INVESTIGATIONS INTO CASES OF CEREBROSPINAL FEVER IN THE NORTHERN COMMAND OF THE ARMY DURING 1931, CONCLUDING WITH A PLEA FOR THE EARLY DIAGNOSIS OF THE DISEASE.

By Major W. Walker, M.C., Royal Army Medical Corps.

(Concluded from p. 15.)

CONTACTS AND CARRIERS.

On a case suspected to be cerebrospinal fever occurring in barracks, the remaining men in the barrack-room were isolated in their quarters, which, of course, included messing in their quarters until the arrival of the pathologist. The question as to who were to be regarded as immediate contacts and who were to be swabbed rested entirely with that individual.

This is only right because this type of work is in a special class by itself, especially when it has to be undertaken at a long distance from the laboratory. Very few persons outside a bacteriological laboratory realize the work entailed in getting the special media plates prepared, conveying them at a suitable temperature in their cumbersome boxes, together with other necessary apparatus, to the abode of the contacts; the time taken in the deliberate swabbing behind and beyond the soft palate and in the careful spreading of the material over the surface of the medium, and finally, the after-work in the laboratory in the differentiation of the meningococcus from the other numerous denizens of the nasopharynx. The technique required is so specialized that it cannot be carried out by subordinates. There is therefore a very definite limit to the amount of material that can be dealt with efficiently by one bacteriologist.

As a general routine the remaining occupants of the barrack room from which a case had been removed were considered the immediate contacts and as such were all swabbed. This is more satisfactory than the swabbing of the immediate adjacent contacts because the resulting cultures portray the pharyngeal state of the room as a whole, and afford evidence for or against defective hygienic conditions within the barrack room.

Nasopharyngeal disinfection was postponed until the swabbing had taken place, after which the contacts gargled and insufflated a 1 in 5,000 dilution of potassium permanganate in normal saline solution thrice daily. The bacteriological results of the swabbing were notified in forty-eight hours, all the non-carriers being immediately liberated.

The Treatment and Control of Carriers.

Carriers were either isolated in the infectious diseases blocks of military hospitals or, more generally, in special quarters set apart in barrack rooms. In addition to the routine gargling and nasal insufflation, as recorded above,
Cerebrospinal Fever in the Northern Command in 1931

the carriers were given as much out-door employment as possible; in quarters, liberal bed-spacing and free ventilation were strictly maintained. No other routine form of treatment was instituted.

Carriers were swabbed every seven to ten days. No carrier was allowed to return to duty until two successive examinations of his nasopharynx were negative.

Duration of the Carrier State.

Seventy-seven per cent of carriers ceased to be carriers within fourteen days and ninety-two per cent within three weeks. One woman, the mother of the child who caught the infection, persisted in the carrier state for two months, and a contact carrier (giving a pure growth on a plate) of the first Strensall case remained positive for three months.

The Health of the Carriers.

On examination some sixty per cent of carriers were found to be suffering from nasopharyngitis of some degree. In the majority the condition did not give rise to any discomfort, but in ten per cent it was definitely acute. A pure plate culture of the meningococcus has several times been obtained from a carrier with an apparently normal throat. No detected carrier developed the disease, or, as far as I have been able to trace, was admitted to hospital with acute toxic pharyngitis.

General Consideration regarding the Routine Custom of Swabbing Contacts.

Contacts are swabbed with two ends in view. These are: (a) to detect and isolate carriers in the hope of arresting the spread of infection; (b) To make the public feel that something definite is being done to stop the spread of the disease.

