THE TREATMENT OF CEREBROSPINAL FEVER.

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IN spite of the application of lumbar puncture, no appreciable diminution in the heavy mortality-rate of cerebrospinal fever was apparent until after the adoption of treatment by a specific antimeningococcal serum administered intrathecally. The work of S. Flexner was undoubtedly the most important in establishing this method of treatment, now generally accepted as the most efficient we possess. It is true that in 1914-15, when the disease appeared extensively in Great Britain, and especially amongst mobilized troops, the results of treatment with the antimeningococcal serum then available appeared far from satisfactory. An explanation of this failure gradually came to hand in the recognition that the strains of meningococci responsible for the infection differed in the vast majority of cases from those used in the preparation of the antimeningococcal serum employed in treatment.

Early in 1915, however, M. H. Gordon¹ had begun his bacteriological investigation of cerebrospinal fever, and by means of agglutination and 'absorption of agglutinin' tests was able to differentiate three main groups or 'types' (termed Types I, II, and III) among the meningococci responsible for the outbreak of the disease in England; a Type IV was added later. The objection has been advanced by Eastwood² and others that the grouping of meningococci by serological methods is purely artificial and depends upon the arbitrary selection of particular strains as standards. Nevertheless, the practical value of Gordon's classification is undoubted, and it was of the greatest assistance in dealing with military outbreaks in this country. Since 1915, Gordon's 'types' of meningococci have been regularly employed, notably at the Lister Institute and, later, by S. Griffith at Cambridge, in the immunization of horses for the production of antimeningococcal serum for therapeutic use. As a consequence, therefore, of the improved serum available, the results for 1916 onwards showed a remarkable improvement as regards mortality-rate. A more widespread knowledge of the disease and of the importance of its early recognition has also served to improve the results.

Many excellent sera are now on the market, as, for instance, those of the Lister and Rockefeller Institutes and the Medical Research

Committee serum, which are valent for Gordon's four 'types' and are consequently admirably suited for use in Great Britain. More recently, sera monovalent for each of Gordon's types have been prepared by Griffith in the University Field Laboratories at Cambridge, the object being that, whenever it is possible to determine the infecting 'type' of coccus, the polyvalent serum is replaced by the corresponding monovalent serum.

In addition to serum administration, it is essential that the sub-arachnoid space be adequately drained of its exudate. When serum is given intrathecally, the preliminary lumbar puncture provides the necessary drainage. It is a frequent custom, however, when serum administration is discontinued, to perform no further punctures unless the patient becomes much worse. Formerly, this was also my own practice; but being dissatisfied with the results obtained, especially in cases that tended to run a protracted course, I adopted the plan of following the improvement after a certain period of daily serum administration by a routine daily lumbar puncture until cerebrospinal fluid clear to the naked eye was obtained.

Summary of Treatment Adopted.—Antimeningococcal serum is given intrathecally at the earliest possible moment without waiting for the bacteriological report, the initial dose being 30 to 40 c.c. This amount is then administered daily, or occasionally twice daily, until the clinical improvement is quite definite and undeniable, and organisms, if previously present, have disappeared from the cerebrospinal fluid. Owing to the fact that, occasionally, meningococci may neither be seen in nor cultivated from the cerebrospinal fluid obtained by lumbar puncture when clinical symptoms are well marked, the bacteriological findings are inclined to be misleading if relied upon solely. On post-mortem examination it is not unusual to discover meningococci in the ventricles when they have been absent from the cerebrospinal fluid obtained by lumbar puncture for some days before death.

The minimum period for the continuance of serum administration is four days, no matter how great the improvement in the patient's condition may appear. The dose is usually 30 c.c., excepting when it is only possible to obtain less than this quantity of cerebrospinal fluid; in such a case the fluid withdrawn should exceed the amount of serum injected by at least 5 c.c. A few exceptions to this rule will be mentioned later.

When the clinical improvement is quite decided and meningococci have disappeared from the cerebrospinal fluid, serum administration is omitted, lumbar puncture alone being performed and repeated daily until the cerebrospinal fluid is clear to the naked eye, there being no symptoms of hydrocephalus. Should any sign of a

recrudescence of meningitis occur during the period of repeated daily lumbar puncture, particularly mental changes, increased turbidity of the cerebrospinal fluid, or the reappearance of meningococci, serum administration is recommenced and continued on the same lines.

