SOME CLINICAL OBSERVATIONS ON CEREBROSPINAL FEVER.

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From January of this year up to the time of writing, one hundred and sixty-one cases of cerebrospinal fever have been admitted to this hospital. These cases have been gathered from various units in the field and it is noteworthy that from this number in very few instances have more than one or two cases occurred in the same unit. In this paper we do not desire to discuss at any length those signs and symptoms of the disease which are, by this time, familiar to many, but there are just a few points noted by us during the epidemic that we feel should provide interest.

First, a few words as to the carrier problem. It is well known that during epidemics of cerebrospinal fever there are a certain number of apparently perfectly healthy individuals, living either in close contact with actual cases of the disease, or remote from the latter, in whom bacteriological examination of the secretion of the nasopharynx reveals the presence of the meningococcus. These so-called carriers are found at other times when cases of the actual disease are not occurring. Whether carriers are more prevalent during an epidemic than they are during a normal period is a point that we have not had an opportunity of investigating.

Coincident with the admission of our cases to hospital, fifty immediate contacts were also admitted. In each case nasopharyngeal swabs were taken, and in six instances an organism was isolated so closely resembling the meningococcus of Weichselbaum as to be indistinguishable from the latter—that is to say, twelve per cent of the immediate contacts were in all probability carriers.

Although these latter men were isolated from their respective units and sent as soon as possible to the Base no marked decrease was ever noted in the number of actual cases occurring in the few days following their isolation. We think it only natural to assume
therefore that the carriers responsible for the spread of the infection are not necessarily confined to immediate contacts, but that almost certainly many others are infective, though how it is difficult to say, when it is borne in mind that in this particular form of meningitis not one undoubted case of transmission of the disease by direct contact has been proved.

Is the Disease Contagious?

If the word contagious is used in its ordinary meaning we feel obliged to answer this question in the negative. In our experience no case of the disease has occurred among nurses, nursing orderlies, or medical officers attendant on the cases, although latterly no special precautions to avert infection by contact have been taken by the latter. Curiously enough no suspected carriers were ever found among the persons attending the cases, bacteriological examinations of nasopharyngeal swabs taken from time to time proving in all cases negative, although at the same time, as mentioned above, quite a number of carriers were isolated from units in the field.

Diagnosis of the Disease.

Except in very acute or fulminating cases, when diagnosis is obvious, much difficulty has been experienced both by ourselves and by others in coming to a definite conclusion in many cases, especially in the early stages of the disease.

Ample evidence of this is provided in the following statement: Between April 8 and June 2, 109 cases were sent into this hospital either diagnosed as cerebrospinal fever or as suspected cases; of these 43 (that is 39 per cent) were ultimately found to have the disease.

The diseases with which we have experienced greatest difficulty in differentiating from cerebrospinal fever are as follows:—
Influenza.
Some early cases of enteric fever (both true typhoid and para. B).
Acute mania.
A few cases of sub-acute rheumatism.

Besides these conditions the following diseases—examples of which have been transferred to us as possible cases of cerebrospinal fever—also demand attention when diagnosis is being considered:—
Chronic nephritis with uraemic symptoms.
Pneumococcal septicaemia.
Acute irritant poisoning.
Hysteria simulating meningitis.
Cases of état méningitique (of some French authorities), or "simple meningitis" (to be described below and of doubtful origin, no micro-organism having yet been isolated in such cases).

**Differential Diagnosis.**

**Influenza.**

Severe cases of this disease have presented the greatest difficulty of all. Many cases of cerebrospinal fever begin with symptoms practically identical with those usually associated with the disease known as influenza, and it is not until perhaps several days have elapsed that definite symptoms pointing to a meningeal affection make their appearance. On the other hand influenzal meningitis is a very definite complication of a few cases of severe influenzal infection. Both patients suffering from influenza and cerebrospinal fever in the early stage may complain of sore throat, headache, backache, general lassitude and feeling of weakness, shivering and vomiting.

The following points of difference in the two diseases have been used by us in attempting to arrive at a correct diagnosis.

1. **Relation of Pulse-rate to Temperature.**—In influenza the pulse is usually increased in rate, but at the same time somewhat slow in proportion to the degree of pyrexia, rising to eighty or ninety beats per minute with a temperature of 102° to 103° F. at the onset.

In cerebrospinal fever the pulse is usually exceptionally slow at the onset—slow out of all proportion to the temperature—it being quite common to find a rate of anything from fifty to seventy beats per minute with a temperature of 102° to 103° F., or even much higher.

2. **Other Differences in the Pulse.**—The pulse in an influenzal infection is usually soft, of low tension, and frequently irregular in force and rhythm, while that in cerebrospinal fever is as a rule, full, of moderately high tension and regular.

3. **Very frequent occurrence of irregular ciliary hyperæmia** of the eyes in cases of cerebrospinal fever, not seen in cases of influenza.

4. **Tongue.**—A very dry, dirty, furred tongue, almost brown, a few hours after onset in cerebrospinal fever. This is not noticed in cases of influenza.

5. **Blood-count.**—Leucocytosis is a prominent and early feature of cerebrospinal fever. Influenzal affection, on the other hand, produces no leucocytosis, but usually a leucopenia.

The leucocytosis is high, varying from 16,000 to 35,000 in our cases.
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(6) Lumbar Puncture.—Except in a few cases, this procedure always gave us the information we required. In a few cases, however, the cerebrospinal fluid obtained by lumbar puncture for the first time was perfectly clear and showed no increase in cellular elements at all (a cell count being made on a hæmocytometer slide, fifteen cells per cubic millimetre of cerebrospinal fluid being taken as a normal average count); moreover, bacteriological examination of the fluid proved negative. In a certain proportion of these cases the cerebrospinal fluid became turbid within another few hours, when a second lumbar puncture was performed and bacteriological examinations proved positive. However, in one case at least presenting very definite signs and symptoms of cerebrospinal fever, cerebrospinal fluid on several occasions proved absolutely negative both cytologically and bacteriologically.

