THE BACTERIOLOGY OF BRAIN ABSCESS

BY

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This paper reports the bacteriological findings in 48 cases of brain abscess which had been referred to neurosurgical clinics. I am indebted to the surgeons of seven such clinics for sending specimens of pus and for providing data about their patients.

Details of the Cases

Sex and Age.—Of the 48 patients, 36 were male and 12 female. The ages of three were not stated; the ages of the remaining 45 ranged from 5 to 53 years, and the numbers in successive decades were 4, 8, 11, 13, 7, 2.

Site of Abscess.—Forty-two patients had a single abscess, 6 had more than one. The right side of the brain was affected in 27 cases, the left in 19, and both right and left sides in 2. Of the single abscesses 3 were cerebellar, 18 were in the frontal lobe, 5 in the parietal lobe, 15 in the temporal lobe, and 1 in the occipital lobe. In 3 cases abscesses were present in the frontal and parietal lobes, in 1 case in the frontal and temporal lobes, and in 2 cases in the temporal lobe and cerebellum.

Probable Source of Infection.—Ear disease was considered to be the source of infection in 18 cases, sinusitis in 7, lung disease in 7, trauma (penetrating injury) in 3. Staphylococcal septicaemia, subacute bacterial endocarditis, and puerperal sepsis each provided one case. In 4 cases the source of infection was unknown.

Clinical Course.—The duration of abscess symptoms was known in 47 cases; in 15 it was less than one month at the time of admission, in 22 it was between one and three months, in 6 between four and seven months, and in 4 a year or more. Information about capsule formation was available for 39 cases. In 16 of them encapsulation was demonstrated histologically. In 7 of these cases and in 18 others a definite tough or firm wall was noted at operation. Clinical observations indicated the absence of a capsule in 3 cases, and histological observations in 2 other cases. Of the 48 patients 20 were discharged from hospital—13 of them classified as "cured" or "recovered," and 7 as "improved." Four were "under treatment" at the time of the last report. Twenty-four died in hospital. In 19 of the fatal cases death resulted from the brain abscess. In 4 cases (2 of septicaemia and 2 of pulmonary infection) death was due primarily to the condition from which the brain abscess originated. In 1 case in which death was due to pulmonary embolism two healed abscesses were found in the brain at necropsy.

Technique and Results

Films of the pus were stained by Gram and Ziehl-Neelsen methods. In all cases aerobic and anaerobic cultures were made on horse-blood agar plates and in ox-serum broth. When examination suggested the need for enriched or selective media, Fildes's agar, 20% ox-serum agar, or horse-blood agar with crystal violet (1 in 500,000) or sodium azide (1 in 1,000) were used.

TABLE I.—*Organisms found in 48 Brain Abscesses. (The Pus from One Abscess showed no Organisms in Films and Cultures were Sterile)*

	Number of Times Each Organism Appeared		
	In Pure Culture (33 Cases)	With Other Organisms (14 Cases)	Total (47 Cases)
Staph. aureus	13	2	15
Strep. pneumoniae	6	—	6
P. vulgaris	2	4	6
Strep. pyogenes	4	—	4
Strep. viridans	1	1	2
Non-haemolytic streptococci	2	—	2
Anaerobic streptococci	1	9	10
Unclassified streptococci	—	3*	3
Fusiform bacilli	2	8†	10
M. tetragenus	1	—	1
Anaerobic diphtheroids	—	2	2
H. influenzae	1*	—	1
Total number of organisms	33	29	62

* Seen in films only.
† Two strains of fusiform bacilli were seen in films only.

Examination of films and cultures showed in 33 cases a single bacterial species (Table I), in 14 cases more than one species (Table II), and in one case no organisms. It is unlikely that delay in the post was responsible for any errors in the results recorded here, as many were identical with those obtained at the clinic concerned. From some abscesses several specimens were examined and the same organisms found on each occasion. Only in one traumatic abscess due to *Strep. pyogenes* did later specimens prove sterile. In studying the organisms the following points were noted.

TABLE II.—*Combinations of Organisms found in 14 Cases*

	Cases
Fusiform bacilli and anaerobic streptococci	3
" " " Strep. viridans	1
" " " unclassified streptococci	3
P. vulgaris and anaerobic streptococci	4
Anaerobic streptococci and anaerobic diphtheroids	1
Staph. aureus and anaerobic diphtheroids	1
" " anaerobic streptococci, and fusiform bacilli	1

Staph. aureus.—All 15 strains were coagulase-positive.

Strep. pneumoniae.—All 6 strains were bile-soluble. Three were Type III, two Type VII, and one Type XXI. The three Type III strains and the Type XXI strain grew only anaerobically in primary cultures.

Strep. pyogenes.—All four Group A strains were tested with Griffith's sera. One was not typed, one was Type 8, one Type 5, and one Type 2.

Strep. viridans.—The single strain gave α-lysis on horse-blood agar, was not bile-soluble, and produced no soluble haemolysin.