Vaccines are also employed, their use being of chief value in the later stages of the disease. The doses I administer are somewhat larger than those usually given. Administration begins within the first three days of treatment with an initial dose, for an adult, of 250 million organisms; doses are then given every fourth day, each dose increasing by 250 million organisms up to 500 million, and afterwards by 500 million up to 2500 million. Indications for a departure from this routine dosage are dealt with later.

Results of Treatment.—Of 72 cases of cerebrospinal fever of all types treated by the method described above—the daily intrathecal injection of serum, repeated lumbar puncture, and vaccine administration—57 recovered and 14 died (mortality 20·8 per cent). Of those proving fatal, in no case was death due to internal hydrocephalus; 13 fatal cases were of either the fulminating, acute fatal, or progressively purulent type; the remaining case was not received until the third day of a recrudescence (thirty-sixth day of total course), the early part of the patient's illness not being recognized as subacute cerebrospinal fever. The case proved fatal on the forty-third day of illness, from generalized hydrocephalus, due, as shown by post-mortem examination, to a blockage by fibropurulent exudate having occurred in the region of the foramen magnum. Of the 57 cases recovering, only four showed symptoms (temporary) of generalized hydrocephalus subsequent to the first week, and one those of internal hydrocephalus. The average duration of the course, as estimated from the day of onset, irrespective of the day treatment was started, to the day on which clear cerebrospinal fluid was withdrawn on lumbar puncture, was fourteen days.

Importance of Early Treatment.—Early treatment, and consequently early diagnosis, in cerebrospinal fever is of paramount importance. Its great significance cannot be fully shown by statistics, because in every series of cases there must occur some of a fulminating type which die within twelve to forty-eight hours. When first performing lumbar puncture on a suspected case, if the cerebrospinal fluid shows any turbidity, it is advisable to administer serum at once, without waiting for the bacteriological examination. Valuable time is saved, and no harm can be done by the serum to a possible case of pneumococcal or tuberculous meningitis.

Treatment during the Pre-meningitic Stage.—It is now generally admitted that the mode of infection in cerebrospinal fever is by the meningococcus being absorbed from the nasopharynx and carried

in the blood-stream to its site of election—the meninges. Not only do the symptoms at the onset of the disease suggest this mode of invasion, but in several reported cases the meningococcus has been isolated from the blood during the ‘pre-meningitic stage’, that is, at a time prior to infection of the meninges, when meningitis can be shown by the physical signs and examination of the cerebrospinal fluid to be non-existent. It is seldom, however, that cerebrospinal fever is diagnosed in the absence of signs of meningitis, but in cases in which the disease is suspected, especially on account of the presence of a petechial or purpuric rash, and the cerebrospinal fluid is found clear, antimeningococcal serum should be administered intravenously or intramuscularly, preferably the former. As regards intravenous injections, doses up to 200 c.c. of serum may be given. Herrick, indeed, advises doses up to 600 c.c., the resulting serum sickness apparently being no more severe than with the smaller amounts.

In some cases the initial shock may be extremely severe at the onset. This should be combated by the application of hot bottles and rectal or subcutaneous injections of normal saline solution at a temperature of 100°. Camphor (gr. 5), injected subcutaneously in the form of Curschmann’s solution, may also be of assistance.

Even though antimeningococcal serum be given intravenously or intramuscularly, it is nevertheless essential to watch most carefully for the slightest sign of meningitis, such as increased neck rigidity, Kernig’s sign, delirium, or retention of urine. If there be the least suspicion that meningitis has developed, lumbar puncture must be performed, and, if the cerebrospinal fluid be found turbid, antimeningococcal serum is injected forthwith. When the fluid is apparently clear, films stained by Gram’s method are made from the centrifugalized deposit and examined microscopically, as it should be borne in mind that the presence of meningococci in the cerebrospinal fluid may precede an increase in the cell content and give rise to meningeal symptoms. The fluid should also be sown on ‘tryagar’ and incubated.