Enteric Fever.

Onset usually much less abrupt, and malaise at the commencement much less severe than in cerebrospinal fever. Tongue becomes gradually coated with a brown fur. Blood-count shows a leucopenia.

Blood Culture.—The isolation of an organism from the blood belonging to the enteric group, though important, may take some days to complete, and hence does not aid very much in the differential diagnosis between enteric and cerebrospinal fever in an early stage.

It is interesting to note that in a few cases of cerebrospinal fever the meningococcus has been demonstrated in a culture from the blood.

Lumbar puncture is usually conclusive.

Acute Mania.

Especially important to us, in that we were dealing with men who have in many cases been subjected to extreme mental and physical fatigue. On two occasions we were obliged to perform lumbar puncture in order to satisfy ourselves that we were not dealing with one of the most severe types of cerebrospinal fever characterized at the onset by a mental state resembling acute mania.

Sub-acute Rheumatism.

The history of previous attacks is important. Pains are usually confined to the joints of limbs. Malaise not severe. No vomiting.

Lumbar puncture may be deemed advisable in doubtful cases.
Diagnosis by Lumbar Puncture.

In all but one of our cases we were able to confirm our diagnosis by an examination of the cerebrospinal fluid. In one case death occurred before lumbar puncture could be performed, but diagnosis in this case was confirmed post-mortem.

In one hundred and sixty cases the cerebrospinal fluid was shown to contain a large number of polymorphonuclear leucocytes, and in one hundred and seventeen of these intra-cellular diplococci were seen. In addition to this the cerebrospinal fluid in every case examined also showed a marked increase in the cells of the lymphocyte class, both small and large types being represented. The diagnosis having been definitely established, the occurrence of the following signs and symptoms appear to us to be of major importance especially in regard to prognosis.

Ocular symptoms and signs including blepharitis, purulent conjunctivitis, keratitis, optic neuritis, ciliary hyperæmia, nystagmus, ptosis, strabismus, and consequent diplopia.

Our observations have led us to regard these conditions as very ominous in considering prognosis. Many of the cases showed injection of very irregular distribution in the ciliary ring of vessels apart from any associated conjunctivitis or keratitis.

Loss of Control of Sphincters.—Incontinence, especially if prolonged, is a grave symptom. The patients often have a transient incontinence which is of little importance, but we find that prolonged incontinence is only too frequently associated with a hydrocephalic condition, in our experience invariably fatal.

Retention of urine has been the exception rather than the rule in our cases.

Complications and sequelæ.

Complications.

(1) Acute Nephritis.—We believe that acute nephritis is a complication occurring even more frequently than has hitherto been considered the case. In our experience nine cases in a total of one hundred and sixty-one (that is 5'6 per cent) showed evidence of this complication. The presence of a transient albuminuria, unassociated with the occurrence of cellular elements or casts in a catheterized specimen of urine, is almost invariable in cases of cerebrospinal meningitis, and in the majority of cases no trace of albumin is found at the period of convalescence.

Of those cases which had a typical smoky urine, loaded with
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albumin, and containing blood corpuscles and recently formed casts in large numbers (nine in number), four died and all five that recovered still showed a very slight but persistent albuminuria, associated with the presence in the urine of a few hyaline and granular casts, when they were discharged to the base hospital. Edema of face and dependent parts only occurred in one of these nine cases. We suggest that these cases of cerebrospinal fever complicated by acute nephritis may be potential cases of subacute or chronic nephritis, and may suffer from these latter forms of renal disease subsequently.

(2) Otitis Media.—Seen in one case only.

(3) Suppurative Arthritis.—Two cases. In each the knee-joint on one side was the only joint affected. Recovery following repeated aspiration of the joint was practically perfect in each case.

(4) Broncho-pneumonia occurred in four of our cases.

(5) Extreme marasmus occurred in two cases.

(6) Peripheral Neuritis.—Two cases.

(7) Hydrocephalus.—Both forms—acute and chronic—occurred very frequently. This condition was found post-mortem in some degree almost invariably in fatal cases.

(8) Hyperpyrexia.—Seen on two occasions only, both cases died.

Sequela.

(1) Insanity.—Feeble-mindedness occurred definitely in two cases only, though the possibility of insanity ensuing in any of the others that left hospital apparently cured must not be overlooked.

(2) Permanent Strabismus.—Seen in two cases.

(3) Permanent Blindness.—Blindness in one eye occurred in one case.

(4) Permanent Deafness.—Noted occasionally, where no sign of otitis media had occurred in the earlier stages of the disease.

(5) The possibility of a subacute or chronic nephritis following an acute attack has already been dealt with in the preceding paragraph.

Special Treatment of the Cases.

The patients were nursed in a large airy ward with many windows, kept wide open whenever the weather was sufficiently good. On approaching convalescence, they were put out for the greater part of the day in the open air on a balcony adjoining the ward, and in a few cases during the summer months patients were allowed to sleep on this balcony during the night.
Treatment by Lumbar Puncture.

Frequent lumbar puncture has been the main line of treatment in all our cases. Every case, except one, in which death occurred before treatment could be undertaken, has been treated by lumbar puncture, as a rule, repeated daily for the first four to five days, and then every second day for about the next week, unless symptoms (particularly severe headache) called for more frequent puncture, or unless the patient had already arrived at a convalescent stage. A few cases became convalescent very quickly—within a week—and in these lumbar puncture was discontinued. In cases of relapse, which were not at all infrequent, lumbar puncture was invariably performed again.