With regard to (a), I have frequently doubted the practical value of swabbing a collection of contacts and isolating the unfortunate detected carrier in military communities. The soldier father working in an infected area is an exception; he should be prevented, if possible, from carrying home infection to young, susceptible children. In general barrack procedure, when a case occurs, a few carriers are detected and isolated, but a large number of equally dangerous individuals in other parts of the community continue to mix with their fellow men, completely uncontrolled. The individual who gets infected with the identical strain of meningococcus, but who, by virtue of a partial immunity, arrests the infection in the acute catarrhal stage, causes no apprehension among his fellow men, and his immediate contacts remain undisturbed, continuing to harbour some carriers in their midst. When viewed in this light, our present procedure does not appear to be very practical. Can the energies of the pathologist be expended on more useful lines than travelling back-
wards and forwards on long journeys to re-swab some carriers again and again until two negative swabs in succession are obtained from each one? He would be rendering much more useful service if his energies were concentrated on the prevention of the disease rather than following in the aftermath of a case. By keeping a bacteriological control on a community threatened with infection he should be able to give a timely warning, when energetic steps could be taken by those concerned to overhaul the hygienic condition of the unit. If a case occurs in barracks certainly let a non-contact barracks also be swabbed. Compare the two results; if they are equally bad then it can be taken that the whole unit requires immediate attention by the responsible authorities, and appropriate steps having been taken, the pathologist can return in three weeks and estimate the results of their labours. Any carriers detected should be isolated under good hygienic conditions and given outdoor occupation. At the end of three weeks they should be returned to duty without further examination.

The energies of the pathologist should also be directed towards the routine investigation of catarrhal conditions in the upper air passages when meningococcal infections are known to be prevalent. By this means he will be able to detect a case of cerebrospinal fever in its earlier manifestations, and by the prompt application of active and appropriate measures may either abort a meningal invasion, or at least lessen the intensity of its inflammatory activity. His attitude in life must not be of a passive nature, waiting in his laboratory until invited by the clinician to carry out some particular tests on a suspicious case. By so doing he may, sometimes, be anticipating the presence of the undertaker by a short two or three days.

In a controlled community, the pathologist is the mainspring of everything pertaining to cerebrospinal fever, its prevention, early detection and appropriate specific treatment. In this connection he must be prepared to elaborate practical schemes suitable to the area under his control for the best means of dealing with the infection in all its aspects.

With regard to (b) the allaying of public alarm. Until we know much more about the factors governing the mode of infection and spread of this disease we are not in a strong enough position to refuse to take elaborate steps with regard to immediate contacts, especially in a Service supported by the public purse. Until that extra knowledge is forthcoming the present practice, with regard to contacts, must remain in force.

**Summary of Carrier Investigations.**

<table>
<thead>
<tr>
<th>Swabs from suspected cases</th>
<th>Total swabbed</th>
<th>Number positive</th>
<th>Carrier rate per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>26</td>
<td>11</td>
<td>42-3</td>
</tr>
<tr>
<td>2</td>
<td>177</td>
<td>37</td>
<td>21</td>
</tr>
<tr>
<td>3</td>
<td>114</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>4</td>
<td>190</td>
<td>37</td>
<td>20</td>
</tr>
<tr>
<td>Totals</td>
<td>507</td>
<td>114</td>
<td>22-28</td>
</tr>
</tbody>
</table>
The finding of clear cerebrospinal fluid at the diagnostic lumbar puncture is evidence that an early diagnosis has been made. The value of early diagnosis is illustrated by comparing the appearances of the cerebrospinal fluid at the diagnostic lumbar puncture in the cases investigated from the Command Laboratory in 1931, with the mortality-rate against each type.

- Turbid cerebrospinal fluid, 6; mortality 88 per cent
- Clear cerebrospinal fluid, 4; mortality 50 per cent

Early in 1932, six additional cases were investigated. A similar analysis gives:

- Turbid cerebrospinal fluid, 2; mortality 50 per cent
- Clear cerebrospinal fluid, 4; mortality Nil

Combining the findings from the sixteen cases the results are:

- Turbid cerebrospinal fluid, 8; mortality 75 per cent
- Clear cerebrospinal fluid, 8; mortality 25 per cent

With early diagnosis and appropriate treatment the mortality-rate should not exceed twenty-five per cent of cases.

It may be argued that in some cases such early diagnosis is impossible, the fluid being turbid soon after the onset of the acute symptoms. In comparing the dates of onset of the symptoms with the dates of the diagnostic lumbar punctures in the eight cases with turbid fluid, it was found that there was an interval of from thirty-six to ninety-six hours between the onsets and the lumbar punctures, the average being fifty hours.