Reasons for Intrathecal Administration of Serum.—Owing to the fact that the meningococcus produces its chief pathogenic effects by direct and local action on tissues, the full power of antimeningococcal serum can only be exerted when the immune principles on which these effects depend are brought into contact with the organisms in a concentrated form. In the presence of meningitis, therefore, serum injected subcutaneously or intravenously is practically useless; not only does it undergo an extremely high dilution in the blood-stream, but there is no evidence that it ever reaches the subarachnoid space. Dixon and Halliburton³ have shown that, although the lining membrane of the subarachnoid space is permeable to substances

passing from the cerebrospinal fluid to the blood, it appears quite impermeable, except in the case of a few drugs (e.g., hexamine) and oxygen, in the reverse direction—from blood to cerebrospinal fluid. The choroidal epithelium is a stalwart barrier of secretory cells which keeps back even readily diffusible substances and allows only the normal secretion to escape.

The absorption of antibodies from the cerebrospinal fluid into the blood-stream, however, is fairly rapid. Debré,⁴ by means of the sensitive precipitin reaction for a foreign serum, showed that the reaction appeared in the blood about ten minutes after the intrathecal injection of the foreign serum. Hohn,⁵ by determining the content of the cerebrospinal fluid, found that the serum for the most part is absorbed within twenty-four hours.

Consequently, it is evident that for antimeningococcal serum to exert its maximum effect, it must be introduced directly into the subarachnoid space and, in order to make good the loss in concentration sustained by its absorption into the circulation, at intervals of not longer than twenty-four hours.

The Question of Anæsthesia.—There is some difference of opinion concerning the advisability of administering a general anæsthetic for the performance of lumbar puncture. In routine neurological work I do not consider a general anæsthetic at all necessary as a rule. It is, of course, essential in tetanus, but in cerebrospinal meningitis I have used general anæsthesia only when the patient has been particularly violent. Provided one has a competent assistant with a thorough knowledge of the requisite position in which to hold the patient, the operation is performed without difficulty, always allowing the necessary skill on the part of the operator.

Patients when conscious do not often complain of the actual puncture when it is rapidly performed and the canal entered at the first attempt; further, an anæsthetic in meningitis is not altogether free from risk, and when given daily may interfere considerably with the patient's nourishment. In restless cases a hypodermic injection of morphine (gr. $\frac{1}{4}$) and atropine (gr. $\frac{1}{100}$), given about twenty minutes before the puncture is performed, will often assist in calming the patient.

Dosage of Serum.—In contrast to antidiphtheritic serum and tetanus antitoxin, there exists no definite measure of the potency of antimeningococcal serum; consequently, the dose is measured by volume. As a general rule, with certain exceptions that will be mentioned later, the amount injected at a single administration should be at least 5 c.c. less than the quantity of cerebrospinal fluid withdrawn. In my own cases over 15 years of age, the initial dose has varied from 30 to 45 c.c., the usual dose being 30 c.c. The subsequent serotoxic reaction is certainly no more severe in cases

receiving the larger doses than in many of those to whom only 30 c.c. are administered. As regards children, in relation to age, the following doses may be given: 1 to 5 years, 5 to 15 c.c.; 5 to 10 years, 10 to 20 c.c.; 10 to 19 years, 20 to 40 c.c.

Following the first injection, serum is continued in daily doses of 30 to 40 c.c. for adults and adolescents.

As regards the total dosage of serum administered to an individual case, in my own series the quantity has varied from 120 c.c. to 600 c.c.

Administration of Serum.—The serum is much better given by the gravitation method—first introduced by Heiman in 1908—than injected by means of a syringe. However slowly the serum is forced in with a syringe, there is always the risk of respiratory failure occurring from a sudden increase of intracranial pressure. Also, the intrathecal administration of serum is almost invariably accompanied by a fall in blood-pressure; injection with a syringe tends to increase this fall, with the consequent risk of collapse. In many hundreds of intrathecal serum injections by the gravitation method, in contrast to those with a syringe, I have never seen any indications of respiratory failure or collapse. It appears unnecessary, therefore, provided the respiration be carefully watched, to take the further precaution, as advocated by Sophian,⁶ of registering the blood-pressure as an ocular guide to injection by the gravity method.

If the patient is straining, the inflow of serum may be very slow indeed, and scarcely discernible. Also, he may complain of considerable 'cramp' in the legs caused by the sudden rise of pressure acting on the roots of the cauda equina. To obviate the initial pain, the funnel should only be raised slowly from the horizontal level of the needle; the pain is also less when the serum is warmed to body temperature than when it is injected cold.

