OTOGENIC MENINGITIS

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MENINGITIS is gradually becoming less frequently seen as a complication of ear disease. Its incidence has been reduced by the introduction of the sulphonamides and, later of the antibiotic drugs in the treatment of otitis media. The disease remains, however, as a serious and still often fatal complication of otitis media.

Sufficient time has now elapsed to assess the results of treatment of meningitis by the sulphonamides and penicillin. Thirty-two cases of otogenic meningitis are reviewed. These were treated during the period from 1938 until 1952 that is, a period when the sulphonamides and later penicillin came into wide use in the treatment of infective conditions.

Incidence

Cawthorne (1939) stated that 67 per cent. of cases of otogenic meningitis occurred in patients under 16 years of age, but in this series only three cases (9 per cent.) occurred in children of this age. It should be pointed out, however, that these cases were observed in a department which mainly deals with adult patients.

The following figures (Table I) demonstrate that in younger patients,

TABLE I.

Age of patient	Number of cases	Type of middle-ear disease	
		Acute	Chronic
Under 10 years	3	3	0
10-20	5	4	1
20-30	3	1	2
30-40	4	1	3
40-50	10	2	8
50-60	6	2	4
Over 60	1	1	0
Total	32	14	18

meningitis is more likely to be associated with acute otitis media. In the older age groups it occurs more frequently with chronic middle-ear disease. The two age periods, when the disease was most frequent, were in the 0-20 years age group when seven out of eight complicated acute

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otitis media, and in the 40-50 years age group when eight out of ten complicated chronic otitis media.

In the eight patients under 20 years of age the sexes were equally represented. Of patients over 20 years, eighteen were male and six female. This predominance of male adult cases has been recorded previously (Stewart, 1929).

Diagnosis

In a discussion on otogenic meningitis in the Section of Otology of the Royal Society of Medicine in November, 1941, Scott Stevenson stated that the first essential was early diagnosis, the second was chemotherapy, and the third was the removal of the septic focus after chemotherapy had been started in adequate doses.

For diagnostic purposes it is most important that lumbar puncture should be carried out without delay whenever any symptoms suggestive of meningitis occur in the course of an otitis media whether it is acute or chronic. *These symptoms are:*

(1) Uneasiness and anxiety of the patient for his future.

(2) Headache, which is usually frontal but may be deep and boring in the region of the affected ear or may be occipital.

(3) Pyrexia which persists but does not fluctuate.

(4) Neck stiffness.

Drowsiness or coma and paralysis are late signs which should only be of value in assessing the extent of the disease.

In the examination of the cerebrospinal fluid the most valuable guides are the cell count and the bacteriological examination of the fluid.

The cell count can be obtained immediately whereas the biochemical analysis takes a longer time.

The bacteriological examination of the fluid includes direct film and culture of the centrifuged deposit. If a growth of organisms is obtained on culture, their sensitivity to the available antibiotics is measured.

The protein in the cerebrospinal fluid is constantly raised in the presence of meningitis.

Lowering of the glucose content is indicative of bacterial activity. In this series the average of the lowest glucose measurements in cases with a sterile cerebrospinal fluid was 50 mg. per 100 ml. In cases in which organisms were present in the cerebrospinal fluid the corresponding average was 18 mg. per 100 ml.

Watkyn Thomas (1941) has suggested that the chloride level is of prognostic value but this has not been confirmed. The average lowest chloride level in cases which recovered was 666 mg. per 100 ml. compared with 672 mg. per 100 ml. in fatal cases.

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Bacteriology of the Cerebrospinal Fluid

A feature of this series has been the high proportion of cases in which no organisms have been isolated from the cerebrospinal fluid either by direct film or culture.

In 22 cases (69 per cent.) the cerebrospinal fluid was sterile.

In 1929 (i.e. in the period before sulphonamides and antibiotics were available) Stewart in a review of 114 cases of otogenic meningitis found the cerebrospinal fluid sterile in only 8 per cent.

In Stewart's series streptococci were present in 59 per cent., in marked contrast to the present series when streptococci were found in 9 per cent. Smith, Schiller and Cairns (1946) recorded that streptococci were present in 19 per cent. of their cases which had organisms in the cerebrospinal fluid.

TABLE II.