For the purpose of performing the operation a little pure chloroform was almost invariably administered.

At each puncture the cerebrospinal fluid was allowed to run out until all excess of pressure was relieved, the needle being withdrawn only when the fluid was escaping at the rate of about forty to fifty drops per minute.

In a few cases we were unable to relieve the excessive intracranial pressure by lumbar puncture, free communication between the intraventricular system and the subarachnoid space being probably obliterated by purulent exudation.

In addition to lumbar puncture various other modes of treatment were employed, viz. :-

1) Living vaccine prepared by one of us (S. R.) from cerebrospinal fluids obtained by lumbar puncture from our own cases.
2) Dead vaccine, also prepared by S. R. from our own cases.
   These vaccines were given subcutaneously.
3) Various antimeningococcic sera, given intrathecally.

In these cases treated by anti-meningococcic sera, after allowing the excess of cerebrospinal fluid to escape, a quantity of serum was injected very slowly by means of a syringe, always using a volume of serum less than the volume of fluid which had escaped. After each introduction of serum the foot of the patient's bed was raised for about six hours to aid the flow of the serum towards the ventricles of the brain.

The volume of serum given at one time varied from twenty to forty cubic centimetres according to the volume of cerebrospinal fluid which escaped. Not more than six doses of a serum were as a rule given to one patient. In those cases which had received six doses and which still called for further treatment,
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Lumbar puncture was performed as often as deemed necessary, but no further dose of serum given.

The numbers of cases receiving the various kinds of treatment with results are summarized below:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cases treated</th>
<th>Recovered</th>
<th>Deaths</th>
<th>Cases still in hospital</th>
<th>Per cent case mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar puncture only</td>
<td>43</td>
<td>21</td>
<td>21</td>
<td>1</td>
<td>49</td>
</tr>
<tr>
<td>Living vaccine</td>
<td>29</td>
<td>16</td>
<td>13</td>
<td>-</td>
<td>45</td>
</tr>
<tr>
<td>Dead vaccine</td>
<td>52</td>
<td>24</td>
<td>28</td>
<td>-</td>
<td>54</td>
</tr>
<tr>
<td>Serum B and W</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>-</td>
<td>83</td>
</tr>
<tr>
<td>Serum Flexner</td>
<td>16</td>
<td>6</td>
<td>9</td>
<td>1</td>
<td>56</td>
</tr>
<tr>
<td>Serum Pasteur</td>
<td>11</td>
<td>4</td>
<td>7</td>
<td>-</td>
<td>64</td>
</tr>
<tr>
<td>Serum Mulford</td>
<td>3</td>
<td>2</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Untreated</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>161</td>
<td>74</td>
<td>84</td>
<td>3</td>
<td>-</td>
</tr>
</tbody>
</table>

Total cases treated, 161; died, 84; per cent case mortality, 52.

We think it only fair to ourselves to point out here that several cases (five in number) clinically very suggestive of a mild form of cerebrospinal fever, but which were never proved by us to be such, examinations of the cerebrospinal fluid proving negative, are not included in the above table. These cases invariably recovered, and although in all probability they were true examples of cerebrospinal fever, the absence of absolute proof of their identity has caused us to omit them in considering results of treatment.

We feel also that our high percentage case mortality is in some measure due to the fact that many of the cases came to us untreated as far on in the disease as the fifth to sixth day from date of onset—a few even as late as the ninth to tenth day. Had these cases come under treatment earlier, no doubt the percentage case mortality could have been considerably reduced. In no less than twelve instances the cases admitted were of the fulminant variety and were hopeless from the very first.

It will be gathered from the above figures that no one method of treatment employed gave results sufficiently good to enable us to infer that that particular method carried with it any great possibility of recovery, although the series treated by living vaccine together with repeated lumbar puncture has a percentage case mortality four lower than the series treated by lumbar puncture alone. It is to this series of twenty-nine cases treated by repeated lumbar puncture combined with living vaccine that we would draw particular attention.
Post-mortem Examinations.

These were performed in about fifty cases. No special features were discovered that had not been previously described.

In addition to the lines of treatment already mentioned, operative procedures were undertaken in five of the cases; details of these appear below:

**Cases.**

**Five Cases submitted to Operative Procedure.**

*Case* 16.—Private C., aged 17. Admitted to hospital February 11, 1915. Then ill three days. Complained of severe occipital headache, vomiting and pains in the limbs; tongue dirty, appetite poor; drowsy; tendon reflexes all exaggerated; lumbar puncture performed on admission; cerebrospinal fluid found turbid and under increased pressure; microscopical examination of centrifuged deposit showed many pus cells and intracellular diplococci; 10 c.c. of Burroughs Wellcome's serum introduced intrathecally; 500 millions of a dead vaccine (prepared from several strains obtained from our own cases) given subcutaneously. February 13: Some slight improvement; tongue cleaner; appetite better; less pain in the head; lumbar puncture repeated and serum again introduced. February 14: 1,000 millions of vaccine given subcutaneously. February 15: Again slight improvement; less drowsy than previously. February 16: 1,000 millions vaccine. February 17: Not so well. February 18: Violent headache again; lumbar puncture; no serum given; 1,000 millions vaccine subcutaneously; February 19: No marked change. February 20 to March 6: Patient gradually losing ground; frequent headache with no relief from hypnotics and sedatives; mentally very dull and stupid; fundi examined; commencing optic neuritis; during this period lumbar puncture performed without much relief on five occasions and seven doses of vaccine given. March 7: Operation decided upon; in left temporo-frontal region.

