Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Procaine Amide

SIR,—Since our attention was drawn some time ago by Dr. G. E. H. Enderby to the use of procaine amide to augment the hypotensive action of hexamethonium, described by Dr. A. A. Mason and Dr. J. F. Pelmore (*Journal*, January 31, p. 250), we have investigated some of its pharmacological properties. The action of procaine amide has usually been discussed with respect to its direct cardiac action. But, since procaine itself is well known to be able to interfere with ganglionic transmission, a study of the effects of procaine amide on ganglia seemed necessary.

We have found in cats anaesthetized with chloralose: (1) that procaine amide in doses of 15 mg./kg. or more will cause relaxation of the nictitating membrane excited by preganglionic stimulation; (2) that in doses of 15 mg./kg. it will paralyse the slowing of the heart to vagal stimulation; (3) that in doses of 15–30 mg./kg. it does not lessen the depressor effect of acetylcholine or the pressor effect of adrenaline; (4) in doses of 15 mg./kg. or more it reduces the pressor effect of nicotine. In concentration of 20–50 μg./ml. it reduces the contraction of the guinea-pig's small intestine to nicotine without affecting its response to acetylcholine. These observations indicated that procaine amide can interfere with ganglionic function in three ganglia at least, the superior cervical ganglion and the vagal ganglia of the heart and viscera, without modifying the reactions of the effector cells. It remained to determine the mechanism of action.

Procaine amide, 10 mg., injected during perfusion of the cat's superior cervical ganglion caused complete failure of transmission and abolished release of acetylcholine on preganglionic nerve stimulation. With the perfused ganglion, procaine amide antagonized the stimulant effect of acetylcholine on the ganglion. Using the electrical recording of ganglion action potentials, procaine amide was found to be able to reduce these considerably without causing any depolarization of the ganglion. These results show that procaine amide has two actions at the ganglion-inhibition of acetylcholine release, and an antagonism to the effects of acetylcholine. The second of these two actions should, of course, simply sum with that of hexamethonium, if the two drugs are given together. But the interaction of the first action, that of preventing acetylcholine release, with the acetylcholine-antagonizing power of hexamethonium, might present novel features. We find, in fact, that in the cat procaine amide and hexamethonium potentiate one another, and that the effect of a mixture is greater than that expected from simple addition of the two components.

It seems probable, therefore, that this synergism between depression of acetylcholine release and competition with acetylcholine could go some way to explain the clinical synergism observed. The question arises whether any of the hypotensive action of procaine amide can be attributed to a direct cardiac action. Our only evidence on this point suggests that, in the cat, this is not true, since the relative potency of procaine amide to hexamethonium in lowering blood pressure is actually less than its relative potency in relaxing the nictitating membrane.

Procaine amide appears to offer, therefore, a new possibility of supplementing the action of a ganglion-blocking agent with a drug active by mouth, with which it might be possible to attack ganglia at present relatively refractory to such agents.—We are, etc.,

W. D. M. PATON.
J. W. THOMPSON.

London, W.C.1.

A.C.T.H. and Tuberculous Meningitis

SIR,—The results of the treatment of acute disseminated encephalomyelitis with A.C.T.H. by Dr. H. G. Miller (*Journal*, January 24, p. 177) interested me very much, as I am working on similar lines, except that I am applying this treatment in cases of tuberculous encephalomeningitis, against the warning of this author, who supposes that therapeutic use of A.C.T.H. in tuberculous meningitis "might well be disastrous."

My experiments are limited to those cases of tuberculous meningitis in children, treated with antibiotics, which develop acute neurological symptoms in the late period of treatment (after 10 weeks). The clinical behaviour of such cases is very similar to the symptomatology of acute disseminated encephalomyelitis. Here also we observe violent attacks followed by periods of relaxation, and we too suppose that they are caused by attacks of "allergic vasculitis" on the basis of a hypersensitive reaction of altered blood vessels of the brain. Lowered chloride levels in the C.S.F. in such cases suggests that oedema of the brain may follow or accompany the changes in the blood supply. This syndrome occurs in about 50% of our cases of tuberculous meningitis treated with antibiotics. They are refractory to further application of chemotherapeutics and their mortality rate is about 70%. In despair we tried A.C.T.H. in such cases. The effects are very encouraging, especially if A.C.T.H. is applied after previous preparatory administration of intrathecal tuberculin. We give 10^{-7} solution purified protein derivative tuberculin intrathecally every 2–3 days, in successively increasing doses—0.2, 0.4, 0.6, 0.8, and 1 ml.—then 10^{-6} in the same way until a distinct inflammatory reaction in the C.S.F. is provoked as shown by a pleocytosis and increase of protein level. Then the purified protein derivative administration is stopped and A.C.T.H., 15–25 mg., is given intramuscularly four times daily. The mortality rate among children so treated fell from 68% to 33%. In cases of blockade of the circulation of the C.S.F., A.C.T.H. reduces the protein level of C.S.F. and very often re-establishes free communication.

During combined treatment with tuberculin and A.C.T.H. no chemotherapeutics are given.—I am, etc.,

B. HALIKOWSKI,
Paediatric Department of the Tuberculosis Institute.

Warsaw.

"Butazolidin"

SIR,—In your leading article on "Benefits and Dangers of Butazolidin" (December 27, 1952, p. 1401) you commented on the toxic reactions to the drug, particularly emphasizing the risk of damage to the haemopoietic system. The following case may therefore be of interest.

A woman, aged 24 years, who had suffered from rheumatoid arthritis for many years, was given a course of butazolidin, 200 mg. twice a day, from February 9 to February 18. On February 17 she complained of a sore throat and feverishness. A provisional diagnosis of scarlet fever was made and the patient was given a course of sulphadimidine, 1 g. four-hourly, during February 19–23 without any improvement in her condition. She was therefore admitted to hospital on February 24.

On admission the patient was afebrile and was found to have slight inflammation of her fauces, associated with a generalized erythema. A throat swab was taken, but no haemolytic streptococci were isolated. A white cell count on February 25 gave 1,800 cells/c.mm., with 50% polymorphs and 50% lymphocytes. In view of the neutropenia, a further count was done on February 26, which gave Hb 9.2 g.%, red blood cells 4.46 million/c.mm., white blood cells 4,500/c.mm., neutrophil polymorphs 34%, eosinophil polymorphs 3%, lymphocytes 58%, monocytes 5%, platelets 340,000/c.mm. The sore throat persisted for 12 days and the rash for 15, following which there was desquamation. The patient remained afebrile during her stay in hospital. The following white cell counts were done before she was discharged on March 14: March 3, white blood cells, 5,100/c.mm., 44% polymorphs; March 6, white blood cells 4,400/c.mm., 36% poly-