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## TREATMENT OF CEREBRO-SPINAL MENINGITIS.\*

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FOR the first time in the medical history of these islands, cerebro-spinal fever has prevailed as an epidemic, with the usual characteristics, *i.e.*, a low case-incidence, a widespread yet capricious distribution and predilection for soldiers, particularly young soldiers, a high case-mortality, and a rapid disappearance of the disease with the approach of fine weather. The figures of its distribution and prevalence are not yet available. As usual in Europe, the military population has suffered most. In the first year of the war there were, in the home Army, 462 deaths, which places the disease second on the list of causes of death from acute infections—probably a very much larger proportion than among the civil population. When the returns are made, it will be seen that the deaths from cerebro-spinal fever form but a small proportion of the total deaths from meningitis. I hope that one result of the careful studies recently conducted will be a more accurate registration of the forms of the disease.

For the year 1913, the Registrar-General reported 9,269 deaths from meningitis in England and Wales. More than half, *i.e.*, 5,018, were the tuberculous form. Of the balance, 159 were classified as posterior basic, 163 as cerebro-spinal fever, and 3,819 as "other forms." More information is needed concerning this last group, in which a not inconsiderable number may be due to the meningococcus. Cerebro-spinal fever is not only interesting as an epidemic, but as a meningitis it has the fortunate distinction of being the only variety from which recovery takes place in from 50 to 70 per cent. of the cases. Many men of large clinical experience have never seen recovery in the tuberculous, pneumococcal,

\* This symposium is based upon a recent discussion at the Royal Society of Medicine; each paper has been specially revised and amplified by the author for this number of THE PRACTITIONER.

or streptococcal varieties. I have not myself had a recovery in cases under my care of any of those three forms. I have seen one case of doubtful tuberculous meningitis recover; and I saw, last autumn, at the Cleveland Hospital, one case of streptococcal meningitis recover. It was determined to be streptococcal by that streptococcus specialist, Dr. M. H. Gordon. The meningococcus is always present. It may be grown in pure culture; it has specific serological reactions, and the disease may be reproduced in animals. It has "strains," which, however, have not yet been worked out satisfactorily, neither has their existence yet been sufficiently considered, seeing that they present differences in agglutination, opsonization, and complement fixation. I hope that matter will be cleared up in the present investigation.

Two points call urgently for discussion: the prophylactic measures, and the serum treatment. The others, in comparison, are subsidiary and unimportant.

We may, I think, expect a return of the disease this winter. There are instances of a progressive yearly increase in the virulence of the epidemic. What preparations should be made in the prospect of such a renewal? Let us recognize a certain value in the conception of the disease propounded originally by Dopter, and supported in this country, among others, by Arkwright, Lundie, Thomas, Fleming, and Maclagan. These men hold that the epidemic is in the carrier; the meningitis is regarded by them as an incident. The germ is ubiquitous, and is harboured by many who show no symptoms of the disease, but producing in others a mild catarrh, and only in a few reaching the meninges. This is what happened in the case of pneumonia, in which the proportion of cases to carriers is even smaller than in the case of cerebro-spinal fever. The germs may be present in the throat without the occurrence of naso-pharyngeal catarrh; it may be present in a severe case of the disease, without any indication other than that obtained by cultures.

Two broad facts stand out:

- (1) The correlation of the seasonal prevalence with naso-pharyngeal catarrh, and
- (2) The influence of overcrowding in ill-ventilated barracks and houses.

The concentration of human beings, particularly of young recruits in camps, seems to me to be the most important single

factor. Fatigue lowers resistance, wet and cold and the excessive use of tobacco favour pharyngeal catarrh; too often the huts and tents are overcrowded, nights are cold, blankets thin; what wonder that the men close the windows, and lace up the tents tightly, so that the air becomes foul. The carrier does the rest, distributing the germ to a young fellow whose resistance is weakened, or whose naso-pharynx forms a suitable medium.

During next winter, medical officers in charge of camps and barracks and of men quartered in houses should do three things:

- (1) Guard the young soldier especially against over-fatigue. I know that is a very easy thing for me to say, and a very hard thing for the medical officer to ensure.
- (2) Reduce to a minimum the circumstances favouring naso-pharyngeal catarrh.
- (3) Make possible a combination of good ventilation of sleeping quarters with comfortable warmth for the men.

