

**A review of certain aspects of the control of cerebro-spinal fever : in relation particularly to a scheme for collecting the results of serum treatment.**

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REPORTS

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PUBLIC HEALTH AND  
MEDICAL SUBJECTS

No. 65

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A Review of Certain Aspects of the Control of  
Cerebro-Spinal Fever

In Relation particularly to a Scheme for Collecting  
the Results of Serum Treatment

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MINISTRY OF HEALTH

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REPORTS

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# PREFATORY NOTE BY THE CHIEF MEDICAL OFFICER.

The Right Hon. ARTHUR GREENWOOD, M.P.,  
Minister of Health.

SIR,

In accordance with your instructions, I beg to present a memorandum which has been prepared in the Medical Department on certain aspects of the control of cerebro-spinal fever, particularly in relation to a scheme for collecting the results of serum treatment. Cerebro-spinal fever—or “spotted fever” as it is often called—has an abundant literature both in regard to its occurrence throughout the world and in respect of its pathology and bacteriology. The very magnitude of this literature, however, is apt to create difficulties when this relatively rare disease occurs unexpectedly, as it often does, in a district or in a school or special community. There has thus seemed to be need for a convenient summary of the epidemiology and characteristics of this disease and a concise statement of such means of control and specific treatment as we possess. The present memorandum amplifies and replaces that on Cerebro-Spinal Fever which was issued by the Local Government Board in 1918. The fact that during the past year there has been a definite increase in the prevalence of cerebro-spinal fever in different parts of England and Wales affords an additional reason for the present summary.

All investigators recognise the need for collecting and studying from every point of view the results of the specific method of treatment at present available, namely, the administration of anti-meningococcus serum. One of the objects of this review is to indicate the difficulties with which we are confronted in endeavouring to assess the value of available serums, and of the different dosages and methods of administration employed. No such assessment can be made without sufficient data, which are seldom obtainable in any one district or by any one medical observer. It is hoped, therefore, that the assistance of medical officers of health, hospital medical officers and medical practitioners may be forthcoming in supplying the Department with information regarding the serum treatment of individual cases, in the manner indicated on page 19 and in the second appendix of the review.

I should like to express our gratitude for assistance in the preparation of the memorandum which has been given to the Department by many authorities on the subject, and for the information which has been placed at our disposal by the Medical Research Council.

I have the honour to be, Sir,  
Your obedient Servant,

GEORGE NEWMAN.

Whitehall, *July*, 1931.



## CEREBRO-SPINAL FEVER.

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The object of this review is to bring into handy form for the use of medical officers of health and medical officers of institutions as well as of medical practitioners generally the principal considerations which have to be borne in mind when cases of cerebro-spinal fever are notified or otherwise require their attention, and at the same time to invite them to assist the Ministry of Health in assessing the results of treatment by anti-meningococcus serum. The review may be regarded as a substitute for the Memorandum on Cerebro-spinal Fever issued by the Local Government Board in 1918. A recent brief communication regarding this disease, which was issued from the Ministry to the Press on 20th February, 1931, is, for convenience, reproduced in Appendix I.

### I. GENERAL CONSIDERATIONS AND CHARACTERISTICS OF THE DISEASE.

Cerebro-spinal fever (epidemic cerebro-spinal meningitis, posterior basal meningitis or "spotted fever") is an infectious disease of the central nervous system affecting chiefly the meninges of the brain and spinal cord. It occurs sporadically and occasionally also in local epidemics, and is due to the meningococcus, the "*Diplococcus intracellularis meningitidis*" of Weichselbaum.

Although outbreaks described by, *inter alios*, Sydenham were probably of this disease, its recognition is usually attributed to Vieusseaux, who described an outbreak in Geneva in 1805. Danielson and Mason recorded an outbreak in Massachusetts in 1806. Many epidemics, of varying intensity, have since been reported, chiefly in Europe and North America, while there have been notable outbreaks in military camps and garrisons in France, Italy, Denmark and the United States of America, as well as in England. By 1840 tropical and sub-tropical countries were known to be involved, and cases had been reported from South America and from Northern Africa and Western Asia. It may be said that towards the end of the nineteenth century cerebro-spinal fever had become, or at least was generally recognised as, a cosmopolitan disease.

#### Incidence in the United Kingdom.

With the exception of small outbreaks in London and Rochester in 1865 and in Bardney in 1867, England and Wales was comparatively free until the beginning of the present century. In the period 1902-11 limited outbreaks occurred in Sussex, Lincolnshire, Northamptonshire and Cambridgeshire. A small outbreak in Irthlingborough was investigated in considerable detail by the late Dr. Reginald Farrar for the Local Government Board in 1905.\* In 1907-8 there were 1,238 cases, with 838 deaths, in Glasgow.† At

\* Reports of Medical Inspectors of the Local Government Board, No. 218.

† Annual Report of Medical Officer of Health, Glasgow, 1908.



the same time the disease was prevalent in Belfast, where there were 725 cases, and in Swansea, where there were 63. In the years immediately preceding the war the annual number of notified cases among civilians in England and Wales varied from 200 to 300. In 1915, however, they numbered 2,566, followed by 1,306 in 1916, and 1,465 in 1917. Following demobilisation the numbers fell year by year, and by 1923 had reverted to the pre-war level. Since then, however, there has been a gradual, though not uninterrupted, increase, and the same tendency has been observed in other countries of Europe. The number of cases notified annually among civilians and the number of deaths registered in England and Wales since 1912 are set out below.