Non-haemolytic Streptococci.—Two strains produced no lysis on horse-blood plates and no soluble haemolysin. In primary cultures growth was more profuse anaerobically than aerobically.

Anaerobic Streptococci.—Seven strains grew on horse-blood agar as pin-point colonies after 24 or 48 hours' anaerobic incubation. No growth was obtained aerobically with liberal inocula on blood agar or in serum broth. Four of these seven strains gave no precipitation with Group A, C, or G sera. Three other strains produced small coal-black colonies on horse-blood agar after 5 days' incubation. They were apparently similar in this respect to strains isolated by Colebrook and Hare (1933) from cases of puerperal fever.

Fusiform Bacilli.—These organisms appeared in pus films as slender fusiform or diphtheroid Gram-negative bacilli. Films from cultures showed slender, beaded, Gram-negative bacilli, with some cocco-bacilli and filaments. Some strains showed many "ghost forms" and irregular swellings. No growth was obtained aerobically. No spores were seen. Three strains were killed by heating at 60° C. for 30 minutes. The colonies on horse-blood agar plates after two days' anaerobic incubation were in most cases 1 mm. in diameter, round, smooth, and low convex; but a few strains had colonies of 2 to 3 mm. diameter with a rough surface and slightly irregular edge. In serum sugars two strains produced acid and gas, and one strain acid only, in glucose, maltose, lactose, and sucrose. Mannitol and salicin were not fermented. It seemed justifiable to place these organisms in the *Fusiformis* group, but not to assign them to any particular species in it, because individual strains showed some characteristics of *F. fusiformis* and some of *F. necrophorus* (Topley and Wilson, 1937; Dack, 1940).

Anaerobic Diphtheroids.—Two strains of slender Gram-positive bacilli seen in pus films grew only anaerobically. On horse-blood agar after two days' anaerobic incubation the colonies of one strain were 1 mm. in diameter, round, smooth, and convex; the colonies of the other were 2 mm. in diameter, irregularly circular, rough, flat, and sunken in the agar. Films from cultures showed Gram-positive diphtheroid bacilli. No acid was produced in glucose, maltose, sucrose, or starch serum sugars.

Micrococcus tetragenus.—An abundant growth of this organism was obtained from one specimen of pus which showed clusters of Gram-positive cocci in films. A similar result was obtained in another laboratory which had isolated *Strep. pyogenes* and *Staph. aureus* from specimens taken some months earlier when the abscess was first aspirated. The specimens from which *M. tetragenus* was isolated were obtained at the first aspiration of a recurrence.

Some of the strains isolated were used for the production of experimental brain abscesses in rabbits (Falconer, McFarlan, and Russell, 1943).

The Commonest Organism in Brain Abscess

A comparison of the clinical data of cases collected by other authors (Evans, 1931; Atkinson, 1934) with those studied here showed that this series, though small, is a representative one. Analysis of the bacteriological findings in this series revealed no close association between the type of organism and the site of abscess or source of infection, so that the data as they stand are a fair sample for use in estimating the frequency with which various organisms are found in brain abscesses that are referred to neurosurgical clinics. Rapidly fatal cases which do not reach the neurosurgeon might give different results.

Staphylococcus aureus was isolated from 15 of 48 cases. The age distribution of 11 of the cases from which *Staph. aureus* was isolated in pure culture was 1, 2, 3, 1, 4, 1 in successive decades. Thus the organism occurred in roughly one-third of the whole series and of each age group. "Streptococci" were seen in films or

* A report to the Medical Research Council.

isolated from 21 cases, but culture showed 10 strains to be anaerobic streptococci, 4 to be *Strep. pyogenes*, 2 *Strep. viridans*, and 2 non-haemolytic streptococci. Three strains were seen only in films. Thus, although "streptococci" were common, several species were represented. Fusiform bacilli were found in 10 cases; in 7 of these they were accompanied by streptococci of one species or another, and in one case by both streptococci and staphylococci.

The commonest organism, therefore, was *Staph. aureus*. Fusiform bacilli and anaerobic streptococci came next in order of frequency. *Strep. pneumoniae*, *P. vulgaris*, and *Strep. pyogenes* were also found in several cases.

Discussion

Although staphylococci were present in 15 of the 48 cases in this series and in 14 of 27 cases reported by Alpers (1939), other authors (Hasslauer, 1907; Lund, 1926; Atkinson, 1934) found them in only a few of their cases of brain abscess. It is difficult to account for this discrepancy. The predominance of staphylococci in the present series was not due to the inclusion of cases in infants, in which staphylococci are said to be very common (Sandford, 1928). Several authors have stated that streptococci are the commonest organisms, but the results of culture in this series suggest that several species of streptococci may have been represented. It is unjustifiable to group these species together and misleading to state that streptococci are the commonest organisms in brain abscess. Fusiform bacilli and anaerobic streptococci were often found, and on several occasions pneumococci grew only anaerobically in primary cultures. It is clear that anaerobic culture is an essential part of the examination of pus from brain abscesses.