You can get comfortable warmth and good ventilation combined, but you cannot secure comfortable warmth in many of the conditions in which the men are. I saw once six men in a room in which I would not put three; they were quartered in villas. The windows were shut, and the door was shut until I opened it; the men were sleeping on mattresses on the floor. One of them said, "We have got to shut the window to keep ourselves warm." I think the public health authorities and the medical officers in charge of camps should bear these points in mind, with reference to the possibility of a recurrence of the disease this winter.

The prophylactic use of anti-meningitic serum is still on trial; we do not know enough to recommend it or to discourage it. I hope this discussion will elicit the results which have been achieved by those who have employed it. On present knowledge, specific therapy combined with lumbar puncture is the rational treatment, combating the sepsis by means of the one and the pressure effects of the local exudates by the other means. We are agreed as to the value of withdrawal of fluid from the spinal meninges. On the value of specific therapy, however, there is a grave difference of opinion. The use of the serum is based on sound experimental data.

The long study of Flexner and his pupils and others have made possible the production of a serum which has a specific influence on the meningococci in the spinal canal, partly by a direct bacterioidal action, partly by bringing about phagocytosis; and there may be an antitoxic action. No one can have followed the work at the Rockefeller Institute on the meningitis problem, without having been impressed with the fact that it is solid, sound, good work, and that, if there is any truth in the serum therapy, it is just on such researches that it must be based. The specific treatment has been in use for some years, and details of the results are readily to be found, particularly in the recent monograph of Sophian; the last table in his book gives the collected statistics of cases treated with, and without, the serum, and, if they are worth anything, the figures show an overwhelmingly strong case for specific therapy.

The practical points for us to discuss are, first, the experience of the past few months; and, secondly, its lessons for the future. We must be disappointed in many quarters with the serum treatment. The reasons for the failure should be laid open freely and frankly; what we wish is to get a statement of the truth of the matter. The consultant only sees severe cases, and cases which are far advanced. It has been said that when the cases reach us, they are in a condition to receive "extreme unction." The death-rate has been high, and I hope the figures for the whole country will be available.

I was much interested in the outbreak among Canadian soldiers at Salisbury, where 40 cases were treated, with 26 deaths—a mortality of 63 per cent. The sera used were from Burroughs Wellcome, Lister Institute, Mulford, and Parke, Davis. It was said that a few of the patients treated with Mulford's serum suggested that some improvement had taken place, but it was hardly striking enough to justify its use. There was no benefit from the other sera. In one case, the meningococcus was isolated two and a half months after the illness, and after more than 20 intraspinal injections had been given. In another case, meningococci were found in the fluid five weeks after the onset of the illness, during which there were 12 injections. This is the figure from one who is an expert in the technique of intraspinal treatment. I have seen it given by the gravity method, and with great skill. There were no better results at Haslar. There were 30 cases there, with a mortality of 52 per cent., and the use of the serum

was abandoned after eight deaths in 12 cases. Happily, the man with the largest experience, Dr. Gardner Robb, of Belfast, tells a different tale.

We want to know the reasons for this widespread failure. I think there has been one main cause: inert sera. We do not know in how many cases the parameningococcus was present. That does not react to the ordinary antimeningitic serum. There have been as well insufficient dosage, failure to treat cases early, and imperfect technique; these have been minor contributory causes. There are, of course, cases which resist all treatment. We cannot expect, by any form of treatment of cerebro-spinal meningitis, to get a mortality below 20 to 25 per cent.; we have to deal with acute, malignant, fulminating cases, which die in 24 to 36 hours; and there are some deaths from complications. But we have to face the problem, that there is this extraordinary discrepancy between the results obtained in many quarters in this country and the results obtained by Flexner and others, in recent epidemics in the United States and elsewhere. It may be a question, as I suggest, of inert sera. I think this should be made a War Office problem, and be placed by them into the hands of experts who shall investigate sera, so that we can be certain that they correspond to the strain of organisms present in the prevailing epidemic.

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I HAVE always been greatly interested in this subject, for in Belfast and the North of Ireland we have suffered severely from outbreaks of this disease since 1907.