*Cerebro-spinal Fever in England and Wales since 1912.\**

Year.	Notified Cases.	Registered Deaths.
1912	104	342 ( 142)
1913	305	332 ( 163)
1914	315	396 ( 194)
1915	2,566	2,203 (1,974)
1916	1,306	1,368 (1,214)
1917	1,465	1,651 (1,531)
1918	798	926 ( 812)
1919	848	694 ( 573)
1920	583	533 ( 412)
1921	411	416
1922	344	360
1923	301	284
1924	397	301
1925	402	354
1926	385	365
1927	470	430
1928	412	438
1929	650	588
1930	664 (provisional)	632 (provisional)
1931 (1st quarter)	692 (uncorrected)	

\* Cerebro-spinal fever was made compulsorily notifiable by a General Order of the Local Government Board, which took effect on 1st September, 1912. The variety of meningococcal infection termed "posterior basal meningitis" has never been required to be notified under that term, but cases considered to be posterior basal meningitis may be included, though to an uncertain extent, in notifications of cerebro-spinal fever.

In the case of the Registrar-General's statistics, a distinction of deaths certified as due to posterior basal meningitis was made up to 1920, but subsequently, following the international system, deaths, whether certified as due to cerebro-spinal fever, cerebro-spinal meningitis or posterior basal meningitis, have been recorded under a single heading.

In the third column of this table, the bracketed figures for the years 1912 to 1920 are those which were registered under the heading of cerebro-spinal fever, but the deaths given for all the years in the column itself combine those from cerebro-spinal fever and posterior basal meningitis.



It will be seen that in some of the above years the number of registered deaths actually exceeded the number of notified cases. As always with this disease, the notification figures have a much greater relative than absolute value.\*

The increased prevalence amongst the civilian population during the war years is a striking feature of the table. It coincided with a total of 4,238 cases and 1,928 deaths of non-civilians in the Home Commands of the Army from 1914-1918.†

As already said, the disease is world-wide in its occurrence and appears alike in temperate and tropical climates. There is no evidence of any special racial liability or immunity. In this country cases may occur all the year round, but the greatest incidence is usually in the winter and spring, with a maximum in February or March.

It is sometimes considered (e.g., in the United States) that cerebro-spinal fever has a heavier incidence on rural than on urban communities. The notification returns in England, when taken as a whole over a considerable period of years, do not show any very characteristic differences between urban and rural rates.

*Cases of cerebro-spinal fever notified in England per 1,000 population*  
(from the Annual Reports of the Registrar-General).

Year.	Aggregate of County Boroughs.	Aggregate of non- County Boroughs and Urban Districts (excluding London).	Aggregate of Rural Districts.
1916	0.03	0.03	0.02
1917	0.04	0.04	0.03
1918	0.02	0.02	0.02
1919	0.02	0.02	0.02
1920	0.02	0.01	0.01
1921	0.01	0.01	0.01
1922	0.01	0.01	0.01
1923	0.01	0.01	0.01
1924	0.01	0.01	0.00
1925	0.01	0.01	0.01
1926	0.01	0.01	0.01
1927	0.01	0.01	0.01
1928	0.01	0.01	0.01
1929	0.02	0.01	0.01

It may be stated broadly that the majority of cases occur in children under five. The age incidence in particular instances is materially affected by the occurrence of outbreaks among older children and young adults in particular communities. Cases over the age of 40 years are rare.

\* This question is dealt with further on page 11.

† Official History of the War, Medical Services, Diseases of the War, I, 147.



The ordinary sporadic occurrence of cerebro-spinal fever has no notable relation to occupation. Any apparent connection with particular occupations depends, not on the occupation as such, but on the particular occasion which it has given for the association of susceptible persons, e.g., in training camps, naval depots, residential schools, or in coal mines, where serious epidemics have been frequently associated with concurrent conditions of over-crowding, lack of ventilation, excessive humidity, fatigue, inclement weather, and other conditions favouring the rapid spread and local intensification of meningococcal infection. On the other hand sporadic cases appear to have a less direct relation to unsatisfactory conditions, social or sanitary. Epidemics of cerebro-spinal fever may follow in the wake of other infections. This has been observed, in particular, after influenza epidemics, but the sequence is by no means a constant one.

### Clinical Considerations.

The *incubation period* is indefinite, but usually from 3 to 5 days ; suddenness is one of the usual characteristics of the onset but is not invariable. The maximum period may be as long as 9 to 10 days and in some fulminating cases as short as 24 hours.

*Diagnosis*, before its confirmation by lumbar puncture, is mainly 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. The patient appears to be more seriously ill than his moderate temperature and slow pulse would indicate ; cerebration is usually slow or abnormal ; stupor, delirium or coma may be present early in the disease. The vomiting is almost invariably associated with constipation. Stiffness of the neck muscles is an early symptom, whilst retraction of the head comes later ; a nodding motion of the neck is more painful than rotation ; Kernig's sign is pronounced and there is usually little difficulty in distinguishing this definite sign of increased intrathecal pressure from its slight counterfeit which can sometimes be elicited in influenza or measles. It must be remembered, however, that Kernig's sign sometimes appears gradually and may not be well marked until 24 or perhaps 48 hours after the onset of illness.

