Observations

ON

A CEREBRO-SPINAL FEVER OUTBREAK IN THE ROYAL AIR FORCE IN 1931

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Since 1919 there have been sporadic cases of cerebro-spinal meningitis in the Royal Air Force, chiefly among recruits, and the bacteriological examination of swabbings from the nasopharynx of the more immediate contacts has resulted in the prompt detection and consequent isolation of meningococcus "carriers" in each instance. The spread of the disease has been arrested, possibly by this speedy isolation of carriers, or by good fortune, so that more stringent prophylactic measures have not been necessary.

But in the beginning of the present year there occurred a series of cases of cerebro-spinal fever of the fulminating type which were not so readily controlled, and during the investigation of this outbreak certain interesting observations were made regarding the origin, spread, and control of the infection and the treatment of the disease.

F = Fireplace. C.S.F. = Case of cerebro-spinal fever. c = Carrier of meningococcus.

CHART 1.—Showing the general arrangement of beds in barrack rooms and the occurrence of a case of cerebro-spinal fever in a bed in close proximity to the fireplace (see text). The position of contact carriers of meningococcus is also indicated. The space between adjacent beds is approximately 3 feet.

HISTORY OF THE OUTBREAK

The outbreak occurred at Uxbridge, and was coincident with an influx of new recruits of susceptible age, the advent of cold, foggy weather, and the issue of a more liberal coal allowance to mitigate the rigours of the winter. The provision of fires in the barrack rooms led naturally to a crowding together of men around the fireplace in the evenings, and this appears to have played an important part in the dissemination of the infection; it was not purely a question of bed space. The first case occurred on January 4th, 1931, the second on January 5th, and then serially on the 8th, 17th, 24th, 25th, 27th, and 31st, and on February 7th, 10th, 11th, and 14th. In all, there were twelve cases of cerebro-spinal fever of the malignant type, and there was no direct connexion as regards infection between any of them, with the exception of the patients (Cases Nos. 9 and 11) who occupied adjacent beds; in all other instances the patients were drawn from widely separated barrack rooms. This distribution of cases pointed to some common source of infection, such as the cinema, concert room, or canteen. The isolation of contact carriers of the early cases, and the closure of the cinema and the cessation of other forms of indoor entertainment, did not check the spread of the disease. But on February 12th the canteen was closed, and a more extensive search was made for contact and non-contact meningococcus carriers throughout the depot.

Following on this action the outbreak terminated abruptly within forty-eight hours.

ORIGIN OF THE INFECTION

The first patient in the present epidemic came from a barrack room in which there was an airman (G. T. C.) who had been isolated previously as a meningococcus carrier during the examination of contacts of a sporadic case of cerebro-spinal fever which occurred at Uxbridge in May, 1930. This carrier was then proved to harbour Type I meningococcus, and he continued to carry this organism for five weeks. After repeated nasopharyngeal swabbings were found to be negative, he was pronounced free from infection in July, 1930. He returned to duty at Uxbridge Depot on July 20th, and, despite his sojourn among other recruits, there was no recurrence of cerebro-spinal fever until the present outbreak, which commenced at the beginning of January, 1931, in a different barrack room from that which had been occupied by the patient in the sporadic case referred to above.

It is difficult to prove that the present outbreak of fever originated from this old carrier (G. T. C.), but it is significant that he was found, in January, 1931, to be

still harbouring meningococci of the type responsible for the infection; and that he was a close contact of the first case. It is to be observed, however, that cerebro-spinal fever had been prevalent among the civil population since October, 1930, and that

its incidence was increasing rapidly when the R.A.F. outbreak started; this factor undoubtedly added to the number of meningococcus carriers among the newly joined recruits, and so helped to bring the carrier rate at the Uxbridge Depot to the danger level.

SPREAD OF THE INFECTION

This raises the question of overcrowding in barrack rooms. There was no overcrowding as regards the actual bed space, and the barracks were well ventilated. The beds were spaced $2\frac{1}{2}$ to 3 feet apart, and the windows were kept open day and night. Heating was attained by means of two open fireplaces situated towards the centre of each room. One or other of these fires was usually lighted about tea-time, and during the evening the inmates (twenty to twenty-four in number) naturally congregated at the fireside, so that in any barrack room, probably, the air was most impure in this region. It follows that those individuals whose beds occupied this central area continued to breathe this vitiated atmosphere longer than their room-mates, and it is significant that the first and all subsequent cases of cerebro-spinal fever, except Case No. 8, occurred in airmen occupying beds in close proximity to the fireplace in use (see Chart 1).

In this connexion it is interesting to compare the meningococcus carrier rate of newly joined recruits at Uxbridge and at Halton; in the seventh week of this year it was 15 per cent. and 3 per cent. respectively. The local heating arrangements may help to explain this

difference in the carrier rates. The airmen in both places are housed in barracks similar as regards cubic and floor space per man, but dissimilar as regards the mode of heating. The Halton barracks, which have been singularly free from cerebro-spinal fever, are centrally heated, so that each inmate tends to keep his own bed area, and there is no local overcrowding, whereas at Uxbridge the heating is by open fireplaces, leading to central crowding in each room, with results as described above.

Where did the men get the meningococcus into their upper respiratory passages with which to infect the air of the dormitories? As has been stated, the twelve cases occurred in separate barrack rooms (with one exception), indicating some common source of infection. Originally this infection may have taken place in one or in all of several places in which the airmen congregated—for example, cinema, dance hall, concert room, and canteen. The closure of all common meeting places, with the exception of the dining hall and canteen, together with the adoption of routine disinfection of the nasopharynx of all personnel by means of gargles, nasal douches, and sprays, as described later under "Control of the disease," did not stay the epidemic. Two obvious gaps were left in the chain of control—the dining hall and the canteen. In the dining hall the men of each barrack room sat at appointed tables, so that there was little likelihood of the inmates of one room infecting those of another here. In the canteen the men from different barrack rooms mingled freely in a warm and moisture-laden atmosphere, under social conditions conducive to the spread of disease by droplet infection; this was especially the case on a Friday (pay-day), for then the men flocked to the canteen. Strength is given to the supposition that infection took place chiefly in the canteen, and on a Friday, from the observation that cases of cerebro-spinal fever arose usually on the following Saturday, Sunday, Monday, or Tuesday—that is, within the recognized incubation period for the disease—and from the fact that the closure of the canteen was followed by the abrupt cessation of the epidemic (see Chart 2).