	Stewart, 1929	Smith *et al.* 1946	Present series
	%	%	%
Pneumococcus	19	62*	16
Streptococcus	59	19	9
Staphylococcus	1	4·75	
B. proteus	7		
B. pyocyaneus			3
Streptococcus + *B. proteus* ..	3		
Pneumococcus + Proteus ..	2		
B. mucosus capsulatus	1		
Pneumococcus + Staphylococcus		4·75	
Streptococcus + Staphylococcus		4·75	
H. influenzae		4·75	
Gram – ve Bacilli (not further isolated)			3
Sterile	8		69

*Percentage of cases in which organisms were found in cerebrospinal fluid. Figures for sterile cases not given.

It was thought that the relative increase in the number of cases with a sterile cerebrospinal fluid might be due to the administration of chemotherapeutic drugs before admission to hospital. In 29 cases this information was obtained and it was found that of eighteen cases which had a sterile cerebrospinal fluid, fourteen had had no previous chemotherapy, three had been given full doses of intramuscular penicillin, and the remaining one had been given a sulphonamide drug.

Of the ten cases in which organisms were present in the cerebrospinal fluid, five had been given a sulphonamide and five had had no chemotherapy. It demonstrates that the sulphonamides cannot prevent organisms from reaching the cerebrospinal fluid. There were not sufficient cases which had been given previous penicillin to draw the conclusion that penicillin can prevent the invasion by organisms of the cerebrospinal fluid.

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The large proportion of cases with a sterile cerebrospinal fluid, even when previous chemotherapy had been given, suggests that the type of infection in recent years may be of a relatively non-invasive type.

In the present series, the average duration of meningeal symptoms before admission to hospital in cases seen before 1944 was one day. Since 1944, the average duration has been seven days. The average duration of previous meningeal symptoms has been the same whether chemotherapy has been given or not.

Of the twenty-two cases with a sterile cerebrospinal fluid, fourteen recovered; a recovery rate of 64 per cent. Of ten cases with organisms in the cerebrospinal fluid, five (50 per cent.) recovered. There is not, therefore, any marked difference in the prognosis between cases with a sterile cerebrospinal fluid and those with organisms in the fluid. There would appear to be no justification for relying upon sulphonamides alone in the treatment of cases with a sterile cerebrospinal fluid as has been suggested by some authorities.

In one of the three cases in which streptococci were isolated from the cerebrospinal fluid, meningitis was the only complication of the ear disease. In another, meningitis was associated with labyrinthitis and lateral sinus thrombosis. In the third, meningitis accompanied labyrinthitis, osteomyelitis of the petrous bone and a cerebellar abscess. This tends to confirm the suggestion that when the streptococcus is found in the cerebrospinal fluid there are likely to be other complications, particularly a brain abscess (Honer Smith *et al.*, 1946).

Chemotherapy

In the cases treated between 1938 and 1944, before penicillin was available, sulphanilamide and later sulphapyridine were used in normal doses. When these drugs could not be given orally, they were given by intramuscular or intravenous injection of the sodium salts.

When penicillin became available it was administered intrathecally in doses varying from 10,000 to 100,000 units daily. This was in addition to intramuscular injections of penicillin and the oral administration of sulphathiazole or sulphadiazine. In only one did spinal block occur, and this was in a girl, three years old, who was given 25,000 units of penicillin intrathecally daily. She developed a spinal block on the fifth day of treatment. Penicillin was given subsequently by cisternal punctures with her ultimate recovery.

Elimination of the Septic Focus

This has been the subject of much debate and in considering it, one must clearly separate cases of meningitis arising during the course of acute otitis media from those arising in chronic middle-ear disease.

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With adequate chemotherapy, most cases of acute otitis media can be cured leaving an ear free from infection.

Most cases of chronic otitis media which have been complicated by meningitis cannot be rendered safe by chemotherapy alone. An acute exacerbation may be brought under control by chemotherapy but the avenues opened up by the infection remain. With the recurrence of an acute exacerbation further complications may occur at any times. It has therefore been a general principle to perform a radical operation in those cases where the primary source of infection is a chronic suppurative otitis media.

In the cases arising from acute otitis media before penicillin was available, operation was carried out early in the disease. Of eight cases, a cortical mastoid operation was performed in three and radical mastoid operation with translabyrinthine drainage was carried out in a further three.

Since the introduction of penicillin it has not been necessary to carry out any operation other than paracentesis on cases of meningitis occurring with acute otitis media unaccompanied by mastoiditis.

Results

Before 1922 the best published results were those of Mygind who reported a recovery rate of 28 per cent.

