Treatment

Most patients find that phenobarbitone appreciably relieves the symptoms of dyslysis. One patient who had been given phenobarbitone for some other condition reported that, while this treatment failed to effect the improvement expected, it considerably relieved her symptoms of dyslysis. Case 7 at first improved on phenobarbitone, but relapsed later. Iron therapy for the control of anaemia relieved dyslysis in a most dramatic fashion.

Conclusion

From the physiological point of view the disturbance of relaxation of limbs described in this paper is best regarded as "inhibition of inhibition." An analogy is provided by an experiment in which a recurrently elicited knee-jerk in a cat is first inhibited by ipsilateral sensory-nerve stimulation, and later this inhibition is "inhibited" by stimulation of the bulbar reticular formation (Bach, 1950).

The following points may perhaps indicate that dyslysis is a manifestation of a raised excitatory state referable to bulbar reticular activity: (a) exceptionally high voltage of motor unit potentials were observed during minimal effort contractions; (b) pronounced susceptibility of dyslysis to the influence of lowered oxygen tension; (c) the occasional sensory precipitation of myoclonus; (d) a partial improvement obtained in most cases with phenobarbitone.

Summary

A disorder characterized by disturbed relaxation of limbs at rest is described.

Cases are divided into the following groups, in accordance with the chief clinical features: myoclonus group, pain and myoclonus group, pain group, "sleep-pain" group, and "restless legs" group.

Legs are usually, but not always, the only limbs affected in this disorder, which often shows a heredo-familial incidence and tends to have a long, fluctuating course. Myoclonus during sleep is common.

Pregnancy and anaemia greatly aggravate this condition.

During the phase of overt manifestation of symptoms, sensory precipitation of myoclonus may occur.

Differential diagnosis and treatment are discussed.

"Dyslysis" is suggested as a name for this syndrome.

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"The speed with which people grow old depends as much on social factors as it does on purely physical processes. Ageing is quickened by such things as the loss of interests due to compulsory retirement or frailty; loss of relatives and friends due to the inevitable result of living longer; loss of financial security due to a decline in income or in the value of money; loss of emotional security due to changing environment; loss of status through ceasing to be primarily a contributor to society; and loneliness. Singly or collectively, these are responsible for much of the frustration, disappointment, anxiety, depression, and unusual behaviour amongst elderly citizens."—*Notes on Mental Frailty in the Elderly*, a booklet prepared by the National Old People's Welfare Council for the guidance of those concerned with the care of the elderly. The *Notes* (price 1s.) are obtainable from the National Council of Social Service, 26, Bedford Square, London, W.C.1.

STAPHYLOCOCCAL SPINAL MENINGITIS

BY

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During the years 1949–56, 115 cases of pyogenic meningitis were admitted to the isolation ward of the Cumberland Infirmary (Table I). Comparison of the

TABLE I.—Pyogenic Meningitis, 1949–56

Type of Infection	No. of Cases	No. of Deaths
Meningococcal	61	3
Influenzal	15	1
Pneumococcal	16	3
Pyogenic. No growth on culture	16	—
Staphylococcal	7	1
Total	115	8

figures in Table I with other published series showed an unusually high incidence of staphylococcal infection. These cases presented as meningitis without any obvious local sepsis, but, because of their probable relationship to staphylococcal epidural abscess, the term "staphylococcal spinal meningitis" is used to describe them.

Literature

The first proved case of staphylococcal meningitis was described by Galippe in 1889, following suppuration of the jaw. Anthony (1892) reported the first "cryptogenic staphylococcal meningitis" in a robust soldier aged 23. Neal (1924) and MacNeal *et al.* (1943) collected small series of cases, and Teng and Meleney (1950), in an exhaustive review of the literature, recorded 88 cases with recovery.

In approximately one-third of the published cases the source of infection has been described as "haematogenous" or unknown. The infecting organism, in all but a small minority, has been a coagulase-positive *Staphylococcus aureus*, but *Staph. albus*, *Staph. citreus*, and a mixture of organisms have been incriminated. The possibility of contamination of cerebrospinal fluid (C.S.F.) samples makes evaluation of all reported cases difficult, but the criterion adopted has been the presence of staphylococci in direct smears, and their growth on culture, in cases of pyogenic meningitis.