CHART 2.—Showing the relationship between the case incidence of cerebro-spinal fever and the crowding together of men in the canteen on Fridays—that is, pay-days.

A further isolated or sporadic case of cerebro-spinal fever occurred at the R.A.F. Depot, Uxbridge, on March 20th, 1931—that is, eleven days after the general prophylactic measures were relaxed. This patient, a recruit, had four days previously travelled 140 miles along with a number of his comrades in a closed charabanc. Infection in this instance presumably occurred from contact with meningococcus carriers during the long journey in a closed vehicle, as subsequently two carriers were detected among the passengers in the coach.

MENINGOCOCCUS CARRIERS

It has been established by Netter and Debré that the meningococcus carrier rate of a community bears a direct relationship to the development of cases of cerebro-spinal fever; the incidence and severity of the disease usually

run parallel with the number of carriers. The outbreak at Uxbridge proved to be no exception to this rule.

Chart 3 indicates the meningococcus carrier rate and case incidence of cerebro-spinal fever among 542 recruits at Uxbridge during the first eight weeks of 1931. The percentage of carriers in the first week of January was 10;

CHART 3.—Carrier rate shown by continuous black line. Cases of cerebro-spinal fever represented by vertical black columns. Upper limit of normal meningococcus carrier rate indicated by dotted line. A = Adoption of general prophylactic measures and closure of cinema. B, Closure of canteen.

during the third week it was 19½. The practice of general prophylactic measures, such as the spraying of the throats of all personnel, the isolation of all detected carriers, and the closing of the cinema, did not check the epidemic. By the sixth week of the year the carrier rate had reached 32 per cent. This was the acme, however, for in the seventh and eighth weeks, following on the closure of the canteen, the rate fell rapidly to 17 and 5 per cent. respectively. The case incidence of the disease rose and fell with the carrier rate, and ceased abruptly when this rate reached normal limits—that is, below 6 per cent.

In all, 120 carriers were detected and isolated, or, in other words, 22 per cent. of the recruits were found to carry the meningococcus. Moreover, the distribution of these carriers throughout the various barrack rooms was fairly uniform, as was shown by a general swabbing. Of these, 45 (37½ per cent.) were contact carriers, and 75 (62½ per cent.) were non-contact carriers. A contact carrier is defined as one who is known to have been in contact with a case of cerebro-spinal fever. This classification is unsatisfactory, as it is probable that many, if not most, of the so-called non-contact carriers had become infected from cases in the canteen or elsewhere. Most of the known contact carriers had been in very close relation to patients with the fever; they slept in adjacent or opposite beds, or had used the same cups, or had been intimate friends.

The duration of the infectivity of meningococcus carriers who are undergoing nasopharyngeal disinfection daily is of practical importance, and is indicated in Table I. It was found that 55 per cent. of the carriers were free from infection within three weeks, and 75 per cent. within a month. One carrier was of the chronic type; it was proved that he had harboured the meningococcus intermittently for the past ten months—that is, since May, 1930.

TABLE I.—Showing the average length of time that meningococcus carriers, undergoing nasopharyngeal disinfection daily, carried the germ.

Nasopharynx Clear of Meningococcus	Number of Carriers	Percentage of Carriers
In 2 weeks	18	15
3 "	48	40
4 "	24	20
5 "	15	12½
6 "	15	12½

The effect that the meningococcus had on the health of the carriers remains to be considered. None of the carriers, isolated as such, developed true cerebro-spinal fever, but 19 suffered from a pyrexia of the influenzal type and 26 had acute nasopharyngitis; whereas 75 remained apparently in normal health. If the twelve cases of cerebro-spinal fever be included, then 43 per cent. of the carriers showed signs of some acute infection, and 57 per cent. remained healthy; only 10 per cent. of the men who harboured the meningococcus in their nasopharynx contracted the specific meningitis. Table II amplifies these points, and indicates the varying degrees of immunity developed against the meningococcus; thus there may be health, a local throat infection, a more generalized sepsis, or actual meningitis and septicaemia.

TABLE II.—Meningococcus Present in the Nasopharynx of 132 Men

12 (9 per cent.) suffered from cerebro-spinal fever	43 per cent.
19 (15 per cent.) suffered from influenza	unhealthy
26 (19 per cent.) suffered from nasopharyngitis...	carriers.
75 (57 per cent.) remained healthy	57 per cent.
	healthy
	carriers.

MENINGISMUS

Those individuals who had pyrexia of the influenzal type accompanied by severe headache, together with tenderness of the neck muscles, and had meningococcus in their upper air passages, but not in their cerebro-spinal fluid, might have been diagnosed as suffering from meningismus or meningism—a condition referred to by Flack,² Horder,³ and others during the war. In these cases the meningococcus was possibly the organism responsible for the infection, although Pfeiffer's bacillus was present also in many instances. It mattered little whether the diagnosis was meningismus or influenza, so long as it was recognized that these cases were not examples of cerebro-spinal meningitis, otherwise the serum, or whatever other treatment was given, might have been credited with unmerited curative power. This was not purely a matter of academic interest, but one of vital practical importance, as the therapeutic treatment of cerebro-spinal fever was, and still is, *sub judice*. In many instances a dose of antimeningococcus serum was given to a doubtful case pending the diagnosis; this was a justifiable and a wise measure to carry out during an epidemic of cerebro-spinal fever; in fact, the serum may have prevented the onset of meningitis in some cases. The problem, however, was to differentiate between meningismus or influenza and the early stages or milder attacks of cerebro-spinal fever.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of typical cases was easy, but many suspected cases called for a very careful clinical examination, together with a total leucocyte count of the blood and, at times, lumbar puncture. Special attention was paid to the mode of onset of the disease. Early onset of vomiting, especially if continued, severe headache, stiffness and tenderness of the neck muscles (this was best elicited in early cases by performing Kernig's test alone or in conjunction with Brudzinski's, and inquiring

