by the use of different coloured tubes which are available today.

Finally might be mentioned the use of an early tracheotomy in the event of gross respiratory obstruction, or in certain types of respiratory paralysis, whereby the nursing of the patient is facilitated and the evacuation of secretions made more simple and thorough. This is far better done in the early stage of the postoperative period than delayed until it is absolutely essential.

The earlier complications are diagnosed the more easily they respond to treatment. Prophylaxis with antibiotics will help the control of infection. Atelectasis may respond to simple measures, if not, then intubation with suction or bronchoscopic aspiration may be necessary.

The incidence of postoperative headache can be minimized by the use of fine needles and care with the lumbar puncture. The most intractable cases respond to treatment aimed at re-establishing the dynamics of the cerebrospinal fluid. Concerning the postoperative posture following a spinal anæsthetic, it is felt that no great purpose is fulfilled by maintaining a head-low position for twenty-four hours, rather it is considered that the patient should be placed in his most comfortable position if there are no indications to the contrary.

THE TREATMENT OF TUBERCULOUS MENINGITIS WITH CORTISONE AND STREPTOMYCIN

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SINCE THE ADVENT of streptomycin there has been a radical change in the prognosis of tuberculous meningitis which, prior to the streptomycin era, was uniformly fatal. At present the mortality, while showing some variation in different reported series, is probably of the order of 50%. Physicians who have had experience in treating this disease, while encouraged by these developments, have welcomed any therapeutic adjuvant which might be expected to increase the recovery rate. It was early realized that patients with tuberculous meningitis on streptomycin therapy die, not from tuberculous toxæmia, but from mechanical obstruction to the circulation of the cerebrospinal fluid resulting from the accumulation of tenacious exudate and tuberculous granulation tissue within the subarachnoid space.

All the newer therapeutic measures, therefore, have aimed at preventing the formation of tuberculous exudate, its dissolution once it has occurred, or the mechanical circumvention of obstruction to the circulation of cerebrospinal fluid. The earliest of these measures involved the intrathecal instillation of a heparin-streptomycin complex[1] and yielded entirely disappointing results. Cathie's[2, 3] work on the intrathecal administration of streptokinase has seemed to offer distinct promise and his methods are rather widely followed in Great Britain. However, the results of the British workers have not been widely confirmed in Canada and the United States, and there are also some doubts as to the safety of this procedure. A recent report[4] attributes the death of a patient to the intrathecal administration of this enzyme, and this result appears to have been duplicated in one of our own cases. Earlier enthusiastic reports regarding the intrathecal instillation of tuberculin[5] have not been widely substantiated, and this procedure, in our own experience as well as that of others, has failed to prevent a fatal outcome. Neurosurgical procedures,[6] which have aimed at the circumvention of subarachnoid block, have not been enthusiastically accepted in all quarters. Reports have reached us of the occurrence of massive cortical hæmorrhages, apparently resulting from the necessarily frequent trauma attendant on the intraventricular administration of streptomycin by these methods and, in one case with which we have had personal experience, ataxia and epileptiform convulsions have been unfortunate sequelæ.

For at least a year our research group has given consideration, in this connection, to the known ability of cortisone to prevent or modify the inflammatory response to infective agents. This suppression of tissue reactivity has been considered to have a harmful effect upon the healing process in pulmonary tuberculosis;[7 to 10] but it is precisely this effect which is theoretically most desirable in the management of tuberculous meningitis. It has been our reason-

ing that the addition of cortisone to a streptomycin regimen in tuberculous meningitis might be expected to prevent formation or effect dissolution of the tuberculous exudate, an objective which has been as yet largely unrealized. As a corollary, of equal or possibly greater importance, such a result might also be expected to remove barriers which stand between the antibiotic and the infecting agent.

Bearing these factors in mind, we have treated a case of tuberculous meningitis with cortisone and intramuscular streptomycin. To date the results have been so encouraging, in fact dramatic, that we have deemed it advisable to submit this preliminary report.