In my earlier cases a complaint of cramp was almost invariable. I found, however, that by directing the patient, when his mental condition permitted, to breathe deeply with a somewhat long inspiration and a short expiration, the inflow of serum was greatly accelerated and he ceased to complain of cramp and pain. On inspiration there is a considerable lowering of pressure in the intrathecal canal, with a corresponding increase during expiration. When the expiration is long and the inspiration short the serum scarcely moves, but with a long inspiration it flows rapidly.

Some observers recommend the washing out of the subarachnoid space with normal saline before injecting the serum; personally, I have not found this proceeding of any material advantage.

Accidents during Serum Administration.—Such disturbances as have been described during the intrathecal injection of serum are

usually due to a sudden increase in intracranial pressure and a consequent depression of the respiratory centre. The first abnormal sign is some embarrassment of respiration, the breathing becoming shallow, slow, and occasionally irregular. If the serum be forced in with a syringe, respiration may suddenly stop, although the heart continues to act well. At other times such symptoms result from the too rapid administration or the injection of too large a quantity of serum. Should any symptoms of respiratory embarrassment occur, the intrathecal injection must at once be stopped by lowering the funnel and allowing the serum that has already entered the subarachnoid space to escape. Artificial respiration and the injection of cocaine and atropine in full doses will usually suffice to restore the patient.

Using the gravitation method, allowing the serum to enter the intrathecal sac only very slowly, the flow being regulated by alternately raising and lowering the funnel, and watching carefully the patient's respiration, I have never met with indications of respiratory failure.

Occasionally, incontinence of fæces may occur during the inflow of serum. This is no doubt due to the sudden stimulation of the third and fourth sacral nerve roots. Care, however, must be taken to ascertain that such incontinence is not the result of collapse.

Continuance of Serum Administration.—Following the initial dose, serum injection is repeated daily, usually in doses of 30 c.c., after as much cerebrospinal fluid as possible has been evacuated. In acute cases, the second dose may be given twelve hours after the first. Serum administration is then continued daily until clinical improvement, as indicated by a normal mental and sphincter condition, decreased muscular rigidity, absence of meningococci from the cerebrospinal fluid, etc., is quite definite. After the first two or three injections, there is seldom any distinct advantage in repeating the dose of serum every twelve hours. If, however, owing to only a small amount of cerebrospinal fluid being obtainable, the full dose of serum cannot be given at the morning lumbar puncture, a further injection may be given during the evening.

However great the patient's improvement may appear, serum should be given on at least four successive days, and on no account should it be withdrawn if meningococci are still visible in stained films of the cerebrospinal fluid or obtainable in culture, as until meningococci have disappeared there is no certainty that the patient is free from danger.

Should signs of a recrudescence of meningitis appear after the period of serum administration has ceased, the injection of serum must at once be resumed, and repeated daily until further improve-

ment occurs and organisms have disappeared from the cerebrospinal fluid; lumbar puncture is then continued daily until a clear fluid is obtained.

Anaphylaxis.—Owing to the risk of anaphylaxis, serum administration must not be resumed without first inducing anti-anaphylaxis if the period since the last serum injection exceeds eight days. It is of considerable importance, however, to overcome the meningococcal infection, as far as possible, in one continuous course of serum treatment.

The following method of inducing anti-anaphylaxis rapidly, based on the work of Besredka and Friedberger, is described by C. H. Browning:⁷ 5 c.c. of the serum it is proposed to inject are diluted with 50 c.c. of normal saline. Of this mixture, 1 c.c. is injected intravenously, followed by 3 c.c. four minutes later, 10 c.c. after another two minutes, and finally 25 c.c. after two further minutes. The dilute serum is best administered by means of a graduated funnel attached to the intravenous needle by a rubber tube; the latter can be pinched with a clip for the requisite intervals during the injection. Fifteen minutes after the above injections, the full therapeutic dose of serum may be administered.

General anæsthesia and the hypodermic injection of atropine (gr. $\frac{1}{5}$) are also stated to prevent the occurrence of anaphylactic symptoms.