In no case lumbar-punctured within thirty-six hours of the onset has the cerebrospinal fluid been found turbid. The high mortality in cases with a turbid cerebrospinal fluid at the time of the diagnostic lumbar puncture is largely due to a delayed diagnosis.

It might therefore be said that the mortality-rate in this disease is largely in the hands of the clinicians who first see the cases.

What are the chief factors standing in the way of early diagnosis of cases? They are two in number: (a) The possibility of the disease being a meningococcus infection being entirely overlooked. (b) The reluctance on the part of many clinicians to diagnose the disease until some of the textbook symptoms are definitely established.

With regard to the first factor: This is apt to occur when an odd sporadic case presents itself to one who has had little experience of the disease. With increasing experience one acquires a "meningococcal outlook," and all influenzal-like infections are suspected to be of meningococcus origin until they can be proved to the contrary.

If this attitude were adopted at the present day during the prevailing
incidence of cerebrospinal fever, the occurrence of a sporadic case would not take the clinician unawares.

Influenza is the great stumbling-block over which the physician is apt to fall in the diagnosis of an early sporadic case of the disease. When once the physician is convinced that he is dealing with a case of influenza, he may fail to observe the signs of advance of the meningococcus from the nasopharynx until it is definitely established in his patient’s subarachnoid space.

I could cite several cases treated as influenza until one day it was observed that there was definite neck stiffness and that Kernig’s sign was present.

The second factor of delay is caused by waiting for the textbook symptoms of the disease to establish themselves. We are taught that the classical prodromal symptoms are headache, vomiting and pyrexia, soon to be followed up by neck stiffness and Kernig’s sign. The Ministry of Health review on cerebrospinal fever¹ under “Clinical Considerations” reads:—

“Diagnosis before its confirmation by lumbar puncture, is usually determined by five symptoms; intense headache, vomiting, pyrexia (usually moderate and associated with a comparatively slow pulse), stiffness of the neck muscles and Kernig’s sign.”

It naturally follows that the cautious physician, or one jealous of his diagnostic reputation, who waits until those symptoms are established will generally get a turbid cerebrospinal fluid at his diagnostic lumbar punctures. In the circumstances he must not expect a relatively low rate of mortality among his cases.

The early signs are there for those who can read them, but they are not always writ in capital letters.

A Note on Kernig’s Sign.

Confusion arises from the early atypical symptoms found in many of the sporadic cases. There may be little or no vomiting. The temperature may be raised, normal or subnormal. Neck stiffness may be little more than tenderness of the neck muscles. Kernig’s sign may be definitely positive, merely suggested, or absent.

During my investigations I have had more difficulties regarding Kernig’s sign than with any other clinical manifestation of meningeal infection. To many clinicians Kernig’s sign is either definitely positive or is entirely negative, there is no recognized intermediate state. Early in my investigations I learned the value of an intermediate form of this sign—“suggestion of Kernig”—from Captain F. J. O’Meara, F.R.C.P.I., Medical Specialist, Catterick. A “suggestion of Kernig” is present when the leg

can be all but straightened on the thigh, flexed at right angles, but the attempt to straighten it completely causes definite pain in the hamstrings. Subsequent observations have led me to realize the great value of a "suggestive" Kernig in determining the early onset of meningeal irritation. When once it is realized that the presence of a "suggestion" of Kernig is an important sign in the diagnosis of early meningitis, it will follow that laboratory investigations will be sought for such cases at an earlier period than would otherwise happen, and more cases would be diagnosed and treated before the cerebrospinal fluid became turbid.

Again, Kernig's sign may be absent in an early case when a clear cerebrospinal fluid is obtained at the first lumbar puncture. I have four such cases in my records. In all the cerebrospinal fluid subsequently became turbid; two cases were fatal.

