sufficient. The complex is stable under neutral conditions at 0°, but less so at higher temperatures. It is synthetised in brain-tissue when the latter is allowed to respire in the presence of glucose, sodium lactate, or sodium pyruvate. No synthesis takes place under anaërobic conditions. The sodium salts of AcOH, succinic, aceto-acetic, -ketoglutaric, -glycerophosphoric and hexosediphosphoric acids cause no synthesis of the precursor, nor did *dl*-glyceraldehyde. Eserine had no effect on the synthesis or breakdown of the complex. The presence of choline or acetylcholine increases the rate of synthesis. The effect of acetylcholine is no greater than that of choline, and its effect is probably due to choline liberated by choline esterase. The effect of glucose, sodium lactate and sodium pyruvate on the synthesis is much greater than that due to acetylcholine. It is unlikely that acetylcholine is first produced and then converted to the precursor by an adsorption process. A provisional scheme for the synthesis of acetylcholine is given. E. W. SCOTT (Chem. Abstr.).

A Basis for the Acetylcholine Action of Choline Derivatives. (*Journ. Pharmacol., vol. lxii, pp.* 430–48, 1938.) *Renshaw, R. R., Green, D., and Ziff, M.*

The duration of activity of a large number of choline derivatives when injected intravenously in the cat was measured and found to be approximately the same for all compounds studied, while the relative rates of inactivation of the same compounds by whole blood varied widely. The duration of depressor activity of a blood-stable compound, ethoxycholine bromide, was prolonged by prior injection of eserine, and to the same extent as that of acetylcholine. A substance with the characteristics of acetylcholine was present in blood drawn from the heart of an animal undergoing infusion of ethoxycholine bromide. It is suggested that the vasodepressant action of the choline analogues mentioned above is due, at least in part, to the liberation of acetylcholine from an inactive complex by a process of cationic exchange adsorption. The possible fate of choline and its analogues injected into the blood-stream is discussed. L. E. GILSON (Chem. Abstr.).