whether the patient felt any stiffness elsewhere than in the hamstrings), a varying degree of pyrexia, a pulse-respiratory rate of 3 to 1 or even 2 to 1, together with distinct nervous irritability, tache cérébrale, and inequality, dilatation, or contraction of the pupils were strong evidence of cerebro-spinal fever. Whereas in the influenza cases early and distinct pyrexia (103 to 105° F.) was the prominent symptom, there was little or no tenderness of the neck muscles, and the Kernig test was negative, the pulse-respiratory ratio was normal, nervous irritability was negligible, the pupils were normal, and vomiting was rare and not continued.

Two laboratory tests were found to be of great diagnostic value: a leucocyte count of the blood and the examination of the cerebro-spinal fluid. There was invariably a distinct leucocytosis, even early, in all cases of cerebro-spinal fever; while in influenza a leucopenia or normal count proved the rule. A total leucocyte count was performed as a routine in all cases of pyrexia or suspected cerebro-spinal fever. If the blood count showed the presence of more than 13,000 leucocytes per c.mm., without any clinical condition to account for the leucocytosis, a lumbar puncture was performed; the naked-eye appearance of the cerebro-spinal fluid was often sufficient to clinch the diagnosis without awaiting the result of cytological or cultural examination. On the other hand, if the total white cell count was normal or showed a leucopenia, and there was no definite clinical evidence to suggest meningitis, the patient was watched, and a further count done on the following day, unless the symptoms pointed to the need for earlier intervention: the continued absence of a leucocytosis was a contra-indication of cerebro-spinal fever. In all doubtful cases lumbar puncture was performed. The cerebro-spinal fluid, at times even from fulminating cases of meningitis, appeared clear to the naked eye at the first puncture, but examination in the laboratory showed an increased cell count (60 or more polymorphs per c.mm.), together with an increased albumin content (0.1 to 0.4 per cent. or more) and frequently meningococci in the direct smears, certainly in culture during the next twenty-four to forty-eight hours. Cases of meningismus had clear, sterile cerebro-spinal fluid, with low cell count (about 10 cells per c.mm.) and a practically normal albumin content (0.03 to 0.05 per cent.).

No case was diagnosed as cerebro-spinal meningitis unless the specific organism was seen in, or isolated from, the cerebro-spinal fluid.

FULMINATING CEREBRO-SPINAL FEVER

The twelve cases of cerebro-spinal fever which form the basis of this paper were of the fulminating or malignant type. It might be argued that these were not all fulminating cases, as the patients did not die within three days, but it is maintained that they probably would have done so had it not been for the treatment given to them. The general description of the cases should dispel doubt on this point.

Etiology

The occurrence of cerebro-spinal fever in the recent R.A.F. outbreak was confined to newly joined recruits who were apparently in robust health. The average length of service was ten weeks, and the age incidence varied between 18 and 23½ years, the average age thus being 19½. In four out of the twelve cases there was a history of influenza commencing five to ten days prior to the onset of the meningitis.

Meningococcus Type I, so far as could be ascertained with the high titre agglutination serums available, was isolated from the cerebro-spinal fluid in every instance. In one of the fatal cases *B: influenzae* Pfeiffer was also present in the cerebro-spinal fluid.

Strains of the meningococcus isolated were forwarded to the Ministry of Health Laboratory and to the Lister Institute in connexion with the preparation of a new anti-meningococcus serum.

Clinical Picture

Onset was always abrupt. The earliest symptoms were severe headache and repeated vomiting, often in the absence of pyrexia. Lumbar puncture, when performed at this stage, usually revealed a clear cerebro-spinal fluid containing 30 to 60 leucocytes per c.mm. Within six to eight hours the fluid became opalescent and showed a cellular content of 10,000 to 15,000 leucocytes per c.mm., also a high albumin content, even in cases where serum was not administered during the first puncture. At the same time there was marked exacerbation of the clinical symptoms—the temperature rose to 102° to 105°, there was violent delirium, followed rapidly by coma and accompanied by generalized petechiae. Head retraction was marked, and breathing became of the Cheyne-Stokes variety. The following notes bring out these points.

Case Illustrating Rapid Death

J. McK., aged 18 years 4 months (five weeks' service), reported sick at 9 a.m. on February 11th, 1931, complaining of headache, vomiting, and pains in back and legs; his temperature was normal. In the afternoon his temperature rose to 102°, he vomited several times, and became violent. Shortly afterwards he passed into coma. He was admitted to hospital at 8 p.m. in a deeply comatose condition, with stertorous breathing, pupils fixed in semi-dilatation, marked head retraction, Kernig's sign positive, knee-jerks and superficial abdominal reflexes absent, and generalized purpuric rash; temperature 102°; pulse rate 60; respirations 24. Lumbar puncture was performed at once and 60 c.cm. turbid fluid withdrawn—the cerebro-spinal fluid contained 15,000 leucocytes per c.mm., and meningococci were numerous. Antimeningococcus serum was administered—40 c.cm. intrathecally and 20 c.cm. intravenously. The clinical symptoms, however, gradually got worse, pulse rate and respirations increased (pulse rate 160, respirations 52), the patient became markedly cyanosed, and died suddenly at midnight, within fifteen hours of the onset of the disease.