*Decompression.*—A large scalp flap turned down, and a disc of bone trephined over the left Rolandic area. Opening in skull enlarged a little in all directions; no very marked bulging of dura found; pulsation of the brain good; dura not opened; scalp wound closed. March 8: Patient had a quiet night following operation; headache slightly better. March 9: Given a dose of vaccine subcutaneously. March 10: Still some headache; patient drowsy; taking food fairly well. March 16: Patient brighter; taking interest in his surroundings; speech hesitant and slow; no pain;
temperature normal for the first time. March 20: Fundi examined again—right optic disc still indistinct; vessels partly obscured and apparent bending over at the edge of disc. Left optic disc—outer edge partially clear; rest of edge blurred; inner edge clear; vessels partially obscured. March 23: Progress good; mentally bright and rational; speech clear. March 24: Fundi examined; right disc very much clearer; left disc as before. March 25: Progress satisfactory; no headache; transferred to base hospital; convalescent.

Case 53.—Lance-Corporal D., aged 20. Admitted to hospital March 7, 1915. Appeared to be a case of moderate severity; ill several days before admission; diagnosed by examination of cerebrospinal fluid on day of admission; Flexner's serum introduced intrathecally. March 8: Lumbar puncture repeated; serum given again. March 9: Shows slight improvement. March 10: Lumbar puncture again; serum given. March 11: Lumbar puncture again; serum given. March 13: Violent headache again; lumbar puncture; serum introduced; cerebrospinal fluid still under much pressure. March 14: Not so well; head retracted; headache persists. March 15: Transient diplopia; unequal pupils; lumbar puncture; serum given. March 17: Patient has developed a facial erysipelas beginning in a small septic spot on the left cheek. March 18: Lumbar puncture; serum given; mentally inaccurate; delirious. March 20: Erysipelas has spread over nose to the right cheek; incontinent. March 21: Lumbar puncture; serum given. March 23: Extreme head retraction; semi-conscious; erysipelas has subsided. March 25: No improvement; lumbar puncture; no serum given; cerebrospinal fluid shows no increase of pressure; taking food very badly; commencing bedsores. March 27: Quite comatose; purulent conjunctivitis; fundi examined; optic neuritis present.

March 28: Operation.—Decompression. A large area of bone removed in the left temporo-parietal region; dura not bulging unduly; pulsation of brain good; wound closed. Patient after leaving the theatre and despite stimulants died nine hours later.

Post-mortem.—A generalized meningitis, with a hydrocephalic condition was found; ventricles hugely distended with turbid fluid and convolutions flattened.

Case 66.—Lance-Corporal C., aged 23. Admitted to hospital March 20, 1915: Then ill five or six days; violent occipital headache; vomiting; pain in the back, neck and limbs; head retracted; reflexes brisk; Kernig's sign marked; mentally dull and drowsy;
lumbar puncture performed; cerebrospinal fluid very turbid; high pressure; bacteriologically positive as regards meningococcus; dead vaccine 500 millions given subcutaneously. March 21: Lumbar puncture performed. March 22: Living vaccine 200 millions given subcutaneously (this vaccine also prepared from cerebrospinal fluid of our own cases). March 23: Semi-conscious; taking food badly; incontinent; paralysis of left face; paralysis of left external rectus; left cornea clouded (iritis present). March 25: Lumbar puncture performed again; 500 millions living vaccine given; tongue now deviated to right side on protrusion. March 28: 500 millions living vaccine given. March 31 to April 19: No improvement; marked loss of flesh, mentally extremely dull and apathetic; during this period lumbar puncture on four occasions and two further doses of living vaccine given.

April 21: Operation.—Decompression over the right frontal lobe; incision of dura and puncture of the anterior horn of the right lateral ventricle; dura found very tense, no visible pulsation and even when dura had been incised pulsation of brain very feeble; brain bulging up into the wound: on puncture of the ventricle a slightly opalescent fluid escaped; about 5 drachms removed; brain pulsation now more distinct; we had intended introducing into the ventricle at this stage 10 c.c. of Pasteur's antimeningococcic serum, but after about 5 c.c. had been put in patient strained and began to vomit (anaesthesia, open ether and very light). Patient showed signs of collapse; it became necessary to close quickly; dura being left open. Patient died the same day at 7 p.m., nine hours after operation.

Post-mortem.—A condition of chronic hydrocephalus was found; anterior horn of right ventricle very much enlarged but collapsed; posterior horn of right ventricle distended with fluid, likewise the left lateral ventricle and third and fourth ventricles; pineal gland enlarged and cystic; choroid plexuses pale and atrophied.

Case 102.—Second Lieutenant M., aged 24. Admitted to hospital April 18, 1915. Then ill five days. A typical case of severe type; mentally confused; slight head retraction; purpuric rash; violent headache; lumbar puncture had been performed once before admission; cerebrospinal fluid found bacteriologically positive. For the next six days lumbar puncture repeated and Pasteur's serum given intrathecally each day. Progress seemed to be fairly good; patient became brighter, mentally clearer and had less pain; there was occasional incontinence. May 25: Patient losing ground rapidly; very drowsy, stupid and frequently delirious; lumbar puncture again and serum given. No improvement.
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May 26: Operation.—A large sub-temporal decompression performed. Dura left unopened; no undue bulging of latter and pulsation of brain good; scalp wound closed. Patient left the theatre fairly fit and not showing any signs of collapse. Patient lived for ten days after operation but went slowly downhill and died comatose.

Post-mortem.—A generalized meningitis, with purulent exudation chiefly marked at the base of the brain. A marked hydrocephalic condition also present.