Before the introduction of the serum of Flexner, there occurred in Belfast a severe outbreak. In the first seven months of that outbreak, I had under my care in the Fever Hospitals 275 cases, and the death-rate was over 72 per cent. Then I received from Dr. Flexner a supply of the serum, on the preparation of which he had been working for a long time. It had already been tried in a few scattered cases in America with good results. I began its use in the beginning of September, 1907. The change in results was dramatic. The death-rate fell at once to one-third of what it had been. The death-rate in our hospital cases had been over 80 per cent. in

the three months *immediately before* the serum arrived. Of 45 cases admitted in those three months 37 had ended fatally. In the first four months *after* the use of the serum was begun, the mortality in hospital was 26 per cent. Only half the cases occurring in the city at that time were sent into hospital, and, during the same four months, the mortality in the cases not sent into hospital, and not treated with serum, was 85 per cent. Since then I have from time to time reported the results I have obtained with Flexner's serum, and in no series of cases, up to the beginning of last winter's epidemic, did the mortality in our Belfast cases so treated exceed 30 per cent.

No one who has had any considerable experience in the treatment of this disease without intra-spinal injections of serum, and has then had an opportunity of observing the results of such injections, can have any doubt as to the enormous value of this treatment; and I believe I am correct in stating that *every one* who has had such opportunities is enthusiastic regarding the success of this method of treatment. To this I think there is not any exception, as shown by the writings of Dunn, Emmett Holt, Ladd, Royer, Sophian, Fulton, and many others in America; of Netter and Dopter in France; of Claude Ker of Edinburgh, and of Christomanos, with his large experience, in Greece. The same unanimity is to be found in the records from Germany, where similar success was obtained after the adoption of the intra-spinal route for the administration of the antiserum.

At the discussion in the Epidemiological Section, held here last February, I reported my results to that date. The number of cases was then about 120, and the mortality had been under 24 per cent. These are gross mortality results, *all* the deaths are included, and I would again plead that gross mortality rates should be given in records of serum-treated cases for two reasons. First, because the death-rates of 60 to 80 per cent. commonly reported in outbreaks in America and Europe before the introduction of intra-spinal injections of serum were gross mortality rates; and secondly, because, from my experience, I believe it is quite impossible to say in the first few hours of illness that any case is hopeless.

In a recent and very excellent work on cerebro-spinal meningitis, the author, who had large experience of the serum treatment in a comparatively recent epidemic, and had a gross mortality rate of 25 per cent., excludes over 40 per cent.

of his fatal cases, because they were "hopeless from the first," or died within 24 hours, etc. He then publishes a table of cases reported from various places all over the world. The mortality from these places is a gross rate, whereas the author's is a "corrected" rate. Naturally, his results are about twice as good as those obtained by others.

To illustrate how impossible it is to give a definite prognosis, I may be allowed to mention one case which occurred last February. I was asked late one night to see a young man who had only been taken ill that morning. He had been in excellent spirits on going to bed the night before, but was unable to rise in the morning on account of severe headache; he soon became delirious, and then unconscious. When I saw him, some 15 or 16 hours after the onset, he was unconscious, the pulse could not be counted at the wrist, there was great rigidity, and he was covered with large patches of subcutaneous hæmorrhages and a plentiful petechial eruption; on his feet were large hæmorrhages into the skin measuring 2 ins. by 3 ins., his ears, hands, knees were covered with deep purple patches of hæmorrhage, and there were large sub-conjunctival hæmorrhages. Though it seemed doubtful to me and to his own medical attendant if he could survive the four or five miles journey to the hospital, it was his only chance, and we sent him in. He was punctured immediately after his admission, the cerebro-spinal fluid was purulent, and meningococci were plentiful, both intra- and extra-cellular. He was given 40 c.c. of serum. Twelve hours later he was given 20 c.c., but seemed no better, and the whole cornea in one eye was steamy with pus in the anterior chamber. He was given injections daily for several days and slowly improved. Eventually he recovered with the loss of one eye. Some patches of skin became necrosed and sloughed. He left hospital after 10 weeks' detention, and lately I heard from his doctor that he now reports himself in better health than ever before, and he is earning his living as a carpenter on munitions work. I quote this case to show how impossible it is to separate cases which "have no chance" from other severe cases. If this case had died, he might readily have been put in the category of cases which were "hopeless from the first."