The rashes, which give rise to the term "spotted fever," are more common in some outbreaks, such as the epidemic of 1921 in Denmark, than in others. They include petechiae, maculae and large purpuric patches. Labial herpes is common and occurs late. Incontinence of urine, which is usually due to a retention overflow needing catheterisation, is a valuable positive sign but its absence does not in any way negative the diagnosis.

The clinical appearances in cases in which the invasion of the meninges of the brain and cord is of moderate severity are not difficult of interpretation, but this is not so either when the invasion is severe—the fulminating type in which the patient succumbs to a rapid intoxication—or when it is mild and the symptoms are chiefly



those of a general infection. During an epidemic among adults the great majority (probably 90 per cent.) of all the cases which occur will show a fairly typical clinical picture, as described above. Among the remaining *atypical cases* there will usually be some 2 or 3 per cent. of "fulminant" cases in which the meningococcal septicaemia is so rapid and overwhelming in action that the patient scarcely has time to develop meningeal symptoms before coma and death supervene; in such cases the cerebro-spinal fluid may be comparatively clear. These cases often exhibit a purpuric rash.

Abnormal types of the disease are common among children and include the posterior basic meningitis of infants which is a chronic and loculated form of meningococcal meningitis. Among the anomalous types of cases in adults, one of the most usual is that which begins with a long initial pyrexia, and is often mistaken for typhoid fever. In this type the systemic infection, which in the "fulminant" case kills outright, is less severe and may last for days before the infection becomes localised in the meninges.

Mild attacks lasting from six to nine days are occasionally met with at all ages, particularly towards the decline of an epidemic or as part of the sporadic occurrence of cerebro-spinal fever among adults. In such cases there may be malaise or sore throat followed by increasing headache and generalised pain; there may be vomiting. The mental condition is usually unaffected and the temperature reaches 100° F. to 103° F., with a gradual and steady fall to the normal. These cases may be mistaken at first for influenza or typhoid fever, but some degree of neck rigidity and Kernig's sign are usually present, and the cerebro-spinal fluid is slightly turbid with relatively few meningococci.

In other cases of short duration and quick recovery there may be an acute onset with rigors, headache and vomiting, which subside almost as rapidly as they appear and within a few days convalescence appears to be established. Neck rigidity and Kernig's sign are nearly always present and there may be retention of urine. Sometimes a recrudescence or a second and more severe attack follows within three or four days of apparent recovery.

The duration of illness varies from a few hours in the fulminating type to weeks or even months in the subacute recrudescent type. Ordinarily patients are seldom acutely ill for more than two weeks. If they do not die or recover within this period the condition becomes subacute. Complete recovery may take place, or there may remain various forms of cranial nerve paralysis or even a monoplegia or hemiplegia, more rarely also some mental impairment. The figures of case mortality obtained in particular epidemics and in particular series of cases need to be used with much caution either as absolute figures or for comparative purposes. It may be said that the ordinary case mortality rate for cases untreated with anti-meningococcal serum in different epidemics, and in different phases of the same epidemic, varies from 25 per cent. to 90 per cent.



Contrasts of the official figures of notifications with those of deaths often exaggerate the case mortality, particularly when they relate to the usual sporadic prevalence in the country, when only the pronounced cases are reported and associated mild and abortive cases, being overlooked or not diagnosed as cerebro-spinal fever, are not notified.

### Pathological and Bacteriological Features.

It is probable that cerebro-spinal fever most often follows an infection of the naso-pharynx. Various theories of the route by which the meningococcus passes from the nasal cavities to the brain have been advanced. The most widely held of these is that the cocci are disseminated by the blood stream,\* but on the other hand le Gros Clark† has shown that certain fluids dropped into the nasal cavities of rabbits reach the surface of the brain within one hour, passing by way of the perineural sheaths of the olfactory nerves to the subarachnoid space, and this direct path of invasion must be considered possible with the meningococcus.

The cerebro-spinal fluid in the early stages may be clear or only slightly turbid, but the pressure is much increased. Ultimately, and sometimes almost from the beginning, the fluid becomes purulent. Polymorphonuclear leucocytes are found and meningococci are commonly present in them, as well as free in the fluid. If, as may occur in cases with marked cerebral symptoms, the communication between the cerebral ventricles and the spinal subarachnoid space is occluded, the fluid obtained by lumbar puncture may be scanty and almost clear and free from meningococci.

The characteristic kidney-bean-shaped, Gram-negative cocci are to be found—usually in pairs, but occasionally as tetrads—in the exudations from the meninges, enclosed in polymorphonuclear leucocytes or free. They may also be present in the secretions of the eyes, nose and pharynx of both patients and “carriers” and in the very early stages they may be found in the patient’s blood. Outside the body the meningococcus is a delicate organism requiring special media for its cultivation; it will not grow below 25° C. nor above 40° C. When sufficient care is taken there is no difficulty in making a laboratory diagnosis by means of cultural tests which determine the presence of the meningococcus.‡

For the ordinary purpose of confirming the clinical diagnosis of a case, the determination of the presence of meningococci in the

\* A System of Bacteriology II, 317, Medical Research Council (1929).

† Reports on Public Health and Medical Subjects, No. 54, Ministry of Health (1929).