CASE REPORT

O.B., a 28 year old white female, was admitted to Point Edward Hospital on October 1, 1951 with bacteriologically proved tuberculous meningitis. Treatment was immediately begun with our usual intensive regimen consisting of intramuscular dihydrostreptomycin, 2.0 gm. daily; intrathecal streptomycin, 50 mgm. daily; and oral PAS, 12.0 gm. daily. Although clinical improvement occurred rapidly, there was evidence, within two weeks, of the development of a lumbar intrathecal block. By October 26, 1951, the block had become complete, and it was impossible to obtain cerebrospinal fluid except by the cisternal route. On October 29, 1951 a cisternal puncture was performed and 6,000 units combined streptokinase-streptodornase together with 25 mgm. streptomycin were instilled. That evening the patient's general condition became very alarming. Her skin was cold and clammy and her temperature was subnormal. She was semi-conscious and did not respond to external stimuli. Although her pulse was of fair quality she appeared to be moribund and the last rites of her church were administered. During the next 48 hours, however, she rallied slightly, but still remained in a serious condition. On November 1, 1951, cortisone therapy (Cortone Acetate, Merck)* was begun in a daily dosage of 300 mgm. intramuscularly; intramuscular streptomycin and oral PAS were continued. Within 48 hours the patient showed marked clinical improvement and was able to take food in small amounts and liquids freely. Potassium chloride, 3.0 gm. daily, was added to her therapeutic regimen on November 2, 1951. Cisternal punctures have been performed at weekly intervals and the cerebrospinal fluid thus withdrawn has been examined on each occasion for cells, protein and chlorides. On November 1, 1951, the results were: W.B.C., 898 per c.mm.; protein, 82 mgm. per 100 c.c.; chlorides, 660 mgm. per 100 c.c. There has been a gradual but continued improvement in these findings and, on February 4, 1952 the results were: W.B.C., 22 per c.mm.; protein 34 mgm. per 100 c.c.; chlorides, 740 mgm. per 100 c.c. All attempts to culture tubercle bacilli from the cisternal fluid have been unsuccessful.

The first attempt to re-enter the lumbar intrathecal space was made on December 6, 1951, and on this date a very small amount of yellowish cloudy fluid was obtained. Lumbar punctures were repeated at intervals of two weeks, but it was only on January 17, 1952, eleven weeks after cortisone therapy was begun, that a free flow of spinal fluid was obtained by this route. The patient's clinical condition has continued to improve and she now has no symptoms. One week after the crisis, intra-muscular cortisone acetate was replaced by the oral preparation in a dosage of 200 mgm. daily and subsequently decreased to 100 mgm. daily, on which dose she is at present being maintained. With the exception of slight rounding of the facial contours, which has not been striking since the maintenance dose was begun, no evidence of hypercortisonism has been encountered. Repeated x-ray examinations of the chest have shown no evidence of pulmonary tuberculosis.

*The cortisone for this patient was generously supplied by Merck & Co. (Canada), through the courtesy of Dr. John H. Laurie.

DISCUSSION

It would appear that the outstanding deduction to be made from this case report is that the institution of cortisone therapy proved to be a life-saving measure. Another equally striking feature is the partial resolution of the lumbar subarachnoid block which, in our opinion, should be attributed to the cortisone therapy. If this is actually the case, the implication is obvious that the earlier institution of cortisone treatment would have the much-desired effect of preventing the occurrence of block. The dramatic clinical improvement, which has been maintained to date, is obviously a most desirable result of any form of therapy, and particularly so in a disease in which all the patient's resources must be husbanded for a prolonged period of time. We would also stress the point that, paralleling this clinical improvement, there has been a progressive improvement in the cytological and biochemical findings in the spinal fluid. This has occurred in the absence of intrathecal therapy and, judging from our own experience, is at least equal in degree to that resulting from any intrathecal regimen. This is a highly important consideration, especially where block has already occurred and intrathecal treatment has become impossible except via the cisternal route which, in our experience, is not without danger.