It appears from Table I that more than one species of organism was present in a large proportion of the abscesses from which anaerobic organisms were isolated. Wámoscher and von Vásárhelyi (1933) showed that the injection of agar furnished a nidus in which tetanus spores could germinate, and it is possible that the use of agar in the inoculum was responsible for the production of abscesses in rabbits' brains with anaerobic streptococci and fusiform bacilli by Falconer *et al.* (1943). It seems therefore quite probable that brain abscesses due to anaerobic organisms originate in foci of lowered O-R potential (Fildes, 1927) produced by a vascular accident or by aerobic organisms which later die out.

In this series clinical evidence of encapsulation was obtained in 5 cases two months after the onset of symptoms, and in 8 cases with three months' history. Histological examination showed well-marked fibrous walls in 2 (pneumococcal) cases with six weeks' history, in 3 cases with two months' history, and in 6 cases with three months' history. However, the clinical observations concerned the superficial part of the abscess wall, where encapsulation is more rapid than in the parts nearer the ventricle (Northfield, 1942; Falconer *et al.*, 1943). Moreover, a deeper unencapsulated loculus was present in several abscesses which had apparently been present for six months or longer. It was therefore impossible to draw any general conclusion about the time relations of capsule formation or to compare the speed of encapsulation of abscesses due to different organisms.

Of the two cases without a capsule, one in which cerebral symptoms had been present for a week was due to anaerobic streptococci, and the other, in which symptoms had been present for a fortnight, was due to *Strep. pyogenes*. It is clear that no deductions as to delay in capsule formation should be drawn from these two presumably recent abscesses. The same argument applies to the three abscesses in which the absence of a capsule was noted at operation. One of these with a fortnight's history was due to *P. vulgaris* and anaerobic streptococci, one with a three-weeks history to fusiform bacilli and anaerobic streptococci, and one with a four-weeks history to *Staph. aureus*.

There are repeated statements in the literature (Neumann, 1909; Alpers, 1939; Grant, 1941) that anaerobic and Gram-negative bacilli inhibit capsule formation. Histological examination demonstrated well-formed collagenous capsules in two cases in this series from which fusiform bacilli were isolated (in one case together with anaerobic streptococci and in the other with streptococci seen only in films). One of these cases has already been cited by Falconer *et al.* (1943), who found that encapsulation occurred in brain abscesses caused by the intracerebral inoculation of fusiform bacilli or anaerobic streptococci in rabbits. There is therefore both clinical and experimental evidence that encapsulation does occur in the presence of fusiform bacilli or anaerobic streptococci. Similarly the authors just cited showed that encapsulation occurred in experimental abscesses due to *P. vulgaris*, and well-formed capsules were found in two abscesses in this series in which *P. vulgaris* was present. These observations agree with Atkinson's (1934) statement that *P. vulgaris* is apparently not highly virulent in brain abscesses, but do not support the statement, probably derived from Lund's (1926) record of twelve fatal cases due to coliform bacilli, that Gram-negative bacilli inhibit capsule formation. Thorotrast, which favours encapsulation (Falconer *et al.*, 1943), had not been introduced into the abscesses considered here.

Summary

Specimens of pus from 48 brain abscesses were examined. Details of the cases, of the bacteriological technique, and of the organisms isolated are set out. Of the cases 33 yielded a single organism and 14 more than one species of organism. One specimen was sterile.

Staph. aureus was present in 15 cases, fusiform bacilli and anaerobic streptococci each in 10 cases. *Strep. pneumoniae*, *P. vulgaris*, and *Strep. pyogenes* each appeared in several cases. "Streptococci" were found in 21 cases, but several species were represented, and the statement that streptococci are the commonest organisms in brain abscess is misleading.

Anaerobic culture is a necessary part of the examination of pus from brain abscesses both for the isolation of obligate anaerobes and for the isolation of some strains of pneumococci.

Data concerning the encapsulation of the abscesses were not sufficient to permit any general conclusions about the rate at which the capsule is formed or the effect on that rate of the species of the infecting organism. Two abscesses from which fusiform bacilli were isolated were shown histologically to be well encapsulated, as were two abscesses from which *P. vulgaris* was isolated. These cases and some experimental studies (Falconer *et al.*, 1943) are at variance with the statement that anaerobic and Gram-negative bacilli inhibit capsule formation.

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ON THE HANDLING OF SMALL BIOPSY MATERIAL

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The increasing frequency of diagnostic biopsy, especially of the epithelium of the uterus and the respiratory tract, has prompted this description of the technical procedures used in this laboratory. First, however, it is important to state that biopsy material removed with a blunt scalpel or curette, or subjected to squeezing, tearing, crushing, or deep coagulation during removal will, no matter how good the technique of the pathologist, show nuclear changes that are characteristic of intravital trauma; it should be more widely known that these changes may make the difficulties of histological diagnosis insurmountable.

Many of the methods to be described are of long usage, and are due to predecessors or colleagues; a few are personal innovations, but all have formed an established and satisfactory routine for several years. The importance of scrupulous technique in the handling of such delicate material can scarcely be over-