Case 69.—Private M., aged 21. Admitted to hospital March 22. Severe case, hardly conscious on admission, who improved somewhat under treatment by repeated lumbar puncture and living vaccine for a week. Between March 22 and March 28 lumbar puncture was performed and vaccine given as follows:

<table>
<thead>
<tr>
<th>Date</th>
<th>Living vaccine</th>
<th>Lumbar puncture</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 22, 1915</td>
<td>200 millions</td>
<td>Performed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No special treatment.</td>
</tr>
<tr>
<td>&quot; 23, 1915</td>
<td></td>
<td>Performed.</td>
</tr>
<tr>
<td>&quot; 24, 1915</td>
<td></td>
<td>No special treatment.</td>
</tr>
<tr>
<td>&quot; 25, 1915</td>
<td>500 millions</td>
<td>Performed.</td>
</tr>
<tr>
<td>&quot; 26, 1915</td>
<td></td>
<td>No special treatment.</td>
</tr>
<tr>
<td>&quot; 27, 1915</td>
<td></td>
<td>Performed.</td>
</tr>
<tr>
<td>&quot; 28, 1915</td>
<td>500 millions</td>
<td></td>
</tr>
</tbody>
</table>

During the next two days patient was very dull and apathetic. Some delirium; incontinent. Marked left-sided facial paralysis.

March 30: Operation. Lavage of Spinal Theca.—Patient anaesthetized (chloroform). Lumbar puncture needle introduced through spinal theca into sub-dural space between the second and third lumbar vertebrae; patient lying on left side and curled up. About 15 c.c. of turbid cerebrospinal fluid escaped. About 40 c.c. of sterile normal saline at normal body temperature (37° C.) were introduced through the needle into the spinal theca by means of a sterilized rubber tube and funnel, at a water pressure of four and a half inches. This accomplished, a second lumbar puncture needle was introduced into the sub-dural space between the seventh cervical and first dorsal vertebrae. Turbid fluid immediately escaped under considerable pressure from the upper needle. A sample of this fluid was taken in a test-tube. Next, about 40 c.c. of saline were run in from below, and the excess allowed to flow out from the upper needle, thus irrigating a large part of the spinal sub-dural space. Two further samples of fluid were taken from the upper needle.

Examination of the Samples of Fluid Escaping.—(1) From the lower needle at commencement of operation; very turbid. (2) (3) and (4) From the upper needle, showed a definite gradual decrease
in turbidity, and also in height of coloration; the first sample being greenish yellow in hue, the last just milky and opalescent. A microscopical preparation of each sample showed a corresponding decrease in the number of polymorphonuclear leucocytes present in the fluid.

This operation was not followed by any distinct improvement.

March 31 to April 29: Between these two dates lumbar puncture was performed twice and two further doses of living vaccine were administered. Patient became extremely emaciated and died comatose on April 29.

Two Cases of exceptionally long duration with Recovery.

Case 101.—Private E., aged 22. Admitted to hospital April 14. A typical case of moderate severity. Complained of violent occipital headache, pain at the back of the neck and down the spine; vomiting. A generally distributed rash—partly petechial and partly urticarial in character—but particularly marked on extensor aspect of forearms, hands, legs and feet. Lumbar puncture performed on admission; cerebrospinal fluid very turbid, under high pressure. Centrifuged deposit shows many polymorphonuclear leucocytes with typical intracellular diplococci—also a marked lymphocytosis—large and small mononuclears being present. Pasteur's serum introduced intrathecally. April 15 to April 20: Daily lumbar puncture and Pasteur's serum introduced intrathecally. April 27: Patient had progressed fairly satisfactorily and was transferred to a convalescent ward. He had lost a considerable amount of flesh and had had recurrent urticarial eruptions. He was mentally clear and rational. May 13: Not so well. Irregular pyrexia, anorrhexia, and vomiting. The latter was sudden, copious and unaccompanied by nausea or abdominal pain. He also complained of occasional severe headache. There was no ocular or facial paralysis. Movements of head and limbs, however, were tremulous. Remains mentally rational. Lumbar puncture without introduction of serum was followed on May 14 by marked improvement. The cerebrospinal fluid was slightly turbid, under increased pressure. Microscopical examination of centrifuged deposit showing cells only. Irregular pyrexia with headache and vomiting however recurred, and on May 21 and May 23 lumbar puncture was again performed. May 25: Patient had a severe rigor. May 26: Another rigor; vomiting continues. May 29: Patient now shows double foot-drop; is extremely emaciated; pyrexia as before; pulse rapid and feeble at times. He continues to take a fluid diet well, and though querulous, his mind remains clear. He complains of tingling.
and numbness, and also of muscular tenderness in the calves of the legs. There has been no interference with the action of the sphincters. June 21: Massage has relieved pain in legs. He is much brighter mentally, and is taking more food. Irregular pyrexia however persists. Still occasional headache and vomiting as before.

July 15: No noticeable change. July 21: Temperature now remains down; generally improved; still occasional pain in the feet and in the muscles of the abdominal wall. August 11: Progress continues to be satisfactory, and to-day patient was transferred to Base Hospital. September 15: Patient was able to walk a few steps for the first time, aided by crutches. October 16: Patient can now walk a short distance unassisted. His mental condition is satisfactory. Duration of pyrexia, ninety-six days.