‡ Cerebro-spinal fluid to be examined for meningococcus may be sent, packed in accordance with the regulations of the Post Office, to the Pathological Laboratory of the Ministry of Health, Dudley House, Endell Street, W.C.2. The fluid should be collected in a sterile bottle with aseptic precautions; a short statement of the circumstances of the case should accompany it, including a note of the hour the fluid was obtained. Delay in transmission may result in the organism failing to grow.



cerebro-spinal fluid is all that is required. Reference, however, must here be made to the different serological types of meningococcus, which were the subject of such notable contributions to pathology during the war.\* It was, by 1918, often possible, with the aid of particular type agglutinating serums, to report on the individual case as one which was infected by meningococcus of a particular serological group or type (e.g. Gordon's I, II, III or IV). This information proved its value in relation to the epidemiological studies and the methods of serotherapeutic treatment which were being pursued at that time, and bacteriologists now receiving specimens from cerebro-spinal fever cases are consequently often asked to specify in their reports the type of the meningococcus present. Such reports cannot now be given with the same confidence since the standard type strains and serums formerly in use have deteriorated in the intervening period and it has not been possible in the absence of epidemic prevalence of the disease to replace them. Their preparation so far as the material now available permits is, however, in progress. Further reference to the question of serological types is made below under the heading "Treatment."

### **Infectivity and mode of spread by healthy carriers.**

The transmission of the meningococcus from person to person must almost always be effected by rapid and direct transference of infection from the mucous surfaces of the mouth and nose, as the result of sneezing, coughing, loud speaking or other means of "droplet" infection. Under ordinary conditions the meningococcus is incapable of growth or survival at temperatures much below that of the human body, so that indirect infection is of relatively little importance.

While the transmission of the meningococcus from person to person is common, it is unusual for a patient to have been infected by another patient suffering from cerebro-spinal fever. For every case of meningococcus infection which results in cerebro-spinal fever, there are many more which do not. Neither the one class nor the other may ever have been in known contact with a cerebro-spinal fever patient; they have derived their infection from persons who, if they have been ill at all, have shown no certain signs of infection of the cerebro-spinal system. In other words, the great majority of infections are derived from persons who, for the time being, are unrecognised carriers of the meningococcus. Most populations in this country would probably be found at some period or other to yield healthy meningococcus carriers if a good sampling examination were made of nasopharyngeal swabs. At times when cerebro-spinal fever is locally prevalent and particularly when it is occurring in

\* M.R.C. Special Report Series Nos. 3 (1917) and 50 (1920).

L.G.B. Reports New Series Nos. 110 (1916) and 114 (1917).

For general observations on the epidemiology of Cerebro-spinal Fever, see also MacNalty, "Epidemic Diseases of the Central Nervous System" (1927), and Rolleston, H., Lumleian Lectures, *The Lancet*, 1919, 541, 593, 643.



institutions containing aggregations of children or young adults, the proportion of carriers is specially high.

These considerations must be kept in mind when advice is given on the danger of infection from an individual cerebro-spinal fever patient. It must be assumed that the great majority of patients contract their infection from carriers. If then clinical cerebro-spinal fever is considered apart from symptomless meningococcal infection, it must be termed a disease which has a very low case-to-case infectivity, and in this respect to be on quite a different plane from diseases like smallpox and measles. Multiple cases in one house are not common except in severe epidemics. Doctors, nurses and others in specially close association with acute cases are sometimes themselves attacked, but the occurrence is fortunately rare.

The duration of the carrier condition in healthy persons is usually said to be from two to three weeks and in actual cases of cerebro-spinal fever the carrier condition may continue throughout and beyond the illness itself. Chronic carriers, both among convalescents from cerebro-spinal fever and among apparently healthy persons, who remain carriers for a year or more are, however, known to occur, especially those in whom some naso-pharyngeal abnormality, such as a deflected nasal septum in contact with an enlarged turbinate, exists.

Virulence tests which are so useful in diphtheria cannot ordinarily be applied in cerebro-spinal fever owing to the insusceptibility of all ordinary available laboratory animals to meningococcus infection.

## II. CONTROL AND TREATMENT.

### Notification.

Cerebro-spinal fever has been compulsorily notifiable in England and Wales since the issue of the Local Government Board's Order of 15th August, 1912. It is important that all cases should be notified to the Medical Officer of Health as soon as the clinical diagnosis is made. This diagnosis may, of course, be arrived at clinically before bacteriological evidence has been furnished that the meningococcus is present. It is part of the system implied by notification that the Medical Officer of Health should be informed immediately the disease is even suspected in order that any facilities at his disposal for aiding diagnosis and facilitating treatment should be promptly available.

### Hospital provision, etc.

The Medical Officer of Health should give his first attention to the question of securing that the best available treatment of the patient is obtained, under reasonable conditions of isolation. If these are not already provided at the patient's home, treatment in hospital should at once be offered; a bed in an observation or special ward at the isolation hospital serving the district will usually be the most appropriate, but sometimes the equivalent accommodation in



a general hospital may be more suitable. If the patient is too ill to be moved, any necessary and practicable assistance in home nursing which is at the disposal of the public health department should be made available. It should be remembered that one patient may require hours of attention daily from the doctor, and the services of more than one nurse. It may therefore be necessary, when the patient is treated in the isolation hospital, to provide additional medical and nursing staff. Where there is a part-time medical superintendent, it may sometimes be better to give him assistance in his outside work, thus leaving him free to devote more time to the hospital.

The measures of disinfection required in connection with a cerebro-spinal fever patient are simple ; practically they can be limited to articles likely to have been soiled by discharges from the nose and mouth.