Prior to 1932 the only successes in treatment were reported from France, where it was recognized that many of the so-called primary infections were secondary to latent spinal infection. This type of case was called "la forme rachidienne primitive," and treated by laminectomy and drainage (Sicard and Paraf, 1925; Benoit, 1929; Chavany and George, 1929). Benoit (1929) recognized the danger that lumbar puncture may precipitate generalized meningitis and cautioned against unnecessary spinal taps.

Staphylococcal bacteriophage (Schless, 1932) was given intrathecally with some benefit, and sulphonamides alone (Tolan, 1943) assisted recovery in one case, but it was the introduction of penicillin by intrathecal and intramuscular injection, used in conjunction with sulphonamides, that first gave a prospect of cure in the majority of cases (Evans, 1944; McCune and Evans, 1944; Worth, 1945; Johnson and Walker, 1945). With the emergence of penicillin-resistant strains of organism, other antibiotics have been used with success. Intrathecal and intramuscular bacitracin (Teng and Meleney, 1950; Teng, 1950), chlortetracycline (Almklov and Hansen, 1949), and intrathecal and oral chloramphenicol (Anderson and Ellis, 1951) have all been proved of value in small numbers of cases.

Because of the high incidence of spinal block in cases of staphylococcal meningitis, streptokinase-streptodornase by

intrathecal injection has been advocated by Lièvre *et al.* (1952), but results in the treatment of tuberculous meningitis make it doubtful whether there is any place for the intrathecal use of this drug.

Present Series

The present series comprises seven patients (Table II), aged 18 months to 47 years, admitted to the isolation ward of a general hospital over the period 1949–56. The immediate past history was significant in four of them, but often leading questions were needed to obtain the information.

TABLE II.—Age Incidence and Primary Site of Infection

Case	Sex	Age	Possible Primary Site of Infection
1	F	11 years	Right hip bruised 14 days before admission
2	F	11 "	Not known
3	M	1½ "	Not known. L.P. by family doctor 8 days before admission
4	F	28 "	? Left perinephric cellulitis
5	M	47 "	Boil on neck 5 weeks before admission
6	F	3 "	Bruised left thigh 7 days before admission
7	F	29 "	Not known

In Case 3 the lumbar puncture by the family practitioner eight days before admission might at first sight be blamed as the cause of the infection, as he obtained a clear fluid with a normal cell count on that occasion but the child was already ill with a stiff neck and rigid back at that time. The same sequence was seen in Case 2: an 11-year-old girl was admitted with staphylococcal septicaemia, associated with severe neck and back stiffness. Initial lumbar puncture yielded clear C.S.F. with 1 cell per c.mm., yet five days later thick staphylococcal pus was aspirated from the same interspace. Both these cases confirm Benoit's (1929) warning that in the presence of staphylococcal septicaemia the stiff back and neck may be due to epidural rather than meningeal infection, and lumbar puncture may induce a generalized meningitis.

In Case 5 the boil on the neck five weeks previously was remembered only after cross-questioning. Both Case 1, with marked bruising of the right hip 14 days before admission, and Case 6, that of a little girl who fell off her tricycle seven days before admission and bruised her left thigh, seemed to suggest the possibility of local osteomyelitis, but no clinical or radiological confirmation of this was obtained. Case 4 was of interest. A 28-year-old woman presented with a history of left lumbar pain, vomiting, and pyrexia for five days. There was tenderness and guarding in the left renal area, but no neck stiffness. Microscopy of the urine showed no excess of pus cells, but the urine was coloured golden brown with urobilinogen. There was moderate anaemia (haemoglobin 10 g./100 ml.) and polymorphonuclear leucocytosis (80% of 22,000 white blood cells per c.mm.), and a presumptive diagnosis of perinephric cellulitis was made. Three days later there was a sudden onset of neck stiffness, and lumbar puncture revealed purulent staphylococcal meningitis, with a C.S.F. protein level of 2,600 mg./100 ml. The spontaneous rupture of an epidural abscess again seemed to be the likely explanation, but an initial perinephric cellulitis could not be excluded.

Clinical Picture

The overwhelming complaint in each case was of back-ache rather than headache, which was virtually absent in three cases. A striking feature was the absence of mental clouding, disorientation, and convulsions, and the picture was that of a predominantly spinal, rather than cerebral, irritation. Fever, generalized muscular pains, vomiting, and restlessness were commonly present, but the general condition was remarkably good for such an obviously severe infection. Rigors were not recorded by any case, even in the presence of a frank septicaemia.