Case Illustrating Average Recovery

H. W. P., aged 19 (two weeks' service), reported sick on February 7th, 1931, and was treated for influenza at his unit. The salient features of his illness were headache and backache, together with a moderate degree of pyrexia. The usual antipyretic remedies were given, and he had apparently recovered on February 12th. During the following night he had severe headache, and vomited several times. At noon on the 14th his temperature rose to 104.6°, and he became semi-comatose while being transported to hospital.

On admission he was comatose; temperature was 103.8°, pulse rate 104, and respiratory rate 36, breathing being stertorous. Pupils were dilated and scarcely reacted to light; eye-balls wandering. Knee-jerks were sluggish, and abdominal reflexes were absent. Kernig's sign was present, and neck muscles were spastic. A widespread petechial rash was present on trunk and limbs. A blood count showed a leucocytosis of 23,000 per c.mm., 91½ per cent. being polymorphs. Lumbar puncture was performed immediately, and 50 c.cm. turbid fluid were withdrawn under considerable pressure. The cerebro-spinal fluid contained 10,800 cells per c.mm. (97 per cent. were polymorph leucocytes), and showed the presence of many Gram-negative diplococci, which were chiefly extracellular. On culture, meningococcus Type I was isolated.

After draining off 40 c.cm. of the cerebro-spinal fluid, the subarachnoid space was irrigated with 160 c.cm. of normal saline. Then 20 c.cm. of concentrated globulin solution anti-meningococcus serum were injected intrathecally. Consciousness was partly regained soon afterwards.

Eight hours later lumbar puncture was repeated, and 60 c.cm. cerebro-spinal fluid were withdrawn. This was followed by saline irrigation, and the administration of 25 c.cm. antimeningococcus serum intrathecally and 20 c.cm.

intravenously. The patient was now conscious, although cerebration was slow. Temperature was 104°, pulse rate 108, respirations 26. Spasm of neck muscles had greatly relaxed.

Lumbar puncture, the withdrawal of 40 to 60 c.cm. of cerebro-spinal fluid, followed by saline irrigation of the subarachnoid space, and the administration of 20 c.cm. of antimeningococcus serum intrathecally were carried out twice daily for the first four days of illness, and then once a day for the next six days—that is, four days after the meningococcus was last isolated from the cerebro-spinal fluid. Anti-serum was also given intravenously (10 to 20 c.cm. daily) for the first four days of the disease to counteract the septicaemia.

Under this treatment the patient's temperature for the first two days oscillated between 104° and 99°, the pulse rate remained relatively low (70 to 90), and the respiratory rate was 28. From the third to eleventh day of the disease the temperature varied daily between 100° and normal, pulse rate was 80 to 90, respiratory rate was 20 to 28. On the tenth day of illness the temperature was 100°, there was a well-developed and generalized serum rash, and the larger joints ached. Adrenaline (1 in 1,000) was given subcutaneously in 1/2 c.cm. doses at four-hour intervals, but there was no amelioration of symptoms. The following day 0.125 gram contramine was injected intramuscularly; improvement occurred quickly, and the rash disappeared completely in twenty-four hours. Progress thereafter was uneventful, the patient being allowed up a fortnight later.

This case illustrates the rapid onset of the septicaemic type of cerebro-spinal fever, and the method of treating this condition by means of intrathecal lavage with saline prior to the injection of antimeningococcus serum; also the apparent influence of contramine on the late serum manifestations.

Case Illustrating Slow Recovery and Complications

C. L., aged 23 (eight weeks' service), complained on January 5th, 1931, of severe headache, pains in limbs, and sore throat. Tongue was furred, and temperature was 101°. The following morning he had a rigor; headache was worse, there was vomiting, rigidity of neck, a positive Kernig sign, and extensive purpuric eruption over trunk and limbs. He rapidly became stuporose. Lumbar puncture was performed, and the cerebro-spinal fluid was found to be under pressure and very turbid. Laboratory examination of the fluid showed a cell count of 12,800 leucocytes per c.mm., 96 per cent. of these being polymorphs, a protein content of 0.9 per cent., and the presence of numerous meningococci, both extracellular and intracellular; cultures and serological tests proved the organism to be meningococcus Type I.

For the first four days the patient was lumbar-punctured twice daily, and once a day during the next six days. Only 20 to 30 c.cm. of cerebro-spinal fluid were removed at each puncture, and then 10 to 20 c.cm. of antimeningococcus serum (globulin solution) were given intrathecally without any previous saline irrigation. In addition, small doses of the serum (10 to 20 c.cm.) were given intravenously and intramuscularly each day. In all, 160 c.cm. of cerebro-spinal fluid were removed, and 125 c.cm. of antimeningococcus serum given intrathecally, 120 c.cm. intramuscularly, and 50 c.cm. intravenously.

During this time the patient had been extremely weak, often so delirious and violent that sedatives were much required. But by the eleventh day of the disease (January 16th) the meningeal symptoms were almost nil, and the meningococcus had disappeared from the cerebro-spinal fluid. The temperature, however, was raised, and ranged between 99° and 102° for the first three weeks of the illness, the pulse rate varied between 80 and 120, and the respiratory rate between 20 and 30.

The following complications arose: suppurative arthritis of the left knee commenced on the ninth day of illness and took two weeks to subside; acute orchitis (left) began on the twelfth day of disease and resolved in ten days; acute nephritis manifested itself on the twelfth day but cleared up within three weeks; otitis media, both ears, was first noticed on the seventeenth day of illness, and persisted for ten weeks.