### Treatment.

No attempt is made in this review to advise on the general and special management of the individual case. For this the accounts given in the standard textbooks and monographs should be consulted. The following may, however, be here noted :—

Apart from good nursing, which is of great importance, the essential treatment of cerebro-spinal fever comprises

- (1) Early and repeated lumbar puncture to relieve pressure and to promote drainage of the cerebro-spinal system. This is in itself a therapeutic measure of great importance.
- (2) Anti-meningococcal serum should be administered with the first possible lumbar puncture. The administration of serum should be continued at intervals usually of 24 hours until recovery appears to be well established and the cerebro-spinal fluid has become clear, the tendency to relapse being borne in mind. It should not necessarily be discontinued on the ground that the first examination of the cerebro-spinal fluid has shown no meningococci. Lumbar puncture should not be delayed if the serum be not immediately available.
- (3) It is best to rely primarily upon the intrathecal route, but in certain cases intravenous or intramuscular administration of serum has been tried and found beneficial. Repeated doses from 100 to 150 c.c. can, with the necessary skill and patience, be given intravenously even to young children.\*

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\* According to Professor Cantacuzène, very satisfactory results have been recently obtained in Roumania, especially with adults (recruits), by using a serum polyvalent against many races of meningococcus, given intrathecally in daily doses (usually of 20 to 50 c.c.) and at the same time administered intramuscularly in doses of about 60 c.c. per day for at least three or four days.



- (4) As regards symptomatic treatment, adrenalin is said to have some effect in combating shock in fulminating cases. Morphia or heroin should be freely used once the diagnosis has been established.

### *Lumbar puncture.*

For safe and easy puncture it is essential to have the patient in the correct position, the knees being drawn up on to the abdomen as far as possible and the right knee accurately upon the left. The following instructions for performing lumbar puncture were given by the late Professor Ker.\*

"The needles used for lumbar puncture should fit an ordinary Record syringe or the metal attachment of the rubber tube which is used by those who prefer to introduce the serum from a funnel by gravity. The patient is usually placed on his left side with the knees well drawn up and with the head and shoulders bent forward as far as possible. The under arm should be pulled well forward. The puncture is made in the fourth lumbar interspace, which can be readily identified by the fact that a line connecting the summits of the iliac crests intersects the fourth lumbar vertebra. The skin in the neighbourhood is thoroughly cleansed and painted with iodine. The needle must be carefully sterilised and, especially at a first puncture when bacteriological results are of most importance, it is advisable for the operator to wear rubber gloves. The theca can be reached by two routes, *between the spines* or between the laminae. Of these the first is by far the easiest and, universally practised in the case of children, is equally applicable to adults. The interspinous ligament being firmly grasped between the finger and thumb of the left hand to prevent its being laterally deflected, the needle is inserted, exactly in the middle line and just above the lower spine, and pushed gently and firmly forward, either directly or with a very slight upward slant. After piercing the tough ligament, and for this purpose the needle should be both strong and sharp, one can usually feel a slight sensation of something giving way a little deeper in the back before the point of the needle as the dura is punctured. The stylet is then withdrawn and the fluid is collected first in sterile tubes for examination and then in a graduated glass measure. The depth at which fluid is struck varies much with the age and size of the patient, say from half an inch or less in a small infant to  $3\frac{1}{2}$  inches or more in a muscular or fat adult. Too deep a thrust is apt, by passing across the space and penetrating the venous plexus behind, to cause bleeding which, always unfortunate, is particularly annoying at a first puncture,

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\* "Infectious Diseases," by C. B. Ker, Oxford Medical Publications. Oxford University Press (1920).



as the blood prevents a definite decision as to whether the fluid is clear or turbid. For this reason, when puncturing very young infants I prefer to use an ordinary antitoxin syringe needle without a stilette so that, if the space is reached sooner than is anticipated, the spouting of the fluid at once announces the fact and avoids the risk of too deep a thrust.

If there is much pressure and, as not infrequently happens, the fluid spouts or comes out in a continuous stream, it should be checked by retaining the stilette partly in position, as the too rapid withdrawal of large amounts does not appear to be altogether free from risk. As a rule, if the process is not too hurried, it is safe to let the fluid flow until it exudes slowly, about one drop in three or four seconds. Amounts up to 80 and 90 c.c. are not infrequently obtained in the case of adults, and in one fatal case punctured on the second day 115 c.c. were obtained without difficulty. . . . More common amounts in adults suffering from cerebro-spinal meningitis are from 50 to 70 c.c. and the quantity of fluid obtained remains much the same at subsequent punctures except in the so-called "suppurative" cases, in which it usually decreases steadily. In children in the acute stage about 30 or 40 c.c. may be expected, while in chronic cases of hydrocephalus in infants this amount may be doubled or almost trebled in some instances.

If the puncture is to be made *between the laminae*, a point midway between the spines and a quarter of an inch external to the middle line is selected and the needle is directed inwards and slightly upwards. There is less resistance to be overcome in this route, and its advocates claim that it allows greater delicacy in manipulation. But it is certainly more difficult and should be avoided by beginners. If a syringe is used, moreover, for the introduction of the serum, it is thrown at rather an awkward angle for the injection, an objection which does not apply if the tube and funnel is used.