We remained free from the disease in Belfast in 1913, and to the end of 1914. When there was a reappearance of cases last winter, I fully expected that we might look forward to

getting even better results, for, owing to the experience we had had, the diagnosis was more likely to be made quickly and, the value of early injection of serum being fully recognized, the cases would most probably be sent into hospital without delay. It was apparent, too, that we should have many cases from the camps, and these would generally be in good physical condition, and at a time of life when good results were to be expected. But, unfortunately, the results, instead of being better, have not been so good. Since the beginning of last winter I have had 92 cases in hospital, and have treated 8 cases in various places outside, making exactly 100 cases. Of these, 36 have died, a case-mortality of 36 per cent. In the total number we had previously, the death-rate had been 24 per cent.

In trying to find an explanation of the cause of this increase several questions occur to one:—

- (1) Was the disease of a more virulent type?
- (2) Was there any marked difference in the average age of the patients, which might make for a higher mortality?
- (3) Can the increase be accounted for by differences in the strains of the meningococcus?
- (4) Was the serum available of as high standard of immunity value?

(1) Regarding the virulence of the type, it is very difficult to make a correct estimate, but my opinion is that the recent outbreak was not more severe in type than formerly; although, so far as I have been able to ascertain, no case occurring in the North of Ireland during the past winter and spring, which was treated without serum, recovered. There were several. Unfortunately, the disease is not notifiable in all our sanitary districts, so that it is not possible to obtain exact figures.

(2) The average age of the patients has been higher in the recent outbreak. This should, on the results generally reported in former outbreaks, make rather for a lower case-mortality, but my own experience has been that young children give very good results when treated with serum, provided they come under treatment reasonably early. It is in the infants that the greatest improvement in results has been obtained, since the serum treatment became general. In

children under one year treated without serum, a death-rate of 90 per cent. had been common. With the serum they do quite as well as cases in other age periods. In the present outbreak, I have had 17 cases in children under five years with only four deaths—less than 25 per cent. One of these fatal cases had already been over 50 days ill, when admitted from a country district 25 miles from the city.

(3) Is the increase in the mortality to be accounted for by differences in the strain—strains not provided for in the polyvalent serum available? In the discussion here last February, I believe that the general impression held by many of those taking part was that the resistance to the serum treatment, shown by many of the cases then occurring, was thus to be accounted for. During the early spring, I had several cases which were received into hospital quite early in the attack, but, though living long enough to receive several daily injections, they showed only very temporary improvement or none at all, and ended fatally. I am aware that cases of this kind have been met with amongst the serum-treated cases elsewhere; personally, I had not met with such cases in my former experience in the use of the serum. My experience had been that, if a case lived for ten days or a fortnight, it recovered. In this outbreak that did not hold good I may instance one case which occurred amongst my recent cases. A robust soldier of 20 years was admitted with a severe attack on the first day of illness; he received repeated injections, showed some improvement at first but only for a short time. In all, he was given 15 injections—480 c.c. of serum—and had over 1,100 c.c. of fluid drained off from the canal. He went steadily downhill, and died after four weeks. The meningococcus was present in the cerebro-spinal fluid till the end. In my former series, I had not met with such cases. Having had some correspondence with Dr. Flexner on these resisting cases, I collected specimen cultures of the organism from cases in various places, and took them over to New York for comparison with the strains being used in the preparation of the serum. Through the kindness of Dr. Martin, I obtained several from the Lister Institute; from Dr. Robertson I received some from Birmingham; I also received cultures from Professor Beatty's laboratory in Liverpool, and from Professor McWeeny, of Dublin. Most of these I tried to take out in sealed tubes, but they all died off on the voyage; I had, however, taken a small

incubator, and transplanted samples from all these places on the voyage, so that strains from the various districts were available for comparison. They showed no marked differences, when compared with those in use in the preparation of the serum now being made at the Rockefeller Institute. Some of them did not agglutinate with the serum in quite so high dilutions as those in use there, and these have been used in the preparation of the serum now. With the recent improvements in culture media, interchanges of cultures for comparison should be less difficult.