This case illustrates the slow recovery of a patient treated by the withdrawal of small quantities of cerebro-spinal fluid and the administration of relatively small doses of antiserum.*

The Leucocyte Count of the Blood

The total leucocyte count of the blood was increased very early in the disease to 14,000 or more per c.mm., and in the next twelve to twenty-four hours it increased rapidly to 20,000 to 40,000 per c.mm., depending on the severity of the case. After the second day, in favourable cases, the count fell rapidly to 12,000 to 15,000 per c.mm., and remained about this level for the next fortnight (see Table III). In unfavourable cases there was usually an increase in the leucocytes up to 30,000 to 50,000 per c.mm. during the second day, and thereafter there was no tendency to fall. A persistently high leucocytosis was found to coincide with a thickening and holding up of the cerebro-spinal fluid. The total white cell count proved in many instances to be a valuable aid in deciding whether further lumbar puncture was necessary.

The differential leucocyte count showed usually that 90 to 96 per cent. of the total white cells were of the polymorph variety. The Arneth index during the first four days of the disease read somewhat as follows: 5:50:30:10:5. The differential count was therefore of little clinical value.

The Cerebro-spinal Fluid

The most important characteristics of the cerebro-spinal fluid, as regards diagnosis, were the naked-eye appearance, the leucocyte and protein content, and the presence or absence of meningococci.

The naked-eye appearance and cellular content of the fluid ran parallel; thus the greater the cell content, the more opalescent was the fluid. In favourable cases the

the fluid became and remained like thick cream, while the cell content rose and remained at a high figure—50,000 or even 90,000 leucocytes per c.mm. This thick fluid tended to stagnate in the subarachnoid space, and thus complicated intrathecal medication. A differential count of the leucocytes in the cerebro-spinal fluid of these cases showed that 90 to 97 per cent. were usually of the polymorph variety.

The protein content was invariably high, ranging between 0.4 and 1.2 per cent. Even at the beginning of the disease, when the fluid was clear and the cell count was low, the protein content was found to be about 0.5 per cent., and this increased rapidly during the next twelve hours. The protein figure, prior to intrathecal serum injection, was in direct proportion to the severity of the disease; the higher the protein content, the more grave was the prognosis.

Meningococci were found in smears made from the deposit of the cerebro-spinal fluid that was withdrawn at the first puncture in every instance. At times they were very numerous, extracellular and intracellular cocci being present in every microscopical field. On other occasions they were so scanty that they were found only after prolonged search, and then they were usually extracellular: culture verified their identity. A rough estimate was made each day of the proportion of extracellular to intracellular cocci, and the finding confirmed Horder's statement referring to the intracellular position of the meningococcus—"The more marked this is, the better the outlook, and vice versa."³ The correctness of this observation was striking in two instances in which the cocci tended to remain extracellular, and yet the patients appeared to be doing well clinically; both these cases terminated abruptly in death.

The meningococcus was readily obtained in pure culture from the cerebro-spinal fluid, even of patients under

TABLE III.—*Tabular record of a severe case of cerebro-spinal fever ending in speedy recovery. This indicates the more important clinical facts that should be recorded during the treatment of a case of cerebro-spinal fever.*

Day of Disease	Temperature	Pulse Rate	Respirations	Blood. Leucocytes per c.mm.	Cerebro-spinal Fluid			Treatment			
					Amount Withdrawn c.cm.	Leucocytes per c.mm.	Meningococcus	Saline Washout c.cm.	T. c.cm.	V. c.cm.	M. c.cm.
1	104.0	100	36	23,800	45 and 60	10,800	Numerous E	160 80	20 25	— 20	5 —
2	103.0	96	20	17,600	40 and 60	26,000	Numerous EI	100 160	20 20	20 10	— —
3	100.0	72	24	12,600	50 and 45	14,800	Moderate I	95 100	20 20	— 10	— —
4	100.4	88	20	10,400	50 and 35	4,000	Few I	140 100	20 15	— —	— —
5	98.8	88	20	11,600	50	2,000	Few I	80	15	—	—
6	97.4	70	18	12,000	50	3,000	Nil	80	15	—	—
7	100.4	80	20	12,500	60	400	Nil	60	10	—	—
8	99.4	80	20	15,000	50	200	Nil	40	5	—	—
9	98.8	88	18	14,000	45	320	Nil	50	—	—	—
10	98.4	72	18	13,800	50	300	Nil	80	—	—	—
11	97.4	76	20	11,600	—	—	—	—	—	—	—
12	98.0	70	18	10,800	—	—	—	—	—	—	—

E = extracellular. I = intracellular. T = intrathecal serum injection. V = intravenous serum injection. M = intramuscular serum injection.

fluid became more opalescent and the leucocyte count rose for twenty-four to forty-eight hours (to 20,000 or 40,000 cells per c.mm.) after the first administration of serum intrathecally, but the following day the opalescence diminished distinctly and the cell count fell rapidly to less than 10,000 per c.mm., and the figure gradually became lower daily (see Table III). In some unfavourable cases, the cerebro-spinal fluid was only slightly opalescent, but contained extracellular cocci in large numbers; in others

serum treatment up to the fifth to tenth day, depending on the case. The routine procedure was to incubate the fluid as withdrawn for six to eight hours at 37° C., subculture heavily from the deposit on to blood agar slopes previously warmed to body temperature, and to incubate these at 37° C. for one to two days.

The mortality rate was 50 per cent. There were 12 cases, 6 of which ended fatally; all the deaths occurred by the fifth day of disease. This rate compares favourably with that recorded by most observers for the fulminating type of cerebro-spinal fever.

* These cases of cerebro-spinal fever were treated at the R.A.F. Infectious Diseases Hospital, Halton.