Occasionally fluid is not struck. This may be due merely to the blocking of the needle, which should be cleared with the stilette. Or the dura may have been pushed before the point of the needle and remained unpunctured. Or, again, the pierced membranes may have wrapped themselves round the point, and rotating the needle may meet the difficulty. Adhesions, moreover, may have occluded the canal, though in this case a few drops of fluid usually exude. Lastly, the fluid may be too purulent and sticky to flow. Whatever is the cause of the difficulty, a "dry tap" should always be regarded with great suspicion and the presumption always is that the theca has not been properly penetrated. It is advisable to try a higher space, and it may be remarked here that the second and third spaces seem to be as safe as the fourth. If it is believed that the fluid is too thick to flow, an attempt may be made to wash



out the canal between the second and fourth spaces, two needles being inserted and saline solution injected into the upper one.

It is usually wise to give an *anaesthetic*, particularly if it is intended to inject serum. Many patients are delirious and cannot be properly controlled, and a needle broken in the back is a very awkward accident. Again, the daily treatment, if an anaesthetic is not given, becomes a real terror to the patient, as intrathecal injection causes a considerable amount of pain in the back and legs. Chloroform is, as a rule, excellently tolerated, but it is none the less wise to avoid anaesthetics in the case of infants, who can easily be held steady and who do not stand injection of serum at all well, both the pulse and respiration often giving cause for an anxiety which is only increased if chloroform is employed."

#### *Cisternal puncture.*

Where lumbar puncture has resulted in failure to obtain cerebro-spinal fluid, cisternal puncture is sometimes substituted. The following description of the method of performing this operation is given by Goodall.\*

"The apparatus and the general preparation are the same as for lumbar puncture, but a stouter needle is necessary in order to pierce the *ligamentum nuchae*, and the needle should be graduated in centimetres so as to gauge the depth. The patient is laid on his right side (for a right-handed operator), with his head flexed on his chest. The spot for puncture is the depression which can be felt immediately above the spinous process of the second cervical vertebra. The needle is made to enter the skin in the middle line just above this process, and is pushed upwards and slightly forwards in the plane in which lie the point of puncture, the upper edge of the external auditory meatus and the glabellum. The occipito-atlantoid ligament between the posterior margin of the foramen magnum and the upper border of the posterior arch of the atlas has to be pierced, and it lies 4 to 5 cm. beneath the skin. The width from before backwards of the *cisterna magna* at this spot is  $1\frac{1}{2}$  to 2 cm. The needle should only just be pushed into the cistern, for fear of injuring the floor of the fourth ventricle. Care must also be taken not to push the needle too acutely upwards, lest the middle lobe of the cerebellum be damaged. This lobe is pushed down when the intracranial pressure is increased. When, therefore, symptoms of increased intracranial pressure are present, puncture of the *cisterna magna* should not be performed."

#### *Administration of serum.*

As said already, the withdrawal of cerebro-spinal fluid is usually a preliminary to the injection of therapeutic anti-meningo-

\* "Infectious Diseases," Goodall and Washbourn, Third Edition by E. W. Goodall. H. K. Lewis and Company, Limited (1928).



coccus serum. If the maximum benefit of serum treatment is to be obtained, it should be administered as early as possible ; the mortality in cases in which treatment begins before the third day has been found to be less than half that in those treated only after seven days (Flexner and others).

The serum should be warmed to slightly over blood heat by leaving the glass container in water at about 110° F. A rubber tube ending in an adapter, also fairly warm, is now placed on one end of the glass serum container which has been previously filed and broken open. The other end of the serum container is then broken open, and the tube filled right up to the adapter by adjusting the level. The adapter is then inserted into the needle and the serum run into the theca, a head of less than 1½ ft. being quite sufficient. Some medical officers of experience prefer to administer the serum carefully by syringe rather than to follow the more usual gravity method. When the injection is completed, the puncture should be sealed with cotton wool and collodion and the foot of the bed should be raised for a few hours to promote the flow of the serum towards the upper part of the central nervous system.

The amount of serum injected should never exceed the amount of fluid drawn off. Thirty c.c. of serum is the usual intrathecal dose for adults. With an anaesthetic 60 c.c. to 100 c.c. of cerebro-spinal fluid can usually be drawn off, and one of the advantages of general anaesthesia is that it increases, sometimes to fourfold, the amount of fluid which can be drawn, thereby allowing easy introduction of 30 c.c. of serum. The serum injection should be repeated in twenty-four hours.

### Value of Anti-meningococcus Serum.

In view of the inherent severity and heavy mortality of this disease, it has in the above pages been considered right to emphasise the importance in all cases of giving the one known specific remedy—anti-meningococcus serum—promptly and under the optimum conditions. But it must not on this account be supposed that the evidence of the frequent failure, or alleged failure, of specific serum therapy in recent years has been overlooked or minimised. Serum therapy has undoubtedly proved useless, or almost useless, in many cases, and some good authorities assert that none of the different serums which are at present available can be regarded as potent against the meningococcus and that in consequence they are not worth employing. On the other hand, it is common ground that the earlier results of serum therapy were strikingly good, and that they were particularly so towards the end of the war. It is, of course, possible that the difference is due to the fact that at that time most of the prevalent cerebro-spinal fever was found to be associated with one or two identifiable serological types of meningococcus and the serums used with success



were monovalent or polyvalent, prepared from the particular strains which were current.