(4) Was the serum available of as high a standard of immunity value? For two or three years before our epidemic last winter, there had been very little demand for the serum from the sources of supply in America; then suddenly came the great demand from this country. Our War Office ordered large quantities, and much was requisitioned from France, with the result that the available horses were bled as frequently as possible and the immunity value of the serum dropped very seriously. For this, and possibly for other reasons, I think there is no doubt that much of the serum which reached this country last winter was of a much lower standard of value than that formerly supplied. *I think here lies the true reason of the somewhat disappointing results sometimes obtained from its use.* Steps have been taken to correct the deficiency in the quantity and the quality of the serum. Dr. Flexner, too, has again taken up the preparation of serum at the Rockefeller Institute, and that now available, judged by all the laboratory tests, is of higher value than any formerly in use. I brought back with me a supply of this new serum, and, so far, I have treated eight acute cases with it. In these there has been one death. This is very promising, but is much too small a number to judge by. Some of these eight cases were comparatively mild, but some were quite severe types. The latest case, a soldier, admitted nine days ago, then 24 hours ill, was deeply unconscious with normal temperature, cyanosis, stertorous breathing, and the dreaded slow pulse. On puncture, thick syrupy pus was obtained. He was given 40 c.c. of serum; next day he could be roused, but had paralysis of one side of the face, and, on the following day, paralysis of the arm on the same side. He then steadily improved, and when I saw him yesterday he was quite bright, the paralysis of face had cleared up, that of the arm nearly so,

and the meningococcus had disappeared from the fluid. He appeared on the fair way to rapid recovery. He was given five injections of serum, 140 c.c.s. in all.\*

It would be interesting to have views on the advisability of taking continuous blood-pressure readings during lumbar puncture and the injection of the serum, as insisted upon by Sophian, as well as on the use of general anæsthetics. I confess that when I first read Sophian's note on the value of blood-pressure readings, and on the danger of general anæsthetics, I felt uneasy. I had not at that time—some three years ago—had any cases for a considerable period, but I felt that possibly the cases I had treated had not got the best chance; for I had never been guided by blood-pressure readings, either in fixing the quantity of fluid drained off or in the dosage, and I had generally given chloroform.

Early in my experience I received a lesson which I have not forgotten. I did not like giving chloroform to these patients so frequently, though the patients so often asked for it. In one of the first cases I ever had—a powerfully-built man—I had given chloroform at the first injection; when repeating the injection, I explained to him what I was about to do, and he consented to bear it without moving if possible. He allowed me to puncture him with quite a large trocar without fuss; the fluid came freely, and all was going well, when suddenly—I suppose through some slight movement of the trocar—he felt what was evidently excruciating pain. He sprang off his side, and made desperate efforts to bury his back in the bed, so that I would not again be able to touch the trocar. He was immensely muscular; I had one assistant and a nurse, but I was very greatly relieved when I at length succeeded in getting the trocar removed. I completed the injection under chloroform. Since then I have always used a general anæsthetic, unless the patient was unconscious, or in a few cases when there seemed to be some contra-indication. From my experience of some 800 or 1,000 injections, quite 80 per cent. of which have been done under general anæsthesia, I believe these patients give no more anxiety to the anæsthetist than any others, and I would recommend the use of a general anæsthetic, unless when obviously unnecessary or for some reason contra-indicated. I have not been able to obtain suc-

\* This case has made a complete recovery.

cess with "water anæsthesia," as recommended by Sophian.

In some cases, I tried taking continuous blood-pressure readings, but did not think I received any help from them. With general anæsthesia, the variations in pressure do not seem to be marked either during the withdrawal of fluid or the injection of the serum. The withdrawal of fluid often gives rise to very severe pain, and, as Sophian says, the injection at times gives rise to pain which may be almost unbearable. I think the explanation of many of the alarming variations in blood-pressure is to be found in this sudden severe pain set up. With general anæsthesia this is avoided. As the result of his experience in this method of control of dosage, Sophian found that much smaller doses of serum appeared to be the safer course, and recommends that, in young children, the dose should be 3 to 12 c.c. In my cases in young children, I have always given the full dose of 20 c.c.—often more—generally under complete anæsthesia, and the results have been quite good. In the series are included two children under one year—both recovered. These were not mild cases. One, aged six months, admitted on the fifth day, required seven injections, the last on the 19th day; this case received in all 150 c.c. of serum, viz., six injections of 20 c.c. and one of 30 c.c.

The best dosage for any age, infant or adult, has not been as yet worked out. Personally, I am inclined to give full doses, and to repeat them frequently until definite improvement is shown. I am quite sure we often use more serum than is necessary, but at present we have no means of estimating the risk of withholding it in cases not distinctly improving.