Treatment

Treatment was carried out at first along lines that had been found beneficial when dealing with previous cases of cerebro-spinal fever; antimeningococcus serum was the sheet-anchor. Unfortunately, in the recent epidemic, the meningococcus causing the infection was Type I, whereas the bulk of the therapeutic serum available in this country was made chiefly for use against Type II of the organism. It soon became evident that the antimeningococcus serum was not to be relied upon to the same extent as formerly, so that certain details of treatment that were considered previously to be of secondary importance now took pride of place. Particular attention was paid, therefore, to the adequate relief of pressure within the subarachnoid space in order to lessen its injurious effects on the nerve centres, especially those in the medulla; also to efficient irrigation of the subarachnoid space to help to remove the pus and meningococci and to aid in the circulation of the antimeningococcus serum. The question was whether the subarachnoid space should be irrigated by means of saline as advocated by Hirsch,⁴ and Aubertin and Chabanier,⁵ or by promoting the secretion of cerebro-spinal fluid, and increasing the intrathecal pressure by means of a general anaesthetic, as recommended by Flack.² After experience with both methods, the use of saline irrigation was deemed the more suitable, as this conserved the body fluids and cast no unnecessary strain upon the respiratory organs, already the seat of inflammation in most cases; in addition, the sensations of the conscious patient served as guides for both the amount and rate of fluid required to be withdrawn and injected. In two instances there was a local blockage in the subarachnoid space of such degree that after the third day of disease little fluid could be withdrawn by lumbar puncture; a general anaesthetic (ether) was given for three-quarters of an hour, the needle being left in position, and yet no more fluid could be obtained. Cistern puncture confirmed the theory of local blockage of the subarachnoid space, for the cell content of the fluid obtained by cistern puncture was roughly one hundred times less than that obtained by lumbar puncture. In such cases as these it was felt that general anaesthesia might do more harm than good.

The following routine treatment was found to give the most satisfactory results, and was adopted eventually for all definite cases of cerebro-spinal fever.

Immediately on admission to the ward 1/4 grain of morphine was given hypodermically as a sedative, and 5 c.cm. of antimeningococcus serum were injected intramuscularly into the flank to act as a desensitizing dose. By the time that the patient was cleaned (fifteen to twenty minutes) hypnosis was sufficient to permit the lumbar puncture to be undertaken. About 1/2 c.cm. of 5 per cent. novocain solution was injected intradermally over the site chosen for the lumbar puncture, usually the third interspace, and after re-washing the hands the operator made his puncture. The cerebro-spinal fluid was allowed to flow so long as it was under distinct pressure, 40 to 60 c.cm. being always drawn off, more if necessary; in some instances up to 90 c.cm. of fluid were removed with ease. In cases where the flow tended to be very rapid, the stylet was pushed partly home to lessen the rate of flow, and so more gradually lower the intracranial pressure. Relief of fluid usually made comatose patients pass into irritability, less marked when under the action of morphine; judicious handling by attendants controlled this excitability. During the above procedure 200 c.cm. of sterile normal saline were warmed to 37° C. This saline was used to irrigate the subarachnoid space. A 20 c.cm. syringe was filled with the saline and connected directly to the lumbar puncture needle, and the salt solution was injected slowly—about four to five minutes being allowed for the 20 c.cm. The stylet was inserted and the foot of the bed raised on blocks for a few minutes, then lowered, the stylet removed, and the saline allowed to drain off into a measure glass. This process was

repeated until 100 to 200 c.cm. of saline were used and the washings came away fairly clear; great care was taken throughout to see that at least as much fluid was drawn off as went in. The last washing usually consisted of a mixture of 10 c.cm. saline and 10 c.cm. antiserum. The antimeningococcus serum (globulin solution), warmed to body heat, and well shaken so as to include the deposit, the most potent portion of the serum, was then injected slowly by means of the syringe. The dosage was 20 to 40 c.cm., depending on the amount of fluid withdrawn; it was found expedient to inject considerably less serum than the amount of cerebro-spinal fluid removed, otherwise symptoms of increased intrathecal pressure manifested themselves within a few hours. Thus, if 60 c.cm. of cerebro-spinal fluid were obtained, not more than 30 c.cm. of serum were injected intrathecally. The foot of the bed was raised during the administration of the serum, and kept raised for at least two hours afterwards to facilitate gravitation of the serum towards the brain. Finally, 10 c.cm. of antimeningococcus serum were injected intravenously to counteract the septicaemia which was a prominent feature of these cases.

This procedure of lumbar puncture, saline irrigation of the subarachnoid space, and intrathecal injection of antiserum was repeated within eight hours, then given twice daily until the fourth or fifth day, and once daily for at least the next five days. The intravenous administration of serum was practised daily for the first three days only, unless the septicaemic symptoms persisted beyond that time. For two hours prior to each lumbar puncture the head of the bed was raised on blocks to aid in the gravitation of the cerebro-spinal fluid towards the lumbar region and to facilitate the withdrawal of at least 40 c.cm. of the fluid.

Calcium lactate, 10 grains, was given by the mouth thrice daily from the beginning of the treatment to try to prevent serum sickness. Contramine was given intramuscularly in a 0.125 gram dose to those patients with serum rashes; relief followed quickly, but if necessary the dose was repeated after twelve hours.

The above synopsis of treatment is given in the hope that it may be of some service to others, and to awaken constructive criticism. It may be objected that the number of cases treated was insufficient upon which to form an opinion. The number of cases was certainly few, but it should be borne in mind that although various methods of treatment were tried on several of the patients—serum of different brands in small doses, large doses, intravenously, intrathecally, combined, and so on—it was only when saline irrigation was added to the treatment that distinct improvement followed. All those engaged in treating the cases were impressed by the beneficial effects of the irrigation: there was less tendency for the cerebro-spinal fluid to thicken unduly; coma, delirium, and toxæmia disappeared rapidly; and recovery was accelerated. For an example see Case H. W. P. recorded above, also Table III. Of the six patients treated by saline irrigation, four made a safe recovery, or, in other words, the death rate was 33 per cent.; this compares favourably with the death rate of other observers when only cases of fulminating cerebro-spinal fever are considered.