The relation of Kernig's sign to the appearance of the cerebrospinal fluid at the diagnostic lumbar puncture in the sixteen cases cited above is summarized as follows:

<table>
<thead>
<tr>
<th></th>
<th>Positive Kernig</th>
<th>&quot;Suggestive&quot; Kernig</th>
<th>Negative Kernig</th>
</tr>
</thead>
<tbody>
<tr>
<td>8, turbid cerebrospinal fluids</td>
<td>7</td>
<td>1 (a)</td>
<td>0</td>
</tr>
<tr>
<td>8, clear cerebrospinal fluids</td>
<td>Positive Kernig 1 (b)</td>
<td>&quot;Suggestive&quot; Kernig 3 (c)</td>
<td>Negative Kernig 4 (d)</td>
</tr>
</tbody>
</table>

(a) Very acute case. Died within four days.
(b) The only case diagnosed on purely clinical grounds. The case survived.
(c) All subsequently became positive, the cerebrospinal fluid becoming turbid. All survived.
(d) All subsequently became positive. In all the cerebrospinal fluid became turbid. Two cases died.

A Clinical Description of the Earliest Symptoms.

In a clinical description of the disease the earliest symptoms should be detailed to their fullest extent, for by so doing the physician may be guided towards an earlier diagnosis, when the prompt application of appropriate treatment may hold out better hopes for the ultimate recovery of the case.

Such a description, drawn from my recent experiences within the Northern Command, might read as follows:

Clinically the disease is characterized by the sudden onset of headache, vomiting—often continued, with or without pyrexia. At a later period head retraction and Kernig's sign are established. Headache is the most constant early symptom. It is usually very intense and is, at first, frontal in location. Characteristically, it is continuous but sometimes it is only severe during acts of coughing. In the majority of cases vomiting occurs at the onset. This may be continuous or limited to one or two occasions. In some cases there is only nausea at this stage with no actual vomiting. Pyrexia is not invariable. When it occurs it is usually of moderate degree and is often associated with a relatively slow pulse. In some cases the temperature is normal, or even subnormal.
There are two recognized stages of the disease: (1) The premeningitis stage; (2) the stage of established meningitis.

(1) The Pre-meningitis Stage.—This is of variable duration, depending on the intensity of the infection. On the average it lasts from thirty-six to forty-eight hours, but may be extended to ninety-six hours. In this stage the symptoms resemble those of an acute toxic influenza or an acute toxic catarrhal pharyngitis.

The patient looks more seriously ill than his outward condition would appear to warrant. Early in this stage there are three symptoms constantly present: (a) profound toxæmia; (b) intense headache, usually frontal in location; (c) acute catarrhal pharyngitis. This differs from the “dry catarrh” of influenza.

At the earliest stage the mental attitude is characteristic. There is a definite apathy, an air of detachment from things in general. The patient is clear and lucid when spoken to. Later this state gives way to excitability, delirium or coma when the stage of meningitis is established.

Very early in this stage there are usually some manifestations of meningeal irritation. The superficial and deep reflexes are often found to be exaggerated. Soon the former may be difficult to elicit or may disappear while the knee-jerks are still active. Kernig’s sign may be absent at the onset, but it usually manifests itself early in this stage in a modified form—a “suggestion of Kernig.” When this early manifestation is detected, it calls for a thorough investigation of the case. As the premeningitis stage passes into that of established meningitis, so does Kernig’s sign pass from the “suggestive” to the definite.

At first there may be mere discomfort on moving the head, or the neck muscles may only be tender to the touch. A degree of stiffness is next noticed, passing on to some limitation of movement, particularly the nodding movement. The patient’s chin may not quite touch his sternum. When meningitis is established, the head is retracted.

(2) The Stage of Established Meningitis.—The classical symptoms of head retraction and Kernig’s sign are now present. This stage does not fall within the present considerations.

Aids to Clinical Diagnosis.

An early case having been suspected on clinical grounds, a definite diagnosis can be arrived at by applying three aids: (1) Nasopharyngeal swab for direct examination and for culture; (2) total and differential white blood-cell estimation; (3) lumbar puncture and the examination of the cerebrospinal fluid.

(1) Nasopharyngeal Swab.—(a) Direct examination of a smear stained by Gram’s method. In a meningococcus infection there is invariably an intense exudate of polymuclear cells. If the condition appears to be a pure infection of Gram-negative diplococci, the probability is that the case is a simple meningococcal pharyngitis. If Gram-negative diplococci are present
in a mixed infection, it is a point in favour of the condition being an early meningitis.