Though I must confess to some disappointment with the results in this series of cases, and with the mortality of 36 per cent., I think there can be no doubt that, should there be a recrudescence of the disease in this winter, we may look forward to having available serum of much higher value than much of that employed in this country last winter.

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FROM the commencement of the war to July 31st, 1915, there

were 170 cases of cerebro-spinal fever in the Royal Navy. The following is a summary of the results of treatment in 163 cases, 89 of which (or 54·6 per cent.) proved fatal:—

|                                                                     | Cases. | Deaths.    | Recoveries. |
|---------------------------------------------------------------------|--------|------------|-------------|
| <i>Antimeningococccic serum.</i>                                    |        | Per cent.  | Per cent.   |
| Intrathecally - - - - -                                             | 105    | 64 or 61·0 | 41 or 39    |
| Alone - - - - -                                                     | 62     | 43 „ 69·4  | 19 „ 30·6   |
| Combined with vaccines, soamin, hexamine, or serum hypodermically - | 43     | 20 „ 46·5  | 2 „ 53·5    |
| Combined with soamin - - - - -                                      | 18     | 11 „ 61·0  | 7 „ 39·0    |
| „ „ an auto-vaccine - - - - -                                       | 11     | 2 „ 18·2   | 9 „ 81·8    |
| „ „ hexamine - - - - -                                              | 7      | 5 „ 71·4   | 2 „ 28·6    |
| „ „ serum hypodermically.                                           | 7      | 2 „ 28·6   | 5 „ 71·4    |
| Hypodermically - - - - -                                            | 19     | 6 „ 31·6   | 13 „ 68·4   |
| Alone - - - - -                                                     | 4      | 1          | 3           |
| Combined with intrathecal injection of serum - - - - -              | 7      | 2          | 5           |
| Combined with auto-vaccine and intrathecal injection of serum -     | 4      | 1          | 3           |
| Combined with an auto-vaccine -                                     | 3      | 2          | 1           |
| „ „ soamin - - - - -                                                | 1      | 0          | 1           |
| <i>Autogenous vaccine (never alone) - -</i>                         | 16     | 4 or 25·0  | 12 or 75·0  |
| Combined with serum intrathecally -                                 | 6      | 1          | 5           |
| Combined with serum intrathecally and hypodermically - - - - -      | 4      | 1          | 3           |
| Combined with serum intrathecally and soamin - - - - -              | 1      | 0          | 1           |
| Combined with serum hypodermically -                                | 4      | 2          | 2           |
| „ „ soamin - - - - -                                                | 1      | 0          | 1           |
| <i>Soamin - - - - -</i>                                             | 43     | 19 or 44·0 | 24 or 56·0  |
| Alone - - - - -                                                     | 21     | 7 „ 33·3   | 14 „ 66·7   |
| Combined with serum intrathecally -                                 | 18     | 11 „ 61·0  | 7 „ 39·0    |
| Combined with serum intrathecally and hexamine - - - - -            | 1      | 1          | 0           |
| Combined with serum intrathecally and vaccine - - - - -             | 1      | 1          | 0           |
| Combined with serum hypodermically -                                | 1      | 0          | 1           |
| „ „ auto-vaccine - - - - -                                          | 1      | 0          | 1           |
| Lumbar puncture (alone) - - - - -                                   | 13     | 4 or 30·8  | 9 or 62·2   |
| Symptomatic treatment (only) - - -                                  | 14     | 10 „ 71·4  | 4 „ 28·6    |

Naturally, the prolonged and unsatisfactory cases received more varied treatment than the fulminating ones. Some of the latter died shortly after arriving at hospital. The most

noticeable feature about the tabulated particulars was the failure of the intrathecal injection of antimeningococcic serum, though this was obtained from various sources. The cases treated solely by the intrathecal injection of serum and lumbar puncture showed a higher death-rate than that of the whole 163 cases. Flexner, in the *Journal of Experimental Medicine*, 1913, emphasized the importance of injecting antimeningococcic serum intrathecally as early as possible in the disease. In a table of 1,211 cases, he showed that when the serum was injected within the first three days, the mortality rate was 18 per cent.; when between the fourth and seventh days, 36.5 per cent.; and when later than the seventh day, 36.5 per cent. A comparison on the same lines of the cases in the Royal Navy showed:

|                    | Cases. | Deaths.              | Recoveries.          |
|--------------------|--------|----------------------|----------------------|
| 1st to 3rd day ... | 70     | 42 or 60 per cent.   | 28 or 40 per cent.   |
| 4th to 7th day ... | 24     | 14 or 58.4 per cent. | 10 or 41.6 per cent. |
| Later than 7th day | 11     | 8 or 72.7 per cent.  | 3 or 27.3 per cent.  |