Physical signs in the established case were those of meningitis with neck and back rigidity, and Kernig's sign was positive. Cases 1 and 6 had some limitation of hip movement and Case 4 left renal tenderness. In no case was there local vertebral tenderness or evidence of root

irritation or cord compression. No obvious skin sepsis was present, and there was no evidence of cranial nerve involvement or papilloedema. The temperature on admission varied between 101 and 104° F. (38.3 and 40° C.), with an average of 102° F. (38.9° C.).

Blood examination showed a mild anaemia with an average haemoglobin level of 13.8 g./100 ml. in six cases, and a moderate haemolytic anaemia with haemoglobin level of 10 g./100 ml. in the seventh. There was a marked polymorphonuclear leucocytosis in each case, with white blood cell counts averaging 20,000 per c.mm., the highest being 33,700 per c.mm., but comparison with other forms of pyogenic meningitis showed that this had no real value in differential diagnosis. Blood culture was performed in five cases, and was positive for *Staph. pyogenes* in three.

In two cases normal C.S.F. was obtained on initial puncture, but in the established cases thick pus which had to be aspirated was found in four, and opalescent, xanthochromic fluid under reduced pressure in the remaining three cases (Table III). The sugar content of the C.S.F. was

TABLE III.—Initial C.S.F. Findings in Established Cases

Case	Appearance and Polymorphs (per c.mm.)	Protein mg./100 ml.	<i>Staph. pyogenes</i>	Sensitivity
1	Thick pus. Xanthochromic	900	+	Penicillin
2	" " Few drops	—	+	"
3	" " "	—	+	"
4	Clotted. Xanthochromic	2,600	+	Partial penicillin; chloramphenicol; tetracyclines
5	9,000	284	+	Penicillin
6	Thick pus. Few drops	—	+	"
7	5,000. Xanthochromic	1,950	+	"

greatly reduced in every case, but insufficient fluid was obtained in the first sample to estimate it. The organism was a coagulase-positive *Staph. aureus (pyogenes)*, and was seen in direct films and grew on culture in each case. In six cases it was fully sensitive to penicillin, the seventh being partially sensitive to penicillin and sensitive to chloramphenicol and the tetracyclines.

X-ray films of the entire spine were negative in each case, the hip-joints were clear in Cases 1 and 6, and the intravenous pyelogram was normal in Case 4. Chest x-ray films were clear in four cases. Case 1 was initially clear, and later showed a small encysted empyema. Case 2 showed the classical appearance of staphylococcal pneumonia with a small spontaneous pneumothorax, and later "soap bubble" abscesses.

Treatment

The mainstay of treatment was the combination of intrathecal and intramuscular penicillin with oral or intramuscular sulphonamides. Intrathecal penicillin, in daily doses not exceeding 15,000 units, was given for an average of 10 days. A second course of intrathecal penicillin was given in the fourth week of illness in Case 3 following a full-scale relapse, and a modified course in Case 5 when the C.S.F. picture deteriorated.

In the earlier cases intramuscular penicillin was given in doses of 100,000 units three-hourly, and later in doses of up to 1 mega-unit four- to six-hourly for at least 21 days. The sulphonamides (sulphadiazine or sulphadimidine) were given orally unless there was severe vomiting, but the initial loading dose of 2 g. was given intramuscularly. Dosage varied with age between 4 and 6 g. daily for an average of 14 days. Crystalluria was not encountered.

In addition to this routine, streptomycin, 1 g. a day, was given in Case 3 for 13 days, chlortetracycline, 1 g. a day for 17 days, in Case 5, and chloramphenicol for short periods in Case 4, and for 20 days in Case 6.

Clinical Course

There was one death (Case 7). A 29-year-old woman was admitted with a five-day history of back pain associated with stiffness of the back muscles and fever. After three

days she developed frontal headache, and on the day of admission complained for the first time of a stiff neck. On examination she was toxic and ill, with a high fever (104° F.—40° C.) and rapid pulse (148 a minute). She showed gross back and neck stiffness, but no local bone tenderness or signs of cord compression. The C.S.F. was turbid and xanthochromic under markedly reduced pressure, and examination showed 5,000 polymorphs per c.mm., protein 1,950 mg./100 ml., and sugar 35 mg./100 ml. *Staph. pyogenes* was grown from both blood and C.S.F. culture. Treatment was started at once with 10,000 units of penicillin intrathecally, 1 million units intramuscularly, 2 g. of sulphadimidine and 1 g. of streptomycin intramuscularly. Despite this she died suddenly a few hours after admission. Necropsy (Dr. J. S. Faulds) showed multiple staphylococcal lung abscesses, a small splenic abscess, and severe toxic changes in liver and heart muscle. Detailed examination of the vertebrae failed to show any obvious osteomyelitis, and there was no epidural collection of pus. The meningeal changes were marked in the spinal canal, but much less obvious at the base of the brain, and virtually absent over the vertex.