(b) Culture. A pure culture or nearly pure culture of meningococci favours a simple pharyngitis. A few meningococcus colonies in a mixed culture containing many pyogenic cocci, especially *Staphylococcus albus*, favour an early meningococcus meningitis.

(2) Total and Differential White Blood-cell Estimation.—Total count: This is of the greatest value and affords most reliable information as to the type of infection under investigation. The finding of a normal leucocyte count or a leucopenia at once dismisses the possibility of a meningococcus infection. In this way an influenzal meningismus can be detected by its associated leucopenia. In early cases of cerebrospinal fever there is invariably a definite leucocytosis. This has been found to lie between 15,000 and 21,000 cells. In one instance only has an early case of the disease been associated with a leucocytosis of under 15,000. In this case the first count was 11,000, within seven hours it was 19,200. Very rarely does a leucocyte count in a case of over 15,000 occur in a case of simple meningococcal pharyngitis; if it does, there is generally something definite to account for it, usually a superadded streptococcal infection of the tonsils.

A lumbar puncture should be undertaken at once in a case with clinical symptoms suggestive of meningeal irritation associated with a leucocytosis of 15,000 or over.

If with those symptoms there is a leucocytosis of under 15,000, the case should be kept under observation for forty-eight hours, a total white blood-cell estimation being undertaken morning and evening.

Differential Count: This is not such a constant guide. Early cases of cerebrospinal fever are generally associated with a polynuclear count of 80 to 90 per cent. A lesser percentage of polynuclears does not exclude the possibility of the disease.

(3) Lumbar Puncture.—It is better to conduct this under a general anaesthetic. The pressure of the fluid is raised, and more can be drawn off, which is all to the good, especially if the fluid is turbid.

In early cases the fluid may or may not be under great pressure. It may be clear, or only slightly opalescent. In established cases of meningitis it is definitely turbid.

Anti-meningococcus serum must be given regardless of the appearance of the fluid. It should be given without waiting for the laboratory report on the fluid.

The question of the diagnosis has now to be decided. There should be no difficulty when the fluids are turbid or opalescent. A stained smear prepared from the centrifuged deposit of the fluid will demonstrate the type of exudate. A lymphocytic exudate indicates generally tuberculous or influenzal meningitis. A search for the organisms will settle the point. If the exudate is polynuclear in type, meningococci will be found in every case of cerebrospinal fever.
A turbid fluid with no visible organisms is suggestive of a streptococcal or staphylococcal meningitis. In pneumococcus meningitis the pneumococci may not be difficult to find.

In all cases cultures should be taken from the fluid at the bedside and from the deposit of the fluid after centrifuging.

A diagnosis in the case of clear cerebrospinal fluid is not so easy. A cell-count may reveal a definite increase in their number. An examination of the deposit may reveal a few polynuclear cells and perhaps a few meningococci.

If no increase in cells is detected, the fluid should be incubated and the deposit examined microscopically, and, at the same time, cultured. Meningococci, if originally present, will have multiplied and may be detected microscopically or isolated in culture.

In the case of a clear fluid an examination of the patient within an hour or two after the injection of the anti-meningococcus serum will usually settle the point of meningococcus infection. When this infection is present there is a very definite reaction in the patient. There is an intense throbbing headache, neck stiffness and Kernig's sign are more evident. There is generally vomiting of a continued type. At the next lumbar puncture the fluid will be found to be definitely turbid, and meningococci may or may not be seen in the deposit, depending on the efficacy of the serum injected.

If the case is not meningococcal in origin there may be little or no reaction clinically. The fluid may show an increase in the number of cells at the next lumbar puncture, but the number may not exceed 300 per cubic millimetre. They are polynuclear in type.

A clear cerebrospinal fluid at an initial lumbar puncture is greatly in the patient's favour, but for diagnostic purposes it offers little opportunity to the bacteriologist to offer any definite opinion.

Acute Meningococcus Pharyngitis.

A discussion on the diagnosis of cerebrospinal fever would not be complete without a reference to the differential diagnosis between it and acute meningococcal pharyngitis. In the acute epidemic type of the disease, with its rapid train of progressive symptoms, the differential diagnosis is fairly evident and a total white blood-cell count may determine at once the necessity for an immediate lumbar puncture. The mild sporadic case, in its earlier manifestations, gives rise to a great deal of anxiety and uncertainty. It may be indistinguishable from a very acute catarrhal pharyngitis for twenty-four to forty-eight hours.