The failure of the injected serum to reduce the mortality clearly was not due to its being given too late. The serum treatment, which was so successful in the hands of Flexner and Sophian in America and of Robb in Belfast, was given a thorough trial in these cases, but proved most disappointing. Possibly the meningococci were "fast" to the action of the serum, or the organisms were para-meningococci. Alarming symptoms directly after the intrathecal injection occurred in two cases only, showing that the gravity method of administration (which was not in vogue in the Royal Navy) was scarcely necessary when due care was taken. Serum rashes were noted in 20 per cent. of the cases, but may have been more frequent; in a few cases, there were also arthritic pains. No severe anaphylactic symptoms were recorded. In the 16 cases in which Fleet-Surgeon White-side, R.N., gave an autogenous vaccine, the low mortality of 36.7 per cent. was reached. Soamin seemed to give good results, and to have a beneficial effect in the septicæmic stage. Optic atrophy was not noted in any instance, though in one case 42 gr. were given. Hexamine did not appear to exert any effect clinically, and was therefore soon abandoned. Lumbar puncture was performed in 149 of the

163 cases, though in 38 once only, but 14 of these died soon after coming under observation. Six of the other cases, which had a single tapping, died. Of 22 cases tapped twice, 8 died. Three tappings were done in 20 cases, with 9 deaths; 4 in 24 cases, resulting in 15 deaths. Lumbar puncture, he regarded as a palliative rather than as a curative measure, by relieving symptoms due to increased intrathecal pressure. In 13 cases, of which four proved fatal, it was the only form of treatment other than the ordinary symptomatic remedies employed.

In 14 cases, 10 of which proved fatal, symptomatic remedies only (such as morphine for pain) were given.

With regard to prophylactic measures, it seemed advisable to invalid the men who recovered from an attack of the disease, because they might be intermittent or periodic carriers who alternately gave negative and positive results on bacteriological examination of throat swabs for meningococci. Recently, three cases of the disease among boys were traced to a boy who had recovered from the disease, and, when examined bacteriologically, was found to be a carrier.

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EARLY in the epidemic, the Commanding Officer set apart a ward for the treatment of the disease under discussion, and cases were collected from practically all over the Eastern counties and the South Midlands. The first case came under notice about the middle of January—an officer's servant, who was at his work the night before, and, at 2 a.m., was found in bed unconscious. He was moved to hospital with the provisional diagnosis of uræmia. On arrival, he was profoundly unconscious, had tremors all over, could not swallow, and had nystagmus and retention of urine. Only 1½ oz. of urine could be obtained by catheter, and it contained neither sugar nor albumen. Lumbar puncture yielded an ounce of yellowish fluid containing pus. As the bacteriologist had not made his report next day, the theca was again punctured, and 1½ oz. of fluid drawn off. On the third day, the man was definitely

better. The diagnosis being still uncertain, he was again punctured. The following day he could swallow, and had recovered consciousness. On the sixth day he was well and was discharged. On the twentieth day, he returned to duty. Two other cases occurred within a day or two, from the same regiment. They also were punctured and both recovered, but after a somewhat tedious course. The staff then began to employ serum; six cases were treated with it, and two were admitted from outside after having received an injection. Of the eight cases, four died. They concluded that they were not doing very well with the serum, and, bearing in mind the good result from simple lumbar puncture in the first, very acute, case, they treated all the succeeding cases in that way, repeating it as often as the symptoms persisted. By the end of March, 28 cases had been treated, most of them by lumbar puncture. Twenty cases were treated without serum, and there were four deaths, though in the next seven cases there were five deaths. About that date, there seemed to be a peculiarly virulent type of case. Towards the end of the epidemic, they had a series of nine cases with only one death. During the time I had charge of the ward, *i.e.*, to the middle of June, there were 42 cases, 14 deaths.

