

GANGLION-BLOCKING AGENTS

The growth process of modern therapeutics resembles the ebb and flow of the tide, and in the two papers on ganglion-blocking agents published this week both the ebb and the flow are illustrated. Dr. W. D. M. Paton has written a valuable review, clearly explaining in a cautious and yet hopeful manner the peculiar properties of the different substances which paralyse ganglia: his account is suffused with the optimism which should mark the laboratory worker. But Drs. S. Locket, P. G. Swann, and W. S. M. Grieve describe an investigation which pours cold water on the use of these substances in the treatment of hypertension. They have not failed in the clinician's duty to be objective in assessing their results.

One of the points of special interest in Dr. Paton's review is his suggestion that ganglion-blocking agents may be more effective when the ganglia are transmitting more impulses than normally. When the pre-ganglionic fibres to the superior cervical ganglion are stimulated continuously the effect of hexamethonium becomes greater the longer the stimulation is continued. This, he thinks, may be the reason that doses which reduce hypertension or relieve the pain of gastric ulcer do so without paralysing the small intestine and the bladder. The ganglia which transmit more impulses than normal are paralysed by doses which are ineffective on other ganglia. Another suggestion concerns the postural hypotension which develops in patients given hexamethonium. The fall of blood pressure caused by the intramuscular injection of hexamethonium lasts for periods which rarely exceed two hours. At the end of this time the blood pressure is restored. If, however, the patient stands up he may faint because of a fall of blood pressure which then occurs. The hypotension is promptly remedied by exercise, and Dr. Paton suggests that it may be caused by a pooling of blood in the veins, in which the tone is recovered more slowly than in the arteries. The loss of venomotor tone is, however, counteracted by the increase in venous return which muscular work induces. Very little attention is given at the present time to venomotor tone, though there is evidence of its importance. Perhaps it can be studied by the use of ganglion-blocking agents, though it is difficult to imagine how the duration of their effect on ganglia supplying fibres to the arteries and on those supplying them to the veins can differ.

The clinical results described by Drs. Locket, Swann, and Grieve appear to conflict to some extent with the results of earlier workers to whom they refer in their paper. But this is not very surprising. It

has always seemed unlikely that a substance which has an action of relatively short duration, such as one to two hours, can be profitably used to maintain normal blood pressure throughout the day. The last word in this matter has probably not yet been said. It may be that, as Dr. Locket and his colleagues appear to suggest, the good results which have been reported are due to rest in bed and to the use of the bromide salt of the methonium compounds. Time will show. In the meantime we are all learning much more about ganglia than we knew before.

PROGNOSIS AFTER STREPTOMYCIN THERAPY

Though streptomycin is a curative weapon of vast potentialities the occurrence of relapses, including long-delayed relapses, during or after treatment of tuberculous infections has had the effect of restraining optimism about the likelihood of complete cure. Now that observations based on follow-up surveys are becoming available, a more reliable assessment of the long-term results of streptomycin therapy is possible. A report¹ submitted to the Medical Research Council gave the results of treatment with streptomycin of acute miliary tuberculosis in 25 patients, of whom 19 were aged less than 15 years. The 14 survivors have been followed for over two and a half years. In the U.S.A. Bunn² has continued to observe the survivors out of a series of 100 adult patients given streptomycin for acute miliary infection, meningeal infection, or a combination of both. Twenty-one of these 100 patients were alive 19 to 28 months after completion of treatment. Though the two series differed widely in clinical material they both provide additional evidence that in experienced hands streptomycin offers prospects of healthy survival in some 50% of miliary tuberculous infections. What are the factors which determine response to treatment? Available evidence suggests that prognosis is most serious when the clinical state at the onset of treatment is acute and when response to early treatment is sluggish. A threat of complicating meningitis always exists and may materialize at any time, either during treatment of the miliary infection or after treatment has been stopped. The need is to be constantly on the alert for the earliest evidence of meningeal infection. With this object British and American workers are agreed in advocating early and repeated examination of the cerebrospinal fluid in all cases of miliary tuberculosis.

Meningitis complicating miliary infection necessarily makes for a grave prognosis, but a fatal result is no longer inevitable. Age is an important factor. The conclusions reached by the Ministry of Health³ about the streptomycin treatment of tuberculous meningitis are undoubtedly encouraging. It is to be hoped that the results which have prompted the conclusions will be published in greater detail, more especially in so far

¹ *Lancet*, 1950, 1, 841.

² *Amer. J. med. Sci.*, 1948, 216, 286.

³ *British Medical Journal*, 1950, 2, 413.

⁴ *Ibid.*, 1949, 1, 338.

⁵ *Ibid.*, 1950, 2, 1073.