The only safe guide is to watch the degree of leucocytosis. If the total count exceeds 15,000, with no apparent superadded cause, a lumbar puncture should be carried out with no further delay.

As already stated, a pharyngitis case may hang fire for a few days with a fluctuating leucocytosis. Recently I watched a case brought into hospital
with headache, sore throat, neck stiffness of three days duration. The temperature was subnormal. He looked very toxic. There was a suggestion of Kernig's sign in both legs. A nasopharyngeal culture produced a growth of Type I meningococcus and S. albus. His blood estimations were as follows:

<table>
<thead>
<tr>
<th>Day of observation</th>
<th>Total count</th>
<th>Differential count:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st morning</td>
<td>13,000</td>
<td>74 per cent</td>
</tr>
<tr>
<td>1st evening</td>
<td>14,600</td>
<td>69</td>
</tr>
<tr>
<td>2nd</td>
<td>9,200</td>
<td>79</td>
</tr>
<tr>
<td>3rd morning</td>
<td>15,400</td>
<td>69</td>
</tr>
<tr>
<td>3rd evening</td>
<td>14,800</td>
<td>76</td>
</tr>
<tr>
<td>4th</td>
<td>13,800</td>
<td>82</td>
</tr>
<tr>
<td>5th</td>
<td>9,700</td>
<td>68</td>
</tr>
</tbody>
</table>

On the third day he developed an inflammatory condition of both tonsils. Cultures from the throat revealed streptococcus colonies in large numbers.

In another case the leucocytosis rose to 18,600 cells for a similar reason. With the advancing leucocytosis the nervous symptoms subsided. For this reason a lumbar puncture was not done. The case cleared up completely in three days.

**EARLY APICAL PNEUMONIA.**

Apical pneumonia in its earlier manifestations may readily be confused with cerebrospinal fever. As no cases of the former condition were encountered during the 1931 investigations, the disease was not cited in the general discussion on the differential diagnosis in Part I.

Two cases of this condition were seen within a week, early in 1932.

The first was a middle-aged warrant officer who gave a history of the sudden onset of headache and vomiting four days previously. His temperature was 102° F., pulse 120, respiration 26. The vomiting was of the continued type. He appeared extremely toxic. He complained of severe frontal headache, sore throat and tightness across the upper part of the chest. An examination of the chest revealed no signs of pulmonary involvement. Kernig's sign was absent.

A culture from the nasopharynx produced a heavy growth of catarrhal pharyngococci, but no meningococcus colonies were found.

There was a leucocytosis of 35,000 cells, 85 per cent being polynuclear.

A lumbar puncture showed a clear fluid, not under pressure; 25 cubic centimetres were withdrawn and replaced by 20 cubic centimetres anti-meningococcus serum. An examination of the fluid revealed the globulin and glucose content normal. The cell count was also within normal limits. No organisms were seen or isolated in culture.

The patient exhibited no general reaction after the administration of the serum. Next morning there was definite evidence of pneumonia at the apex of the right lung.

The second case was more confusing. The patient was brought into...
hospital at night with the history of having vomited twice and then fainted on guard duty. He was seen by Major W. M. Cameron, O.B.E., Medical Specialist, York, who found the patient in a highly excitable condition. Temperature 102° F., pulse 104, respirations 24. The knee-jerks and other deep reflexes were greatly exaggerated. Kernig's sign was present in its most extreme form. The pupils were dilated. There was an intermittent hysterical internal strabismus of the left eye.

During the night the patient vomited several times. Next morning the nervous symptoms persisted in their exaggerated form. A culture from the nasopharynx revealed no colonies of meningococci.

There was a leucocytosis of 45,000 cells, polynuclears being 86 per cent. At the lumbar puncture, twenty-five cubic centimetres of clear fluid were removed under slight pressure and were replaced by twenty cubic centimetres of anti-meningococcus serum.

The globulin and glucose content of the fluid was normal. The cell count was one cell per cubic centimetre. No organisms were seen or isolated in culture.