Control of the Disease

General prophylactic measures applicable to the control of diseases spread by droplet infection were adopted as soon as the epidemic nature of the disease was recognized.⁶ These measures, as indicated in the beginning of this paper under the headings of history, origin, and spread of the infection, included the search for, and isolation of, contact carriers; special supervision in the spacing of beds and the efficient ventilation of barrack rooms; closure of canteen, cinema, and other places of indoor entertainment; and the disinfection of the nasopharynxes of all personnel by means of nasal douches or sprays. The efficacy of this policy was shown by the prompt termination of the epidemic within forty-eight hours of its adoption. The operation of these measures, however,

interfered greatly with the daily work of the personnel concerned, and threw a lot of extra labour on certain departments and individuals; as the need for some of these precautions was problematic, the opportunity was taken to make observations regarding their relative values for future guidance.

The search for and isolation of carriers was extended to include all the recruits and the members of the permanent staff who came into close contact with them. Wholesale swabbing of the nasopharynges of these individuals showed that carriers of the meningococcus were distributed fairly uniformly throughout all the barrack rooms—a fact that could have been prophesied in advance. The percentage of persons carrying was found to be as high as 32 at one time. This was only a relative figure for the technique used, because, with a more perfect technique and more frequent swabbings, probably many more individuals would have been found to harbour some meningococci. The fact remains that the general swabbing helped to detect the more heavily infected carriers, who were potent sources of further infection.

Prompt isolation limited their sphere of action, and this undoubtedly aided in stemming the epidemic. The isolation of all detected carriers was complete; this was considered advisable, for though simple spacing out would have limited their range of activity, the adequate supervision of scattered carriers would have been impracticable.

The spacing out of beds and efficient ventilation of barrack rooms, as normally arranged by the authorities in charge, was adequate, there being $2\frac{1}{2}$ to 3 feet between adjacent beds, so that this was not a likely factor in the spread of the infection. The inter-bed space was increased, however, to 4 feet, and, as a further precaution, the beds in each row were placed alternately head and foot towards the wall. But the problem of preventing local crowding around the fireplaces remained; this was difficult to control without constant supervision.

The canteen and cinema, well-recognized spots for local overcrowding, lived up to their reputation, especially the former. Reference to Chart 2 and the associated text supplies all the information needed on this subject. The canteen was closed on February 12th, and as a temporary measure the salespeople were permitted, at appointed times, to serve the men in the barrack rooms. The closure of the canteen proved a crucial measure in staying the epidemic.

Nasopharyngeal disinfection was applied to all personnel in the infected unit, first of all by means of a spraying chamber, latterly by nasal douching and gargling. Zinc sulphate (1 per cent. solution) was used in conjunction with Levick's steam spray, and the men were exposed to its action for fifteen minutes daily. Nasopharyngeal swabbings taken from a hundred men the day following their sixth spray treatment showed 32 per cent. to be harbouring viable meningococci—the highest carrier rate detected during the epidemic. It was suggested that this proved the efficacy of spraying, for the coryza induced by its action caused lurking germs to be discharged from their lairs in the nasal sinuses. The use of the spray chamber was discontinued, however, partly on account of the length of time necessary to pass all the personnel through it, and in part because of the danger of spreading infection when the men crowded together during the various stages of coming, going, and entering the chamber. Latterly, nasal douching was adopted instead of the spraying. The douching was carried out thrice daily for a fortnight with either a 1 in 5,000 solution of potassium permanganate or an alkaline douche which consisted of sodium bicarbonate and borax, 2 drachms of each, liquid carbolic acid, 1 drachm, sugar, $\frac{1}{2}$ ounce, water to one pint. The solution was held in the palm of the hand and sniffed up vigorously. In addition, a chlorine gargle was

given according to the following formula: potassium chlorate, 200 grains, hydrochloric acid, 40 minims, to a pint of water. This method of nasopharyngeal disinfection proved simple to administer and efficient as regards its action, as may be judged by the result obtained in the treatment of carriers.

The Treatment of Carriers.—The contact carriers were transferred to special isolation blocks at Halton, where routine treatment was carried out. They were exercised in the open and spaced out as much as possible, and thrice daily for a fortnight they practised nasopharyngeal disinfection by douching and gargling, as indicated above. At the end of a fortnight medication ceased, and nasopharyngeal swabbings were examined for the meningococcus every other day. In any case where meningococci were found to persist, treatment began all over again. Carriers were not pronounced free from infection until six consecutive swabbings proved negative to the meningococcus; 75 per cent. were found to be free from the infection within a month. For fuller details see Table I.

CONCLUSIONS

1. The recent outbreak of cerebro-spinal fever in the Royal Air Force was confined to newly joined recruits, aged between 18 and $23\frac{1}{2}$ years, and appears to have been precipitated by local overcrowding in canteen, cinema, and around barrack room fires.

2. It was not an isolated outbreak, but formed part of an epidemic spread widely over England, and the lessons learned from it can be applied to the problem as it affects the civil community, among which the incidence of this disease has of late years grown to disquieting proportions. It is suggested that the increased patronage throughout the country of cinemas with their continuous performances, cafés in preference to bars, and closed charabancs in lieu of trains play an important part in the dissemination of droplet infections, and may help to explain the increased incidence of cerebro-spinal fever.

3. The control of the disease is chiefly a matter of spacing out, so that special attention should be paid to the number of individuals gathered at one time in canteens, cafés, cinemas, and closed conveyances. The proprietors and public should be suitably warned of the danger of confined atmospheres. Barrack rooms in this country should be centrally heated to ensure efficient warmth and ventilation, without local overcrowding.

4. Nasopharyngeal disinfection by means of simple douching and gargling is efficient, and should be adopted as an additional precautionary measure, especially by those who come in contact with the sick, and by carriers. It should be persisted in for a fortnight after the last exposure to infection.

5. A general nasopharyngeal swabbing of the inmates of an infected barracks is an advisable measure, as it is a rapid method of detecting the more heavily infected and therefore dangerous carriers. Prompt action in this direction, together with adequate spacing out of personnel, should nip in the bud most epidemics of cerebro-spinal fever. Swabbing of the immediate contacts should suffice, if further cases arise.