This unexpected death was all the more tragic when it was found that the staphylococcus was fully sensitive to penicillin.

In the other cases the temperature settled in 10–16 days, and the C.S.F. became sterile in three to nine days. In Case 3 relapse occurred at one month, after the temperature had been normal for a fortnight and treatment discontinued for a week. This patient responded well to a second full course of treatment. In Case 1 a small sterile empyema required aspiration, and in Case 3 staphylococcal pneumonia developed with a small left-sided spontaneous pneumothorax. Both these cleared well without residual signs. In Case 5, after one month, the patient still had a polymorphonuclear pleocytosis in the C.S.F. and continued headache, but made slow progress and recovered completely in six weeks. In Case 6 measles developed on the ninth day in hospital, but the patient suffered no more than a temporary setback.

The time in hospital varied from 23 to 60 days, with an average of 40 days. The condition on discharge was excellent and was maintained on routine follow-up.

Discussion

The predominantly spinal localization of the meningitis in this series makes the theory that this form of meningitis is secondary to epidural suppuration attractive. However, Hulme and Dott (1954) state that epidural spinal abscess follows a fairly constant pattern: (1) constant spinal ache; (2) root pain of the affected trunk; (3) impairment of cord function leading to sphincter disturbances and early motor and sensory loss; and (4) complete paralysis.

As no case in this series showed any sign of root irritation, and the one case coming to necropsy, although presenting with obvious C.S.F. loculation, had no evidence of any sizable abscess, there is no clear confirmation of this theory. Four cases did, however, develop sudden neck stiffness after a variable period of severe back pain, and in two of these the initial C.S.F. had been clear. In the absence of any obvious vertebral osteomyelitis, it seems reasonable to postulate spread from the epidural space, perhaps accelerated by lumbar puncture in two cases, as the probable explanation. Therefore it is felt that these cases should be watched closely for the earliest sign of root pain, cord compression, or localized spinal tenderness, when they should be referred to a neurosurgical clinic without delay.

The finding of so many strains of staphylococcus fully sensitive to penicillin may not be usual, and in future wide-spectrum antibiotics may cut out the need for intrathecal injections of penicillin, but the routine followed was so successful that it seems justifiable to treat penicillin-sensitive organisms along these lines in future.

Summary

Seven cases of staphylococcal spinal meningitis are described. One patient died within a few hours of admission; the remaining six made a full recovery.

The predominantly spinal localization of the meningitis is stressed and its relationship to epidural abscess discussed.

My thanks are due to Dr. J. S. Faulds, who carried out the necropsy in Case 7.

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TABLE FOR ASCERTAINING WHETHER DIFFERENCES BETWEEN PERCENTAGES ARE STATISTICALLY SIGNIFICANT

BY

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Smyth and Bainbridge (1957) suggest a scheme of tabulating data and thereby ascertaining whether any two factors concerning a group of patients are related. This they do by calculating the statistical significance of the difference between the percentage incidence (Pa) of one of the factors (a) and of the percentage incidence of both factors combined (Pab/b). The latter percentage is calculated by dividing the actual incidence of the combination of both factors (Nab) by the actual incidence of factor b—that is, Nb.

If the difference between Pa and Pab/b exceeds 1.96 times its standard error, then the difference is significant at the 5% level, and thus there are 19 chances out of 20 that the two factors are related. The standard error (S.E.) of the difference is given by:

$$S.E. = \sqrt{Pa(100 - Pa) (1/Nb - 1/N)}$$

where N = total number of patients (Yule and Kendall, 1950). It is therefore possible to tabulate values of 1.96 times the S.E. for various values of Pa and of (1/Nb - 1/N). This has been done in the accompanying table. By using this table it is possible to find whether the difference between Pa and Pab/b is significant without having to work out the S.E. When there are many such differences the table should save a considerable amount of time.

Method of Use

To use the table, the percentage incidence of each factor (Pa, etc.) should first be calculated. These are the diagonal percentages in Smyth and Bainbridge's diagram. Then (1/Nb - 1/N) = n should be calculated for each factor. This