LETTERS TO THE EDITORS

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Acetylcholine and Body Temperature

Glaubach and Pick[1] were the first to find that procaine causes a fall of body temperature. The fall has recently been shown by Peczenik[2] to be greatly increased after adrenalectomy. The work of Dawes[3] in this laboratory on quinidine substitutes led him to point out that quinine, quinidine and procaine antagonize the effect of acetylcholine on many types of tissue. They reduce its effect on the heart and on the intestine, and they reduce its effect on skeletal muscle also (Harvey[4]). Thus procaine, in addition to being a local anæsthetic, reduces the action of acetylcholine in all forms of muscle. Recently, de Elio[5] has shown in this laboratory that procaine shares these properties, not only with quinidine, but also with atropine and with the analgesic 'Pethidine' (demerol), while Dews and Graham[6] have shown that the antihistamine substance 'Neoantergan' shares them too.

We have now tested atropine, benadryl, 'Pethidine' and quinidine to see if they affect the body temperature of mice as does procaine. We have discovered that they do, and that the fall they produce is augmented by adrenalectomy. Since the common property of these substances is that they depress the action of acetylcholine, it becomes probable that the maintenance of body temperature depends on a mechanism in which acetylcholine plays a part, and that the adrenal glands support such a mechanism against the depressant action of substances like procaine.

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Cholinesterase Activity in Cerebro-Spinal Fluid

The published finding of Stedman and Stedman[1], that cholinesterase cannot be detected in cerebro-spinal fluid, appears to be generally accepted, for recent literature contains no account of further investigations in cholinesterase activity.

We have found that the cholinesterase activity of the cerebro-spinal fluid of forty-two human subjects was in each case considerably above the range of the spontaneous hydrolysis of the cholinesters.

The cholinesterase activity was determined manometrically by Warburg's method at 37·5° C., and the result expressed in cubic millimetres of carbon dioxide produced by 1 ml. cerebro-spinal fluid in a period of thirty minutes. 1·6–2 ml. cerebro-spinal fluid, with 0·2 ml. 2 per cent bicarbonate, were put in the main vessel of the ordinary conical containers, and in the side arm 0·2 ml. of the substrate solutions, which consisted of 0·3 *M* acetylcholine, or 0·3 *M* acetylmethylcholine ('Mecholyl'), or 0·06 *M* benzoylcholine, respectively. This procedure was adopted in the light of the recent investigations of Mendel and Rudney and Mendel and Mundell[2].

The cerebro-spinal fluid was obtained from psychotic patients suffering from organic (general paralysis of the insane) and non-organic (mania, schizophrenia) psychoses. The cholinesterase activity of individual specimens varied considerably: substrate acetylcholine, between 6·6 and 28·4; substrate acetylmethylcholine, between 5·4 and 23·6; substrate benzoylcholine, between 2·3 and 6·2.

The relation between cholinesterase activity of cerebro-spinal fluid and blood serum was: with acetylcholine as substrate, 1/90–1/150; with 'Mecholyl' as substrate, 1/8–1/40; with benzoylcholine as substrate, 1/125–1/300.

Specimens of cerebro-spinal fluid from a number of patients were mixed; the cholinesterase activity, using the different substrates, is shown in the accompanying table.

For preparatory reasons, we tried to absorb the cholinesterase by different absorbents: 'Permutit' ('Decalso'), kieselguhr and alumina. The result was negative; no activity was lost by treatment with any of the substances (see table).

	Hydrolysis (mm.³ CO_2 evolved by 1 ml. cerebro-spinal fluid in 30 min.) of			Nitrogen content (mgm./ml.)
	Acetylcholine 0·03 *M*	Acetylmethylcholine 0·03 *M*	Benzoylcholine 0·006 *M*	
Cerebro-spinal fluid mixture (16 patients)	23·6	12·4	4·6	1·18
After treatment with kieselguhr	25·1	11·8	5·2	1·19
After treatment with alumina	22·8	10·3	4·9	1·13
Cerebro-spinal fluid mixture (29 patients)	21·4	10·4	4·3	
After filtering through 'Decalso' column	21·5	9·6	4·6	
After boiling for four minutes	13·7	6·7	2·5	

It seems reasonable to suppose that the so-called true cholinesterase of Mendel and Rudney is the predominant enzyme system present in cerebro-spinal fluid.

We are now investigating possible relationships between the level of cerebro-spinal fluid cholinesterase and various disturbances of brain and mental function.

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Bristol Mental Hospitals. Sept. 1.

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Relation of Intermediary Metabolites to the Lowering of the Potency of Pancreatic Insulin in the Animal System

It has long been felt by several workers that adiposity is connected with the onset of diabetes mellitus. It has previously been reported by us[1] that the intermediary fat metabolites such as β-hydroxy butyric acid, aceto-acetic acid and pyruvic acid, when injected into normal rabbits in the form of their sodium salts, give rise to the condition of hyperglycæmia characterized by decreased sugar