The difficulty of assessing the probable therapeutic efficiency of anti-meningococcus serums by laboratory methods has not yet been overcome. A hopeful method, described by Gordon,\* depends on the demonstration of anti-endotoxic action. In the event of a sufficient response being made to the inquiry proposed below into the clinical results of serum treatment at the present time, endeavours will be made to correlate these results with the response to the endotoxin tests. But however this may be, the present use of monovalent as against polyvalent therapeutic serums raises difficult practical questions. While it was possible when dealing with the extensive prevalence of cerebro-spinal fever among special communities under war conditions to differentiate the particular local strains and to prepare monotypical serums, and while, under these conditions, it was often also possible immediately to classify the meningococcus of a given patient and to select the monotypical serum appropriate for his case, it has not so far been found practicable to organise or to maintain any corresponding method to deal with the scattered and unconnected cases which occur in the ordinary population of this country at the present time. Moreover it cannot be assumed that in different epidemic periods the same serological types will prevail or that the serums prepared with strains which were isolated before an epidemic outbreak will possess the complete range of anti-bodies required to combat the new infection.†

Reliance must in these circumstances be placed on the use of polyvalent serums, the result of immunising the horse with a variety of types of meningococci, taking care to include as large an element as possible of meningococci obtained from the cerebro-spinal fluid drawn from new and acute cases occurring in different parts of the country. The principal institutes and laboratories from which local

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\* Med. Res. Council, Spec. Rep. Series No. 50 (1920).

† A rather pessimistic view of this subject is taken by Prausnitz (Memoranda on the International Standardisation of Therapeutic Sera and Bacterial Products, p. 42, League of Nations, Geneva, 1929):—

An appreciable number of strains of American, Danish, English and French origin, taken from the 'National Collection of Type Cultures' of the Lister Institute, as well as twenty-six other Danish cultures, were tested by agglutination and agglutinin absorption with several sera prepared from a number of these cultures. Hardly in a single case was it possible to make a clear division into definite groups or types, but almost without exception one strain was found to pass over by insensible degrees into another. We may ask ourselves whether these conditions have developed in this extreme form in the last few years, during which meningitis has only been occurring sporadically.

It is, indeed, quite conceivable that strains of greater antigenic uniformity might occur in larger numbers in the course of more extensive epidemics. Under present circumstances, at all events, the prospects of producing anti-meningococcus sera of *practical* value are rendered highly doubtful by the existence of this antigenic multiplicity."



authorities or practitioners usually purchase anti-meningococcus serum have adopted this policy, and are utilising material derived from recent cases which the Pathological Laboratory of the Ministry Health has put at their disposal.

Meanwhile, it should be added, the problem of preserving either potent anti-meningococcus serum, or culture material of full immunising potency, or both, during inter-epidemic periods when fresh strains are not available, is engaging the attention of the Medical Research Council.

#### *Collection of Records of Results of Serum Treatment.*

It is obviously desirable to secure the closest and most accurate observation on the efficiency and potency of all the serums thus in use. Seeing that by far the most valuable test of the efficiency and potency of these serums is clinical and that it rarely happens that any one hospital has sufficient cases for useful differential study, the Department is now endeavouring by means of individual case inquiry to collect and examine all evidence available regarding the results of serum treatment, both as to the methods of administration and as to the nature of the serum used. The co-operation of Medical Officers of Health, hospital medical officers and medical practitioners in this matter is obviously essential and is cordially invited. Forms for the purpose will be sent on application to the Senior Medical Officer, Med. I., Ministry of Health. As, however, the data required (see Appendix II) are few, any communication which contains them will be equally useful for the purpose.

#### **Meningococcus Vaccine.**

In treatment a vaccine may find a useful place in the slow convalescence which is not uncommon, whether in acute, severe or more chronic cases. The vaccine should, if possible, consist of killed cultures of the patient's own meningococcus, or, at least, of a strain of similar type and should be administered by subcutaneous injection in fairly large doses, as high initially as 250 millions.\*

As regards its use in prophylaxis no satisfactory data exist; statistical evidence, on which alone its value could be determined, is peculiarly difficult to obtain in a disease of such erratic incidence. In special circumstances, however, such as the entrance of persons from an uninfected area into a community where cases are occurring, its use, at least ten days before such entrance should be seriously considered. Doses of 500 and 1,000 million, as with T.A.B. vaccine, would be suitable and the cocci should consist of a mixture of the types predominating in the infected community.

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\* Proc. R. Soc. Med. 1917, X (Pt. II Section of Epidemiology and State Medicine), 44, 45.



### Measures to be taken with contacts.

It is impracticable to employ "swabbing" of the naso-pharynx so extensively as to detect all the persons in a district who may be carrying the meningococcus, nor has it been found possible to eliminate the "carrier" condition when discovered. Swabbing, if employed at all, should, therefore, be limited to close contacts of the patient; but even here the efficacy of such action in controlling the spread of infection must be relatively slight, and there is little justification (apart from research work) for its routine adoption. There are, however, special circumstances in which the information gained by swabbing may be valuable. In view of the special susceptibility of children to meningococcal infection, it will be undesirable to allow them to pass under the charge of a nurse or other person who has recently been in intimate contact with a cerebro-spinal fever patient, and in such a case the fact that adequate bacteriological examination has proved that the person in question is not a carrier is a substantial and useful guarantee of safety. Similarly, for the proper study and control of outbreaks in residential schools and other limited communities, systematic swabbing sometimes gives valuable indications. If any useful conclusions are to be deduced from the examination of swabs it is necessary that the specimens should be skilfully taken\* and promptly dealt with by immediate inoculation of culture plates. The most careful bacteriologist may sometimes fail to detect the presence of meningococci, particularly when these are masked by other micro-organisms, so that in cases where the establishment of a negative result is of importance, it is well that at least two successive bacteriological examinations of swabs should be made.