Case 141.—Driver M., R.F.A., aged 22. Admitted to hospital June 12—then ill six days. Lumbar puncture had been performed at a casualty clearing station before admission and the meningococcus found. On admission here semi-conscious; head retracted; neck and limbs very stiff; Kernig's sign present; reflexes natural; photophobia; tache cérébrale present. Patient very irritable and difficult to examine. Respirations rapid and laboured; slightly cyanosed; incontinent. Lumbar puncture performed; cerebrospinal fluid found very turbid; no increase of pressure. Microscopical examination of centrifuged deposit shows many polymorphonuclear leucocytes; lymphocytes of both varieties, large and small, and a few typical intracellular diplococci. Flexner's serum introduced intrathecally. June 13: Much clearer mentally. No head retraction; no cyanosis; respirations quiet and slow. Gives an accurate history of illness. Lumbar puncture again performed and Flexner's serum given intrathecally. To-day pressure of cerebrospinal fluid considerably increased. June 14: Lumbar puncture repeated and serum again introduced. June 16: Incontinent; mentally dull; slight purulent conjunctivitis; herpes labialis. Does not complain. Lumbar puncture performed without introduction of serum. June 19 to July 18: Patient gradually lost ground. Mentally always uncertain; taking food badly; incontinence of urine and faeces; frequently delirious. Slight head retraction; very tremulous; marked loss of flesh. Lumbar puncture performed on three occasions. July 18 to August 19: No marked change. Bedsores; taking food slightly better; purulent conjunctivitis; extremely emaciated. Lumbar puncture not performed during this period. August 19 to September 18: Patient's condition now very variable, some days a little brighter and taking food well; other days drowsy,
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dull and extremely difficult to feed. Incontinence as before. No sign of
gaining flesh; marasmus is now even more marked than previously.
Lumbar puncture performed on two occasions. Cerebrospinal fluid
very slightly turbid; pressure slightly increased. September 24:
Wildly delirious—screaming and shouting; hypodermics of morphia
and hyoscin being necessary. September 26: Dull and drowsy
again; has a marked iritis of the right eye. Lumbar puncture
performed. Cerebrospinal fluid shows no increase of pressure.
Incontinence persists. Temperature now remains subnormal for
the first time. October 11: Patient now remains well; brighter
and clearer mentally. Bedsores healing. No incontinence; talking
better. October 20: Progress satisfactory; gaining flesh and
strength. Mentally quite clear and rational; memory fairly good.
Duration of pyrexia, one hundred and forty-one days.

Four Cases of Etat méningitique or "Simple Meningitis."

These cases are examples of a condition in which the physical
signs and symptoms suggest a mild case of cerebrospinal meningitis,
but in which no bacteriological proof of the presence of the meningo-
coccus has been obtained. The cerebrospinal fluid in this condition
shows a marked lymphocytosis only, no polymorphonuclear leuco-
cytes being found. All the cases are said to recover.

Case 1.—Private N., aged 26. Admitted to hospital April 1,
having been ill two days with headache, vomiting, pains in the
back and limbs. Onset sudden. On admission, mentally clear and
rational. Tongue furred but moist. Temperature 99·6°; pulse 60,
full. Slight stiffness of neck; marked photophobia; reflexes very
active; knee-jerks exaggerated; Kernig's sign doubtfully positive.
Lumbar puncture performed, cerebrospinal fluid very slightly turbid;
very high pressure. Microscopical examination of cerebrospinal
fluid shows very marked lymphocytosis; no polymorph leucocytes
or organisms found. Given 500 millions dead vaccine subcutan-
eously. Culture of fluid, in blood-broth sterile at end of forty-
eight hours. Blood culture—in broth—reported sterile at the end
of seventy-two hours. April 2: Patient had a restless night;
headache and vomiting; photophobia and stiffness of neck still
marked; splenic dullness increased; spleen not palpable; knee-
jerks brisk. Lumbar puncture repeated; cerebrospinal fluid as
before, slightly turbid under high pressure. Shows lymphocytes
only. Fundi examined—discs clear. Patient made an uneventful
recovery and was perfectly well within ten days of onset of
symptoms.
Clinical Observations on Cerebrospinal Fever

Case 2.—Corporal P., aged 30. Admitted to hospital April 23. Taken ill on April 19; slight headache; vomiting; general aching of the body and limbs; feverish. He had had a sharp feverish attack a few days before this, and thought this present attack was a recurrence of the same, but symptoms were getting more severe. On admission to hospital, rational; still headache and vomiting; tongue furred but moist; neck stiff and legs very stiff; Kernig's sign present; knee-jerks absent; patellar reflexes flexor. Temperature 101° F.; pulse 88 full. Lumbar puncture performed. Cerebrospinal fluid slightly turbid and under increased pressure. Microscopical examination of fluid showed marked lymphocytosis. No polymorph leucocytes or organisms found. Culture of fluid proved sterile. Blood culture also proved sterile. White blood cell count, 11,000. April 25: Patient much better; no headache or vomiting. April 27: Temperature normal; feels perfectly well. May 3: Transferred to base hospital. Convalescent.

Case 3.—Private N., aged 24. Admitted to hospital April 20, 1915. Ill four days, headache, constipation; on admission mentally dull and drowsy; no accurate account of his illness was obtainable from the patient; tongue very dirty; pharynx injected; slight photophobia; temperature 99° F.; pulse 100; knee-jerks absent; Kernig's sign present; lumbar puncture had been performed at a clearing station before admission here; cerebrospinal fluid reported opalescent, containing lymphocytes only; 20 c.c. Flexner's serum had been given intrathecally. On admission to our hospital lumbar puncture repeated; cerebrospinal fluid turbid and under high pressure, shows lymphocytes only, no organisms found. Culture of fluid proved sterile. Blood culture proved sterile. April 21: White blood cell count, 20,000; still much headache; vomiting again; lumbar puncture; cerebrospinal fluid slightly turbid and under high pressure; microscopical examination as before; culture of cerebrospinal fluid proved sterile; blood culture proved sterile. April 23: No marked change in patient's condition; lumbar puncture; cerebrospinal fluid as before; second culture of fluid proved sterile. April 24: Lumbar puncture; cerebrospinal fluid practically clear; pressure slightly increased; third culture of fluid proved sterile. April 25: Patient now progressing favourably. May 1: Temperature has now fallen to normal. May 3: Complete recovery; sent to base convalescent.