The Amount of Serum Injected in Relation to the Amount of Cerebrospinal Fluid Withdrawn.—As a general rule, the amount of cerebrospinal fluid evacuated by lumbar puncture should exceed by at least 5 c.c. the quantity of serum injected. In certain cases in which the amount of cerebrospinal fluid obtainable is less than the quantity of serum it is desired to administer, an exception may be made. Provided that there is no evidence of increased intracranial pressure, and that the serum is not forced in with a syringe, but merely allowed to flow in at not more than twelve to eighteen inches water pressure by the gravitation method, I have found the administration perfectly safe; as a precaution, however, the patient's respiration should be carefully watched. In such instances, the amount of serum given may equal and even exceed by 15 to 20 c.c. that of the cerebrospinal fluid withdrawn. By the gravitation method, and at the pressure mentioned, the serum will usually cease to flow when the intrathecal pressure is approaching the limits of safety.

When there is distinct evidence of increased intracranial pressure, —c.g., hydrocephalic symptoms—the injection of a larger amount of serum than of cerebrospinal fluid withdrawn must not be entertained.

Repeated Lumbar Puncture.—When clinical improvement is quite decided and organisms have disappeared from the cerebrospinal

fluid, as previously described, the administration of serum is discontinued; lumbar puncture, however, is still performed daily until a cerebrospinal fluid quite clear to the naked eye is obtained, pyrexia being absent and the patient being free from any symptoms indicating hydrocephalus. At each lumbar puncture, cerebrospinal fluid is allowed to escape until the flow of fluid practically ceases. This procedure ensures that the exudate is removed as far as possible, and that the subarachnoid space is flushed out from above by the secretion of fresh fluid by the choroid plexus. It is true that H. D. Rolleston⁸ has considered the possibility of harm resulting from repeatedly withdrawing cerebrospinal fluid, as, to quote this author's own words, "an excessive secretion of cerebrospinal fluid, perhaps comparable to cerebrospinal rhinorrhœa, may be induced". In my experience, however, this has never been the case; on the other hand, I have seen nothing but good result; and there is no doubt that, in addition to shortening the course of the disease, the repeated draining of the exudate from the subarachnoid space tends to inhibit the development of any serious degree of hydrocephalus.

For all practical purposes, when the cerebrospinal fluid becomes clear, sterile, and under approximately normal pressure, no evidence of hydrocephalus being present, the course of disease may be said to have ended. At this stage subjective symptoms are absent, and the only sign is usually some degree of muscular rigidity, as shown by slight stiffness of the neck and a modified Kernig; the latter is usually the last sign to disappear.

Following the cessation of serum administration, the number of days of repeated lumbar puncture in my cases has varied from three to fourteen. By varying the site of puncture from time to time, I have never experienced any trouble with the skin wounds. It is found that the skin can be kept in better condition by avoiding collodion dressings. On withdrawal of the needle after each operation is completed, the wound is merely swabbed with a mixture of equal parts of tincture and liniment of iodine.

Treatment in Relation to Type of Infecting Coccus.—The question of the specificity of the serum is a most important one. Indeed, it is probable that the presence of an inert serum in the intrathecal sac may be positively harmful; horse serum when thus injected gives rise to an aseptic meningitis which, in the absence of any specific antibodies, may favour the passage of meningococci through the tissues. Since it is of paramount importance that the therapeutic serum should correspond with the strain or 'type' of the infecting meningococcus, as well as for the comparison of results, it is to be regretted that several different classifications of meningococci exist, and, further, that there appears to be considerable confusion as

to the correlation of the 'types' of different observers. If a classification of meningococci based on 'types' is to be adopted generally, it is clear that some endeavour should be made to arrive at uniformity. In my experiences with military cases, working in conjunction with A. Mills Kennedy, M. H. Gordon's classification proved of the utmost practical value and the one which we used almost exclusively.

At the initial lumbar puncture and withdrawal of cerebrospinal fluid, an antimeningococcal serum, in the production of which the prevalent types of meningococci have been employed, is injected intrathecally without awaiting the bacteriological report. In my own cases I have usually employed polyvalent serum corresponding to Gordon's four types and prepared by the Lister Institute or the Medical Research Committee. Failing a knowledge of the production of the serum, the agglutinating power of the opsonic reaction towards the particular type of meningococcus isolated from the patient should be tested. Although these tests are of limited value, in the present state of our knowledge it is safer to discard a serum showing little or no agglutinating power towards the type of coccus concerned in the infection. More recently, Gordon⁹ has described a method of testing the immune serum for anti-endotoxin which appears to be a more reliable test of therapeutic activity.