The patient exhibited no after-reaction to the serum.

Next morning his sputum was muco-sanguinous. There were early signs of pneumonia at the apex of the right lung.

It is interesting here to note that with a non-meningococcus infection there was no general reaction on the part of the patients after the administration of anti-meningococcus serum.

**A Few Observations on Four Cases Treated at the Military Hospital, York.**

Early in 1932, several cases of acute nasopharyngitis, exhibiting signs of meningeal irritation, were admitted to the Military Hospital, York. Meningococci were isolated from each case. In those typed the organism was found to be a Type I meningococcus.

This created a "meningococcal atmosphere" and all cases were strictly watched for early signs of cerebrospinal fever. In addition, the medical officer in charge of the medical inspection room was asked to send cases complaining of headache and sore throat to the laboratory for investigation.

In this way four cases of cerebrospinal fever were detected in the early stages of the disease.

The blood and cerebrospinal fluid findings are recorded briefly below. In all cases antimeningococcus serum Type I (Lister Institute product, globulin solution) was administered at the lumbar puncture.

**Case 1.**—Leucocytosis of 21,000; polynuclears 89 per cent. Cerebrospinal fluid faintly opalescent. Globulin in excess, partial reduction of Feiling's solution. Cell count, 50, majority polynuclears. Several meningococci seen, all extra-cellular. Culture, sterile.

**Case 2.**—Leucocytosis of 18,200; polynuclears 85 per cent. Cerebrospinal fluid crystal clear. Faint trace of globulin but normal reduction of
Fehling's solution. Cell count of ten cells. In stained smears from the deposit the majority of cells appeared to be lymphocytes, but several polynuclear cells were found. Eight pairs of meningococci were found, after a prolonged search, six pairs being within one polynuclear cell, two pairs being extra-cellular. Cultures were sterile.

Case 3.—Leucocytosis of 15,000; polynuclears 60 per cent. Cerebrospinal fluid clear, globulin and glucose content normal. Cell count of two cells. No organisms seen or isolated.

The following day the cerebrospinal fluid was turbid, cell count of 1,550 cells. Occasional intra-cellular meningococci were observed. Cultures were sterile.

Case 4.—Leucocytosis of 11,000; polynuclears 76 per cent. After seven hours the findings were 19,200 and 66 per cent respectively.

The cerebrospinal fluid was clear and normal so far as could be ascertained.

Next day the patient was acutely ill. He lay in a state of semi-coma. There was neck stiffness and Kernig's sign was definitely positive. He refused to allow a lumbar puncture. The leucocytosis had risen to 26,000; polynuclears being 91 per cent. The following day he offered no objection to lumbar puncture. There was no coma but the patient felt acutely ill. There was a leucocytosis of 19,800 cells; polynuclears being 90 per cent. The cerebrospinal fluid was turbid, the cell count being 881 cells. No organisms were seen or isolated.

Nasopharyngeal cultures in each case produced meningococcus colonies in varying numbers; in one case only were they numerous. It is now greatly regretted that the meningococci isolated were not typed.

Permission was obtained to retain the cases for treatment at the Military Hospital, York.

The results obtained in the Command during the previous year with various brands of polyvalent anti-meningococcus serum were not encouraging. For this reason, and because the local strain of the organism appeared to be a Type I meningococcus, it was decided to give Type I serum a trial in the first case. That the serum was definitely specific was demonstrated by the fact that, although there was an intense cellular exudate at the second and third lumbar punctures, no organisms were visible or were isolated in culture. The case was intensely ill for three days. On the fourth day a definite improvement set in, which was maintained until the ninth day, when a severe serum reaction developed. He soon became cold, collapsed and pulseless. Cardiac stimulants and subcutaneous injections of adrenalin, 1 in 1,000, had little effect. An intravenous of 1 in 10,000 adrenalin was slowly given up to four cubic centimetres.

This produced a rapid change for the better, which was subsequently maintained by cardiac stimulants. Convalescence was rapidly established and the patient made a complete recovery, no after-effects of any description being detected.
Type I serum was given to the three subsequent cases. In each the reaction appeared to be specific, and only in one case were organisms found at the second lumbar puncture.