I submit that frequent drainage of the cerebro-spinal fluid during the persistence of the symptoms is a satisfactory form of treatment, at all events until a more satisfactory serum is available than there now seems to be. The simple procedure resulted in a very striking relief of symptoms, especially of the very intense headache. A most important matter was the prevention of hydrocephalus. Some of the fulminating cases were absolutely unresponsive to anything. Many cases seemed to recover up to a certain point, then had a return of severe headache, and relapsed, ending in death. The onset of hydrocephalus may be marked by a sudden lapse into an adynamic state with feeble pulse and unconsciousness. The supervention of these symptoms is a sign of increased cerebro-spinal pressure, and an indication for lumbar puncture. Post-mortem, one found that the cord was so tightly bound across that there was no circulation, explaining the impossibility of getting anything from the cord by puncture. I believe that in many cases daily

puncture would prevent hydrocephalus being set up. If the theca could be kept properly drained, there seemed a reasonable chance of a successful result. It is a very safe operation, but I agree with Dr. Robb that it is very difficult to ensure doing it properly without a general anæsthetic. The greatest quantity of fluid which either my colleague, Captain Gaskell, or myself has withdrawn is 2 ozs., and no sign of collapse followed.

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THE fifteen fatal cases mentioned by Captain Foster were all examined post-mortem, and could be divided roughly into three groups: *acute fatal cases*, which did not respond to treatment and succumbed within five days; *sub-acute cases*, dying three to four weeks after onset; and *chronic cases*, lasting six weeks or more, which died with hydrocephalus.

In the *acute cases*, pus was found not merely at the base of the brain, but distributed all over the vertex in the sub-arachnoid space round the blood vessels, a most intense vertical meningitis being present, the whole of the meninges being greatly engorged. Even in fulminating cases, in which the disease had lasted less than 48 hours, a considerable amount of pus was present round the cerebral vessels over the vertex. The pathological condition was such that recovery from it would seem to be almost out of the question. Two of the *sub-acute cases* lasted for about three weeks. At the post-mortem, a most tenacious, inspissated, purulent exudate completely covered the base of the brain, and filled the sub-arachnoid space of the cord. In contradistinction to other cases, excess of cerebro-spinal fluid was entirely absent. Pus was present over the vertex, but in comparatively small amount; the cerebral vessels were not congested. In these cases, lumbar puncture had been performed repeatedly, but the amount of pus present, instead of diminishing, had progressively increased, until finally the fluid became so thick that it would no longer flow through the largest puncture needle. After this, only a drachm or two of thin serum could be obtained. In one of these cases, serum was used in an attempt to dilute the pus, but was entirely without effect.

These cases had initially responded to treatment, but had finally sunk into an adynamic state. In this class of case, the purulent infection had apparently paralysed the cerebro-spinal secretion.

In the *chronic* group, marked symptoms of hydrocephalus were present in life, and, post-mortem, the third and fourth ventricles were found to be widely dilated and filled with fluid. The lateral ventricles were also, as a rule, distended. In two cases, the sub-arachnoid space was completely obliterated by adhesions in the upper dorsal region. Lumbar puncture had, therefore, failed to relieve the distension of the ventricles. In another case, the roof of the fourth ventricle had become completely adherent to the cerebellum. In yet another case, no complete obstruction in the cerebro-spinal circulation was found, but a terminal pneumococcal septicæmia was present.

A common cause of death was respiratory failure; the heart could be kept beating by artificial respiration for some hours.

The efficacy of daily lumbar puncture, commenced as early as possible in the illness, was demonstrated in the cases which had recovered, those punctured on the first or second day having a comparatively short illness. Some had not been punctured before the eighth day, and, in these, the illness had run a very prolonged course. One of these prolonged cases had ceased to show further signs of illness after 5 c.c. of his own serum had been injected intrathecally. This form of treatment was tried, because the agglutinating power of the man's own serum had been found to be much higher than that of any of the artificial immune sera. This effect may have been merely a coincidence, for other chronic cases had similarly ceased quite suddenly to show symptoms. It is, however, intended to test the treatment further. The net result of the cases at the hospital is a mortality of 39 per cent., and most of the cases were treated by lumbar puncture, unsupplemented by any other form of treatment. I contend that the details of the cases showed up as well under that simple procedure as other series in which lumbar puncture and the injection of serum had been carried out.