Monovalent sera for each of Gordon's four types have also been prepared by S. Griffith, at Cambridge, under the auspices of the Medical Research Committee (M.R.C. serum). As soon as the 'type' of meningococcus cultivated from the patient's cerebrospinal fluid is identified by means of the agglutination test, the monotypical serum corresponding to that particular 'type' of meningococcus may be substituted for the polyvalent serum. When, however, the 'type' cannot be identified—as, for example, when the organism, although visible on direct microscopical examination of stained films of the cerebrospinal fluid, fails to appear in culture—the criticism has been advanced that one must continue the polyvalent serum at the risk of greatly diminishing therapeutic potency, or grope blindly after the requisite monovalent serum. Nevertheless, the polyvalent serum, even if used exclusively, will usually be found to give most satisfactory results.

If no response to the polyvalent serum occur, however, the monovalent serum corresponding to the prevalent type of meningococcus in the particular district should be tried. Also, it should be borne in mind that a swab from the patient's nasopharynx may yield the necessary meningococcus, or that there may be several 'positive contacts' to whom one 'type' of meningococcus is common.

M. H. Gordon considers that 80 to 85 per cent of all cases of cerebrospinal fever occurring in England are due to Types I and II

(Gordon) meningococcus. Consequently, he suggests that when a case is seen for the first time, injections of Types I and II sera, pooled, should be given until the type of infecting meningococcus is determined; the corresponding monotypical serum can then be substituted. In the Woolwich Military District (comprising the greater part of outer London) during the war, however, A. Mills Kennedy found Type III quite as prevalent as Type I; Type IV, as elsewhere, was rare. Consequently, it would appear better to begin with a serum valent for Types I, II, and III (Gordon), unless it is definitely known that a particular type has occurred with frequency in other cases of the same origin.

Vaccine Treatment.—The doses of vaccine I administer are somewhat larger than those usually employed. Thus, in adults, a dose of 250 million organisms is injected subcutaneously at some time during the first three days of illness, the second dose consisting of 500 million, each of the subsequent doses being increased by 500 million up to a maximum of 2500 million. The last two doses are not always necessary. In children, the initial dose may be 10 million, the second 50 million, and each subsequent dose increased by 100 million. The vaccine is preferably autogenous, but as this takes some time to prepare, a polyvalent vaccine is given at first and is replaced by the autogenous vaccine as soon as the latter is available. The sensitized polyvalent vaccine I have used (and for much of which I am indebted to Sir Kenneth Goadby) consists of the four types of meningococci differentiated by Gordon. Monovalent vaccine, in the absence of autogenous, should be used in those cases in which the 'type' of infecting coccus has been determined. When the 'type' is not determined, polyvalent vaccine is used throughout.

Vaccine administration should begin within the first few days of treatment with, as stated above, a dose of 250 million organisms; the gradually increasing doses are then given every fourth day. If the reaction to a particular dose is at all pronounced, the same dose is repeated four days later; usually no reaction follows the repetition. The increase of 500 million is then made on the next occasion of administration.

Cases in which the effect of vaccine is certainly beneficial are those subacute ones which tend to run a somewhat long course. In some cases, the third or fourth dose is followed by a transient rise of temperature; subsequent increased doses, however, usually fail to produce any marked rise in temperature or pulse-rate. A slight local reaction may occur in a few cases.

At the present time, as far as I am aware, detoxicated vaccines have not been employed in the treatment of cerebrospinal fever, but they appear quite worthy of trial.

General Management and Treatment of Symptoms. — The ward or room chosen should be isolated and be provided with an abundance of fresh air. Nurses should be specially experienced, as careful nursing is of extreme importance. The patient's head is kept fairly low, and the hair cropped close to the scalp. Unconscious patients should be turned frequently and not be permitted to lie in the same position for hours at a time, as hypostasis is undoubtedly a predisposing factor in the development of pneumonia in cerebrospinal-fever cases. In all severe cases it is desirable that a water-bed be substituted for the ordinary mattress, as, unless this precaution be taken, difficulty with bedsores will be experienced. As regards the transport of patients by motor ambulance, in my experience the danger is negligible.