The isolation in hospital of contacts or known carriers should not be attempted, and, in general, such persons should be dealt with in the light of the knowledge that intermittently the meningococcus is a common inhabitant of the naso-pharynx, and only exceptionally produces disease in the person harbouring it or in others. Temporary carriers in good hygienic conditions clear up rapidly without treatment; indeed, fresh air and exercise have been found to be the best means of freeing a meningococcus carrier. A fine vapour spray, for example of zinc sulphate 1.5-2 per cent., directed through the nostrils and mouth on to the naso-pharynx appears sometimes to have a beneficial effect.

As previously mentioned, cerebro-spinal fever is transmitted by means of "droplet" infection, and young children are especially susceptible to the disease. The kissing of children while cerebro-spinal fever is prevalent is therefore to be deprecated, and persons who are habitually in close contact with clinical cases should be

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\* The upper end of the posterior pharyngeal wall should be swabbed, and every effort should be made to avoid contamination of the swab with saliva. The culture plates should be warmed to blood heat.



kept away from children so far as possible and should be advised to take every precaution to avoid conveying infection to others by sneezing or coughing. As the meningococcus commonly disappears from the naso-pharynx of healthy persons within two or three weeks, it will usually be sufficient if children of school age who have been in contact with a clinical case of cerebro-spinal fever are excluded from school for three weeks. Meanwhile, however, the hygienic conditions in the school should be looked into, in case action is required to prevent overcrowding or to ensure that the children get as much fresh air as possible.

### **General precautions.**

Observance of the general rules of hygiene, particularly in regard to fresh air and avoidance of "droplet" infection, is the best general safeguard. The path of meningococcus infection being by way of the nose or mouth, the general precautions to be taken are such as are appropriate to prevent the spread of catarrhal diseases. On the appearance of cerebro-spinal fever in a residential institution, the nearest approach to open air life by day and night should be aimed at. Overcrowding in sleeping quarters, particularly in cold weather, has been proved by repeated experience to constitute a powerful factor in the spread of cerebro-spinal fever; in dormitories the space left between adjacent beds should be not less than three feet.



## APPENDIX I.

**Copy of Press Communication on Cerebro-spinal Fever (Ministry of Health, February, 1931.)**

Periodical increases of this relatively rare disease are not unusual. It was made generally notifiable in 1912, and from 200 to 300 cases were reported annually before the War. From 1915 to 1917 there was an annual incidence in the civil population of from 1,300 to 2,500. The figures fell to 301 in 1923. Since then their tendency has been upward. In the present year about 230 cases among civilians have been notified in England and Wales.

Of the cases at present occurring and reported about half have proved fatal. The disease is, relatively speaking, more common in the United States. The responsible micro-organism (the meningococcus) is to be found in the nose and throat passages of a very large number of persons who are, and who remain, quite well. Local outbreaks are favoured by overcrowding in barracks, schools, and other residential institutions, and in club premises for young people. It was found, particularly during the war years, that when the individual was given more room in which to live and sleep the incidence fell greatly. In order to prevent outbreaks of the disease in these institutions, no approach to overcrowding should be permitted. This applies particularly to dormitories, where insistence on sufficient space between the edges of adjacent beds (which should never be less than 3 ft. clear), and the maintenance of thorough ventilation are of the greatest importance.

No vaccine or serum effective for the prevention of an attack of cerebro-spinal fever is known. There is, however, an important specific curative treatment by the administration of anti-meningococcus serum. Research workers and bacteriologists in this and other countries are trying to find serums which promise greater success than those now in use.



## APPENDIX II.

**Reports desired by the Ministry of Health on serum treatment of individual cases of cerebro-spinal fever. (Page 19).**

In view of the lack of recent reliable information of the use and results of anti-meningococcus serum treatment, an endeavour is now being made to collect new data on the subject. Medical Officers of Health and the Medical Superintendents of Hospitals as well as medical practitioners in charge of cases are consequently invited to furnish the information asked for below, which should be sent, as soon as possible after the recovery or death of the case, addressed to:—

*"The Senior Medical Officer (Med. I),  
Ministry of Health,  
Whitehall,  
London, S.W.1."*

1. Sanitary District (or Hospital).
2. Initials, age and sex of patient.
3. Date of onset of illness.
4. Date of notification.
5. Date of removal to hospital.
6. Whether any bacteriological confirmation of diagnosis; if so, when and by whom?
7. On what dates and on how many occasions was lumbar puncture performed and how much cerebro-spinal fluid was removed at each operation?
8. Dates on which anti-meningococcus serum was administered intrathecally and the amount on each date.
9. Dates on which anti-meningococcus serum was administered intravenously (or intramuscularly) with amounts on each date.
10. Source of the anti-meningococcus serum or serums used, giving in every case the identification or batch numbers supplied.
11. Date of recovery or death.
12. Observations on the severity of the case and on the apparent effect of serum treatment.

*(Signature of medical reporter  
and date of report.)*