Case 4.—Private W., aged 17. Admitted to hospital April 8, 1915. Had then been ill three days, headache, pain in the neck and lumbar region, stiffness of the neck. Onset sudden. Lumbar puncture had been performed twice at an isolation hospital.
E. A. Bourke, R. G. Abrahams and Sydney Rowland

before admission. April 6: Cerebrospinal fluid found clear, but under very high pressure; no cells or organisms found in the fluid; culture of the fluid proved sterile. April 7: Pain in head and back worse; stiffness of the neck more marked; temperature 99°F.; vomited several times to-day. April 8: Lumbar puncture repeated; cerebrospinal fluid again quite clear, but now shows very distinct lymphocytosis; no polymorphs or organisms found; white blood cell count, 14,900.

On admission to our hospital, conscious, but very drowsy; dull and apathetic; still complains of headache, stiffness and pain at the back of the neck; has very slight head retraction; tongue furred and dry; temperature 100°F.; pulse 70; knee-jerks exaggerated; Kernig's sign present. Given 500 millions dead vaccine subcutaneously. April 9: Much better to-day; no stiffness of the neck; Kernig's sign absent; knee-jerks natural; no headache; tongue clean; temperature normal. Patient remained perfectly well from this date.

A Case clinically identical with Cerebrospinal Fever, but not proved to be such bacteriologically.

Second Airman B., aged 21. Admitted to hospital May 28. Then ill three days with headache, vomiting, pain in the abdomen, shivering. He was mentally rational, but memory a little hazy and uncertain; headache now very violent and worse in the occipital region; there was slight stiffness and pain in the back of the neck; slight abdominal pain and rigidity; there was a generally distributed rash, partly purpuric and partly petechial in character. He had peculiar blotchy conjunctival congestion, and also slight hyperæmia of the ciliary vessels; pupils were equal, and reacted to light and accommodation; slight photophobia; pharyngeal wall injected; tongue furred and dry; marked hyperæsthesia; tache cérébrale present; knee-jerks exaggerated; Kernig's sign absent; patellar reflexes flexor; temperature subnormal; pulse 96. Lumbar puncture performed; cerebrospinal fluid quite clear, but under very high pressure. Fluid contains an excess of albumin, and a few lymphocyte cells were seen in a centrifuged deposit. Culture of fluid proved sterile. Urine examined (catheter specimen); smoky; reaction to litmus, acid; a dense cloud of albumin; no sugar. Centrifuged deposit shows blood cells, and many blood and recently formed epithelial casts. White blood cell count, 60,000; blood culture proved sterile. May 29: Patient dull and quiet; still has headache; no head retraction; marked herpes on lips, chin and nose; Kernig's sign present; has a purulent conjunctivitis; rash
is more marked to-day, especially on the extensor aspects of limbs. Lumbar puncture repeated; cerebrospinal fluid clear, still under very high pressure, contains a few lymphocytes only; culture of fluid again proved sterile. Temperature chart shows slight pyrexia; pulse slow. May 30: Lumbar puncture; cerebrospinal fluid as before; culture sterile. May 31: Urine, still shows many recent casts and blood cells. A second blood culture taken to-day proves sterile. June 1: Patient much brighter mentally, no pain or headache. June 5: Temperature now remains normal. June 8: Progress satisfactory. June 10: Urine shows a haze of albumin and granular casts. June 16: Patient convalescent and transferred to base hospital.

**Case of Hysteria simulating Meningitis.**

Mrs. M. Patient, a young woman, who had been visiting her husband lying ill with cerebrospinal fever in this hospital for the last few weeks. She was known to have been in very close contact with him on the morning of May 26, just previous to an operation being performed on him. After the operation she continued to visit him, and was perfectly well, to all outward appearances, in every respect, at midday on May 28, 1915.

About midnight (May 28) she was brought to hospital with a history of having been suddenly seized that evening, while walking in the street, with violent headache and inability to stand upright. She fell and sustained severe bruising of the right side of the forehead and slight bruising over the outer side of the right thigh. Shortly afterwards she vomited several times.

On admission patient was mentally confused. Complained of violent occipital headache, pain in the neck and back. Slight stiffness of the neck and slight abdominal rigidity present. Marked hyperesthesia and photophobia. Patient very restless, throwing herself about the bed as if in great pain. Temperature 101°, pulse 68. Vomiting continues. Lumbar puncture was performed under chloroform. Cerebrospinal fluid found quite clear—no increase of pressure. No excess of cells in a centrifuged specimen. At 10 a.m. next morning—still much headache; has vomited again; slight head retraction; neck stiff; erythematous blotches on the abdomen; tongue very dry and furred; patient conscious but mentally dull; knee-jerks exaggerated (almost knee clonus); ankle clonus present; Kernig’s sign doubtful; patellar reflexes flexor. Culture of cerebrospinal fluid proved sterile. Patient was removed this morning to a civil hospital, where symptoms
Graphical Record of Epidemic, as it Affected this Hospital.