In a series of cases of otogenic meningitis treated by either sulphonamides or penicillin between 1944 and 1947 Watson (1947) achieved a recovery rate of 84·6 per cent.

In this series thirty-two cases were treated; eighteen recovered and thirteen died, giving a recovery rate of 59 per cent.

Thirteen cases were treated by the sulphonamides alone; five recovered and eight died. This represents a recovery rate of 38 per cent.

Of the cases treated by systemic and intrathecal penicillin and systemic sulphonamides, fourteen recovered and five died giving a recovery rate of 74 per cent.

The cases which recovered on the penicillin and sulphonamide regimen included two complicated by labyrinthitis, two by tempero-sphenoidal brain abscesses and one by lateral sinus thrombosis, labyrinthitis, osteomyelitis of the petrous bone and a cerebellar abscess. Of the penicillin treated cases which died, one had a cerebellar abscess and a second had labyrinthitis and a cerebellar abscess.

The cases treated by sulphonamides alone included three complicated by labyrinthitis and two by brain abscesses. All five proved fatal.

There were four recoveries and four deaths in cases arising from acute otitis media and treated by sulphonamides alone. When penicillin was used three died and one recovered. This would suggest that, when penicillin is

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used in the treatment of acute otitis media, meningitis occurs only when the infecting organisms are resistant to it. In these circumstances, the disease tends to be of the fulminating type and death may occur in 24 to 72 hours.

When meningitis, arising in the course of a chronic otitis media, was treated by sulphonamides alone, one out of five recovered. Under the penicillin and sulphonamide regimen thirteen out of fifteen recovered.

Role of the Newer Antibiotics

In 1949, Ross, Bischoff *et al.* showed that chloramphenicol passes into the cerebrospinal fluid where it reaches a concentration of 30 to 50 per cent. of that in the blood stream.

With this information Prather and Smith (1950) treated fifteen cases of meningitis due to *H. influenzae*, using chloramphenicol with recovery in all cases. Green *et al.* (1950) and McCrumb (1951) have reported successes in similar cases.

Judge and Davis (1950) reported response with chloramphenicol orally in a case of otogenic meningitis due to *B. coli* which had failed to respond to penicillin and sodium sulphadiazine. Cutin (1951) reported a similar case and Appleton (1951) has reported one successful case of otogenic meningitis treated by chloramphenicol.

It seems likely that chloramphenicol will prove a valuable drug in the treatment of meningitis because of its wide range of activity. There is some evidence that aureomycin and terramycin may also be of value. Streptomycin is of value when organisms sensitive to it and resistant to penicillin are discovered in the cerebrospinal fluid.

The treatment of choice at present is still probably a combination of systemic and intrathecal penicillin with oral sulphadiazine. The new antibiotics will probably be reserved for cases not responding to this treatment so that information about these drugs will only gradually be accumulated. It may be that one or a combination of two or more of these drugs will give better results than those at present being achieved.

An account has been given by Garrod (1953) of the results of combining antibiotic drugs in general. Combinations may be used in urgent undiagnosed cases, in mixed infections and to prevent toxic effects. Combinations may also reduce the incidence of resistant strains as in treatment of tuberculosis by P.A.S. and streptomycin.

Combinations may result in a simple addition of the effects of the individual agents. Synergism, however, may occur. This is defined by Jawetz and Gunnison (1952) as "A large increase in the rate of early bactericidal action and in the rate of cure of infections beyond that obtainable by simple additive effects of the agents." It is well demonstrated by the treatment of *Str. fæcalis* endocarditis by penicillin and streptomycin.

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On the other hand the opposite effect, antagonism, may occur.

Jawetz and Gunnison (1952) have classified antibiotics as follows: Group 1 (bactericidal): penicillin, streptomycin, bacitracin, neomycin. Group 2 (bacteriostatic): aureomycin, chloramphenicol, terramycin.

Combinations within group 1 are often synergic. With group 2 they are no more than additive. Combination of the two groups are apt to be antagonistic. This evidence is experimental but should provide a useful guide in the choice of combinations of drugs in the treatment of infective processes.

Conclusion

The prognosis of otogenic meningitis has been completely changed by the introduction of the chemotherapeutic and antibiotic agents.

Further improvement may be achieved by treatment at an earlier stage in the disease and by the administration of the appropriate drug or combination of drugs from an ever-increasing range of antibiotics.

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