All cases, after being acutely ill for two or three days, made a complete recovery.

A daily examination of the fluid was made in each case. Below is a typical example:

<table>
<thead>
<tr>
<th>Day of treatment</th>
<th>Cell count</th>
<th>Percentage of polymorphs</th>
<th>Organisms seen</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1,550</td>
<td>95</td>
<td>Occasional meningococci</td>
</tr>
<tr>
<td>3</td>
<td>370</td>
<td>85</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>475</td>
<td>80</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>140</td>
<td>80</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>145</td>
<td>60</td>
<td>None</td>
</tr>
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No further treatment was given as the patient’s clinical condition was now definitely good.

These four consecutive cases illustrate the immense importance of early diagnosis and the early application of specific treatment. Not only was the mortality rate nil, but no after effects were demonstrable in any of the cases.

In endemic areas every case of pharyngitis in hospital should have at least one total white blood-count performed daily.

Cases attending for treatment with symptoms of sore throat and headache should be detained for laboratory investigation.

The extra work entailed will be more than compensated for by the finding of a case of cerebrospinal fluid in its early, pre-meningitis stage, when a lumbar puncture can be undertaken with the reasonable hope of finding the cerebrospinal fluid clear.

There are two definite rules of action which should be adhered to in every suspected case of cerebrospinal fever:
1. Never omit to do a total white blood-count.
2. When in doubt, lumbar puncture.

**Summary.**

(1) In Part I the investigation of twelve cases of cerebrospinal fever within the Northern Command of the Army is described. Eleven young soldiers and one young child were infected. The outbreak formed part of a generalized epidemic throughout the country.

(2) An endeavour is made to trace the sources of infection in the different cases. In two areas the main cause of cross-infection appeared to be due to overcrowding in canteens.

(3) Suggestions are put forward for future preventive measures. These entail a close watch on the carrier rate, from which much valuable information may be gained.

(4) The technique employed in the isolation of the meningococcus from the cerebrospinal fluid and from the nasopharynx is recorded. Difficulty was met with when attempting to type the various strains of meningococcus isolated. The typing serum available appeared to lack type specificity.
The clinical investigation of cases is given in detail. When the results are set out in tabulated form the atypical nature of many of the cases is realized. The most constant features were headache and catarrhal pharyngitis.

A definite leucocytosis was found constantly. It was invariably over 15,000 cells. (An exception is quoted in Part II.)

The clinical aspect of the cases encountered is described. The mortality is recorded as fifty per cent. In the very acute cases it was one hundred per cent. Examples illustrating the different types of cases seen are given in detail.

A differential diagnosis, so far as it affected the types of cases met with in the Command, is discussed. Many different types of infection are involved and reasons for their differentiation from cerebrospinal fever are given.

The control of contacts and carriers, and the treatment of the latter, are considered. With simple treatment and outdoor employment, ninety-two per cent of the carriers were rendered non-infective within three weeks.

The present custom of dealing with contacts is discussed and some doubts are cast on the necessity for our present-day procedure. It is considered that the bacteriologist's time might be more usefully employed in preventive investigation and also in the early detection of cerebrospinal fever among catarrhal cases in an endemic community.

In Part II, the knowledge acquired is applied towards the establishment of early diagnosis. The criterion of early diagnosis is defined as the finding of clear cerebrospinal fluid at the diagnostic lumbar puncture. The mortality findings with cases diagnosed early and in cases in which the diagnosis was delayed, are quoted from actual experience: In early diagnosis the mortality was twenty-five per cent, while in late diagnosis it was seventy-five per cent.

A plea for the detailed description of the earliest symptoms of the disease is put forward in the hope that an earlier diagnosis of cases may result.

The aids to clinical diagnosis are described, the most important being a total leucocyte count and lumbar puncture.

The difficulty of differentiating an early cerebrospinal fever from an acute meningocoecal pharyngitis is discussed.

Apical pneumonia is added to the previous list of cases in the differential diagnosis of the disease.

Four cases diagnosed early in the disease are described and their treatment is briefly outlined. A Type I monovalent serum was employed. All cases completely recovered.

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