As a rule, the digestive functions are not greatly disturbed in cerebrospinal fever, and the appetite is often well maintained. In the early acute stages fluids are given, and as soon as possible semi-solids should be allowed. There is no need to wait for the disappearance of pyrexia before ordering a fish diet; patients are hungry and take food well towards the end of the course.

For the relief of headache, phenacetin and caffeine may be given and repeated twice daily; cold applications are also of benefit. Acetylsalicylic acid will frequently relieve muscular pain; as a routine measure, I give acetylsalicylic acid (gr. 10) after serum administration. The most efficacious measure for the prevention of vomiting is repeated daily lumbar puncture according to the method previously described. Sulphonal (gr. 20 to 30) will be found useful in promoting sleep. For obstinate insomnia or when delirium with restlessness is present, morphine (gr. $\frac{1}{4}$) should be given. Paraldehyde is of little value in the delirium of cerebrospinal fever, and hyoscine should be avoided. Warm sponging may often assist in relieving restlessness.

Should symptoms of cardiac failure or of a falling blood-pressure develop, hot saline infusions (100°) should be given, either rectally, or subcutaneously in the pectoral region, every eight to twelve hours. Digitalin (gr. $\frac{1}{100}$) hypodermically is also useful. Strychnine, owing to its tendency to precipitate convulsions, should not be administered.

As cerebrospinal fever is an exhausting disease, patients should remain in bed for at least ten to fourteen days after the termination of the course.

Treatment of the Nasopharynx.—As soon as the condition of the patient permits, measures should be taken to free the nasopharynx from meningococci. This is important, true relapses being probably due to a further absorption of meningococci from this situation, as the organism, unless prevented, may often persist in the nasopharynx after recovery has taken place. Sterilization may be effected by

causing the patient to sniff a warm solution of 1 per cent chloramine-T into the nostrils from the palm of the hand, expelling it through the mouth. This is repeated twice daily under supervision until two or three successive nasopharyngeal swabs have proved negative.

Treatment of Complications.—Repeated daily lumbar puncture, following the period of serum administration, largely counteracts any tendency towards the development of hydrocephalus. Nevertheless, symptoms of this serious complication occur occasionally. The question of its treatment is most important, and one with which it is hoped to deal in a further communication.

Cases in which meningococci are cultivated from the bloodstream, in the presence of definite meningitis, should be given antimeningococcal serum intravenously as well as intrathecally. The prognosis is bad, but some cases recover. Pneumonia is treated on the usual lines, its occurrence being no indication for stopping the intrathecal injection of antimeningococcal serum. Arthropathies, as a rule, subside fairly quickly with simple immobilization and warm applications. If much distended, the joint should be aspirated, and 5 to 10 c.c. of antimeningococcal serum should be tried; this procedure usually results in prompt recovery. In pyelitis or cystitis, hexamine is prescribed and almost invariably leads to subsidence of the complication. If iridochoroiditis develop, intravitreal injection of antimeningococcal serum should be performed; instances of suppurative iridochoroiditis have occurred in which this treatment led to rapid recovery, sight being retained.

REFERENCES.

- ¹ GORDON, M. H., *Jour. R.A.M.C.* 1915, xxii, 655; xxv, 410, 456.
- ² EASTWOOD, A., *Reports to L. G. Board*, New Series, 1916-17, Nos. 110 and 114.
- ³ DIXON AND HALLIBURTON, *Jour. of Physiol.*, 1, 198.
- ⁴ DEBRÉ, "Recherches épidémiologiques, cliniques, et thérapeutiques", *Thèse de Paris*, 1911.
- ⁵ HOHN, *Klin. Jahrbuch*, 1909, xx, 357.
- ⁶ SOPHIAN, *Epidemic Cerebrospinal Meningitis*, 1913.
- ⁷ BROWNING, C. H., *Brit. Jour. Surg.*, 1916, iv, 13.
- ⁸ ROLLESTON, H. D., *Lancet*, 1919, i, 645-53.
- ⁹ GORDON, M. H., *Brit. Med. Jour.*, 1918, i, 110.