It is of interest that, on admission, this patient showed no evidence of pulmonary tuberculosis and that no such evidence has appeared since the institution of cortisone treatment. It is possible that the presence of associated pulmonary tuberculosis, miliary or otherwise, might give rise to hesitation in prescribing cortisone therapy. It is our opinion, however, that the concomitant administration of full doses of streptomycin and PAS should provide adequate insurance against any such extension of tuberculous disease.

It is quite clear that the present situation provides no assurance that relapse will not occur when cortisone therapy is discontinued. It is our hope, however, that, by very gradual withdrawal of cortisone together with prolonged administra-

tion of streptomycin and PAS, such an exacerbation will be avoided. A progress report, together with results of this form of combined therapy in other cases, will form the basis of a subsequent communication.

It is of interest to theorize as to the cause of the sudden deterioration of this patient's condition immediately prior to the institution of cortisone treatment. There is published evidence, again substantiated by our own experience, that untoward reactions have been encountered following the intrathecal instillation of both streptomycin[11] and streptokinase-streptodornase.[4] Any form of therapy, therefore, which renders unnecessary the intrathecal administration of either agent would appear to constitute an important therapeutic advance.

PROGRESS NOTE

A progress note in April, 1952 shows the patient to be in good health, with no x-ray evidence of pulmonary tuberculosis. Cisternal punctures are within normal limits, except for 10 to 20 W.B.C. Lumbar punctures also show 34 W.B.C., with 280 mgm. of protein and 680 mgm. of chloride.

SUMMARY

1. A case of tuberculous meningitis is reported in which the addition of cortisone to the streptomycin regimen resulted in dramatic and continued improvement in both the clinical condition and the cerebrospinal fluid findings.

2. The partial resolution of an established intrathecal block was apparently accomplished by this treatment.

3. The theoretical considerations underlying the administration of cortisone in tuberculous meningitis are discussed.

NOTE.—In a "Morning Lecture" entitled, "The Clinical Application of Pituitary Adrenocorticotropic and Adrenal Steroid Hormones," delivered at the 1951 Annual Meeting of the American College of Physicians, and later published (*Ann. Int. Med.*, 35: 615, 1951), Dr. Laurance W. Kinsell briefly outlined his experiences in two cases of tuberculous meningitis treated with ACTH. These experiences appear to be quite similar to ours with cortisone.

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AN ARTIFICIAL BILE DUCT*

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A SEARCH OF THE LITERATURE concerning transplantation of skin revealed no record of its application in the reconstruction of tubular structures within the abdomen. In view of the success of MacLean and Gerrie[1] in the replacement of portions of the male urethra by split thickness grafts it seemed reasonable to suppose that skin might be so used, especially in the reconstruction of portions of the biliary tract. Our preliminary report[2] covers the earliest results of this experiment.

Several investigators have studied the fate of buried skin for periods of several years. Peer and Paddock[3] examined specimens of skin buried subcutaneously at intervals of one week to one year. Mair[4] used whole thickness skin grafts in the repair of herniæ in man and studied specimens excised at various intervals after implantation. Uihlein[5] described tissue from an area where skin had been used four years previously in the repair of a hernia. The above reports, concerning the fate of buried skin, include observations which differ from one another although the conditions under which they were made were similar. Mair and Uihlein noted eventual metaplasia of buried skin, whereas Peer and Paddock recorded survival of skin elements over equally prolonged periods. These reports agree, however, in one important respect, that buried skin heals on its dermal aspect to the tissue bed in which it is implanted and acquires a rich vascular supply.

Price and Lee[6] planted free full thickness skin grafts on the anterior serosal surface of the stomach and on the parietal peritoneum near the stomach. Later they implanted these grafts, with their new blood supply intact, in windows in the

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