6. Detected carriers should be isolated to limit their radius of infectivity. They should practise nasopharyngeal disinfection by douching thrice daily for at least a fortnight before swabbings are examined for the meningococcus. No carrier should be liberated unless at least six swabbings, taken on alternate days, are negative to the meningococcus. Alternatively, all carriers might be liberated at the end of six weeks without the examination of nasopharyngeal swabbings, provided they had carried out the nasopharyngeal disinfection daily during that period.

7. Early diagnosis is most important both for the sake of prevention and of cure. Most cases can be diagnosed by careful clinical examination, but a simple total leucocyte count of the blood is of material aid in the differential diagnosis between influenza and the early stages of cerebro-spinal fever.

8. The globulin content of the cerebro-spinal fluid and the position of the meningococci, whether chiefly intracellular or extracellular, are valuable prognostic guides.

9. There is a tendency to regard antimeningococcus serum as a magic cure for cerebro-spinal fever, but, although some batches of the serum have been possessed of remarkable curative powers, others have proved of little therapeutic value. This variability of potency has been noted in many epidemics, and it would appear to be due to difference in the technique of preparing the serum, also to the nature and proportion of the types of meningococci used. Thus, the recent epidemic has been caused by Type I meningococcus, whereas the polyvalent antimeningococcus serum available has been prepared chiefly against Type II of the organism. In addition, the success of the treatment depends greatly on applied physiology. The aim should be to reduce the increased intrathecal pressure to normal limits, to replace as far as practicable the purulent cerebro-spinal fluid by a bland fluid such as normal saline, and to ensure the uniform distribution of antiserum throughout the subarachnoid space. For this purpose about 60 c.cm. of cerebro-spinal fluid should be withdrawn, the subarachnoid space irrigated with 100 to 200 c.cm. of saline, and up to 30 c.cm. of antimeningococcus serum injected intrathecally, once or twice daily, until at least three days after meningococci have disappeared from the cerebro-spinal fluid. This treatment by subarachnoid lavage is not new: it is apt to be ignored, however, possibly because of the extra work entailed; but this is labour well spent, as those who care to try it will be able to testify.

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SPONDYLITIS DEFORMANS

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(With Special Plate)

This paper is based upon a clinical and radiological study of 150 cases of spondylitis of various types treated in the Devonshire Hospital during the last three years. In order to narrow down the scope all cases in which there were no obvious bony changes on x-ray examination, in spite of stiffness of the back, have been excluded, as well as cases of osteitis deformans.

The most notable investigations prior to the general use of x rays in diagnosis are those of Pierre Marie, Strümpell, and von Bechterew, with whose names certain types of spondylitis have come to be associated. It is, however, worthy of note that Dr. Bernard Connor, writing in the *Philosophical Transactions* in 1700, describes a skeleton displaying the characters of spondylitis ankylopoietica with

an exactitude that can hardly be improved upon, and deduces the clinical features of the disease.

"All these bones which naturally are separate and distinct from one another were here so straightly and intimately joyned, their ligaments perfectly bony and their articulations so effaced, they readily made but one uniform and continuous bone, so that it was as easie to break one of the vertebrae in two as to disjoyn or separate it from the other vertebrae or the os sacrum from those of the ilia. The roots of the ribs made but one equal smooth and plain superficies with the vertebrae and their apophyses. . . . The cartilaginous edge of the vertebrae themselves were turned to perfect bone. But when I had sawed two of the vertebrae asunder at the commissure I found that this uniting did not enter above two lines deep . . . their middles were separated as they usually are, and touched each other only at their edge which was raised up a little above the middle part."

It is also clear from other parts of his description and from the illustration he gives that there were no osteophytes, and that the ankylosis was due to ligamentous ossification. Hilton Fagge in 1877² described a similar case which came to necropsy, but adds the observation that there was great softening and fragility of the bones (a point of much importance also stressed by Leri³), which is a characteristic feature of this form, the "spondylose rhizomelique" of Marie and Strümpell. The type described by von Bechterew differs from that of Strümpell and Marie. Fraenkel⁴ contrasts the two types as follows:

Bechterew Type

Stiffening of the spine from above downwards, descending.

The ankylosis results in a very bent attitude; kyphosis is always present.

Nerve-root symptoms and irritation phenomena are always present.

Joints of the extremities are never involved.

Paretic condition of the muscles with slight atrophy.

Process begins as an infection of the pia spinalis.

Etiology: heredity, trauma, infection.

Marie-Strümpell Type

Stiffening of the spine from below upwards.

The ankylosis results in an erect attitude; kyphosis is seldom seen.

Nerve manifestations may be missing in some cases.

The root joints of the extremities are always, and other small joints often, ankylosed.

Atrophy of the musculature is often very pronounced.

Primary process is an ossification of the spine.

Etiology: rheumatism and infection.

The first five of these points of difference are not diagnostic, but appear to depend on the degree of severity, on the treatment of the case, and on the site at which the disease begins. The commencement as an affection of the spinal meninges is the essential difference, but much more evidence is required before it is proved that the two types are distinct. I am therefore adopting the classification of spondylitis into two main groups: spondylitis ankylopoietica or ankylosing spondylitis, which includes both the above varieties, and spondylitis osteo-arthritis, the degenerative or hypertrophic form, one of the outstanding features of which was indicated by Sir Samuel Wilks in the name which he gave it—"labourer's spine." To these may be added traumatic, tuberculous, and possibly syphilitic spondylitis.

SPONDYLITIS ANKYLOPOIETICA

As the name implies this is distinguished by its striking tendency to ankylosis of the vertebral and adjoining articulations, the end-result of which is so vividly described by Connor. Of my series sixty were of this type, and the age incidence was as follows:

Below 20	20-30	30-40	40-50	50-60	Over 60
1	17	20	15	5	2

There were six women in the series, which, so far as I am aware, is a higher proportion than has previously been