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Cases</th>
<th>Deaths among those same cases</th>
<th>% Case mortality</th>
<th>Treatment (i.e., the main line of treatment during each week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan. 17-23</td>
<td>5 3 100</td>
<td></td>
<td></td>
<td>L.P. + Serum.</td>
</tr>
<tr>
<td>24-30</td>
<td>1 1 100</td>
<td></td>
<td></td>
<td>L.P. + Serum.</td>
</tr>
<tr>
<td>31-6</td>
<td>4 3 75</td>
<td></td>
<td></td>
<td>L.P. + Serum + Vaccine.</td>
</tr>
<tr>
<td>Feb. 7-13</td>
<td>12 6 50</td>
<td></td>
<td></td>
<td>L.P. + Vaccine.</td>
</tr>
<tr>
<td>14-20</td>
<td>16 5 31</td>
<td></td>
<td></td>
<td>L.P. + Vaccine.</td>
</tr>
<tr>
<td>21-27</td>
<td>6 5 83</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>28-3</td>
<td>10 7 70</td>
<td></td>
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<td>L.P. + Vaccine.</td>
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<tr>
<td>Mar. 7-13</td>
<td>7 6 85</td>
<td></td>
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<td>L.P. + Flexner's Serum.</td>
</tr>
<tr>
<td>14-20</td>
<td>8 6 75</td>
<td></td>
<td></td>
<td>L.P. + Serum + Vaccine.</td>
</tr>
<tr>
<td>21-27</td>
<td>9 5 56</td>
<td></td>
<td></td>
<td>L.P. + Living Vaccine.</td>
</tr>
<tr>
<td>28-3</td>
<td>15 5 33</td>
<td></td>
<td></td>
<td>L.P. + Living Vaccine.</td>
</tr>
<tr>
<td>Apr. 4-10</td>
<td>8 4 50</td>
<td></td>
<td></td>
<td>L.P. + Living &amp; Stock Vaccine.</td>
</tr>
<tr>
<td>11-17</td>
<td>4 3 75</td>
<td></td>
<td></td>
<td>L.P. + Pasteur's Serum.</td>
</tr>
<tr>
<td>18-24</td>
<td>7 2 29</td>
<td></td>
<td></td>
<td>L.P. + Pasteur's Serum.</td>
</tr>
<tr>
<td>25-1</td>
<td>7 5 71</td>
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<td></td>
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</tr>
<tr>
<td>May 2-8</td>
<td>6 5 50</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>9-15</td>
<td>2 0 0</td>
<td></td>
<td></td>
<td>L.P. only.</td>
</tr>
<tr>
<td>16-22</td>
<td>1 1 100</td>
<td></td>
<td></td>
<td>L.P. only.</td>
</tr>
<tr>
<td>23-29</td>
<td>4 3 75</td>
<td></td>
<td></td>
<td>L.P. only.</td>
</tr>
<tr>
<td>30-5</td>
<td>8 2 25</td>
<td></td>
<td></td>
<td>L.P. + Flexner's Serum.</td>
</tr>
<tr>
<td>June 6-12</td>
<td>3 1 38</td>
<td></td>
<td></td>
<td>L.P. + Flexner's Serum.</td>
</tr>
<tr>
<td>13-19</td>
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<td>L.P. + Flexner's Serum.</td>
</tr>
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<td>20-26</td>
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</tr>
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<td>27-3</td>
<td>1 1 100</td>
<td></td>
<td></td>
<td>L.P. only.</td>
</tr>
<tr>
<td>July 4-10</td>
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</tr>
<tr>
<td>11-17</td>
<td>1 0 0</td>
<td></td>
<td></td>
<td>L.P. only.</td>
</tr>
<tr>
<td>18-24</td>
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<td></td>
<td></td>
<td>L.P. only.</td>
</tr>
<tr>
<td>25-31</td>
<td>0 0 0</td>
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<td></td>
<td>L.P. only.</td>
</tr>
<tr>
<td>Aug. 1-7</td>
<td>2 2 100</td>
<td></td>
<td></td>
<td>L.P. only.</td>
</tr>
<tr>
<td>8-14</td>
<td>1 1 100</td>
<td></td>
<td></td>
<td>L.P. only.</td>
</tr>
<tr>
<td>15-21</td>
<td>0 0 0</td>
<td></td>
<td></td>
<td>L.P. only.</td>
</tr>
<tr>
<td>22-28</td>
<td>4 1 25</td>
<td></td>
<td></td>
<td>L.P. only.</td>
</tr>
<tr>
<td>29-4</td>
<td>2 1 50</td>
<td></td>
<td></td>
<td>L.P. only.</td>
</tr>
<tr>
<td>Sept. 5-11</td>
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<td></td>
<td>L.P. only.</td>
</tr>
<tr>
<td>12-18</td>
<td>2 0 0</td>
<td></td>
<td></td>
<td>L.P. + Mulford Serum.</td>
</tr>
<tr>
<td>19-25</td>
<td>2 0 0</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Total cases 161  Case incidence shown thus
Deaths 84  Deaths occurring among those same cases
% Case mortality 52  Percentage case mortality
Clinical Observations on Cerebrospinal Fever

described above persisted for some days, and lumbar puncture was repeated on two further occasions, but the fluid was found clear and quite normal each time. Recovery was rapid, patient becoming quite rational in every way within a week.

We heard later that the patient after leaving France suffered with sciatica, which at first she feared might be meningitis. The entire absence of any evidence derived from examinations of the cerebrospinal fluid suggestive of meningeal infection, together with the history of this case and rapid recovery have led us to believe that the illness was entirely of a functional nature.

The bacteriology of the meningococcus is notoriously difficult. This arises from the difficulty in growing the organism. Growth can often be obtained from an obviously infected fluid on blood agar; in many cases, however, no growth is obtained on this medium. Blood broth on the other hand never failed to give a growth from an obviously infected fluid. Blood broth (prepared by adding fresh blood to broth with a little citrate), however, suffers from the disadvantage common to all liquid media.

The identification of the organism is also, especially in the case of throat and nasal infections, often very problematical. No differential medium or method of isolation, such as we have in the case of the enteric group of organisms, has yet been devised. This fact must always be borne in mind in considering the application of any series of observations on the presence of the meningococcus in the naso-pharynx. Consequently the whole question of the significance of carriers in this disease despite the enormous amount of work that has been done, should still be regarded as sub judice.

Concluding, we wish to record our most grateful thanks to Colonel Sir Wilmot Herringham, Consulting Physician to the British Expeditionary Force, for his kindness and interest in superintending our work all through, especially with regard to the employment and dosage of the sera and vaccines used in the treatment of the cases.