

## A Review of acute bacterial meningitis in childhood

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**ABSTRACT:** This paper reviews the epidemiology, pathogenesis and management of acute bacterial meningitis in childhood. The epidemiology of this infection has undergone significant changes with the implementation of effective immunisation, antibiotic therapy and chemoprophylaxis. The reported incidence of bacterial meningitis in children in the Maltese Islands is low compared to other countries. A high index of suspicion is required to diagnose the onset of bacterial meningitis especially in infants. Third-generation cephalosporins are currently the antibiotics of choice for the acute disease. The timely administration of penicillin may be life saving in cases of meningococcal septicaemia. Adjuvant therapy such as dexamethasone may reduce the occurrence and the severity of sequelae, in particular sensorineural hearing loss. Chemoprophylaxis with rifampicin has played an important role in curtailing epidemics of meningococcal disease. The Haemophilus influenzae type b (Hib) vaccine has made a significant impact on the incidence of H. influenzae meningitis in children. Effective vaccines against pneumococci and meningococci (type b) do not yet exist, however ongoing research seeks to produce these vaccines in an effort to emulate the successful outcome attained by the Hib vaccine.

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### Introduction

Bacterial meningitis is a common disorder of the central nervous system encountered in childhood. Unless recognised and treated early, this infective condition can result in massive destruction of the central nervous system. Moreover, sequelae of bacterial meningitis such as sensorineural hearing loss, hydrocephalus and seizures may seriously impair the development of the child.

### Incidence

The real incidence of bacterial meningitis is not known as there is substantial under-reporting<sup>1</sup>. In England & Wales approximately 1400 cases of bacterial meningitis occur in children per year giving an incidence of 3.3 per 100,000. Approximately two-thirds of these cases occur in children under 5 years of age. Until recently a large number of cases of bacterial meningitis in children were due to Haemophilus influenzae but this has dropped dramatically in the UK following the introduction of the Haemophilus influenza type b vaccine (Hib) in October 1992. This drop has in turn led to a relative increase in the percentage of meningococcal disease<sup>1</sup>. A similar shift in the causative organisms for bacterial meningitis was noted even earlier in Boston, Massachusetts since the licensure of Hib vaccine was endorsed in 1987<sup>2</sup>.

Varying incidences of bacterial meningitis are found in other parts of the world. In the U.S.A. the reported incidence is about 6 per 100,000 per year<sup>3</sup>, while in Barcelona, Spain an incidence of 24 per 100,000 has

been recorded<sup>4</sup>. In a three year study by Carroll & Carroll, a particularly high incidence of 134 cases of bacterial meningitis per 100,000 children has been found in Vanuatu in the Pacific Islands<sup>5</sup>. Increasing incidence of HIV infection may have an important impact on the future incidence of bacterial meningitis<sup>6</sup>.

The reported incidence of bacterial meningitis in the Maltese Islands is about 1.3 cases per 100,000 per year<sup>7</sup>. Figure 1 depicts the number of cases of bacterial meningitis in children in the Maltese Islands over the last 10 years<sup>7</sup>. Cases of meningococcal septicaemia during this period are also shown

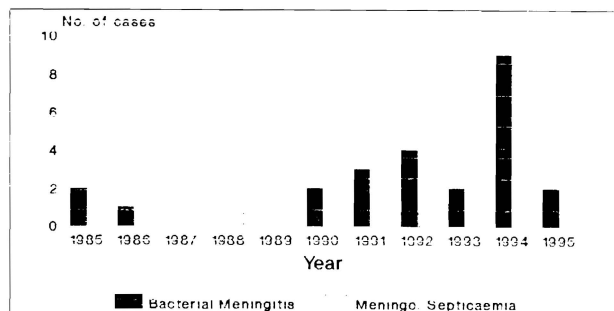


Fig 1 - Bacterial Meningitis in children in the Maltese Islands (1985 - 95)

*Source:* Department of Health, Malta

### Microbiology

Neisseria meningitidis and Haemophilus influenzae are the most common causes of bacterial meningitis in

many parts of the world. Meningitis due to *Streptococcus pneumoniae* tends to occur in children over 5 years of age. A similar microbiological pattern for bacterial meningitis is found in the Maltese Islands (Figure 2) <sup>7</sup>.

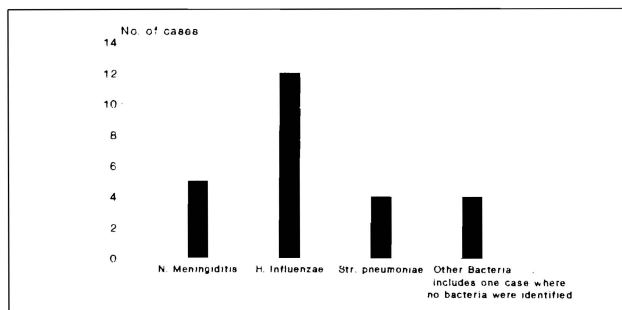


Fig 2 - Microbiology of bacterial meningitis in children in the Maltese Islands (1985 - 95)

Source: Department of Health, Malta

Other pathogens less commonly causing bacterial meningitis include: *Staphylococcus*, enteric bacteria, Group B *Streptococcus* and *Listeria*. These occur mainly in neonates, children with immunodeficiencies or following neurosurgical procedures including ventriculo-peritoneal shunts and head trauma <sup>3</sup>. Tuberculous meningitis is now a rare occurrence in developed countries.

### Pathogenesis

Most cases of acute bacterial meningitis progress through four stages: Initially, infection of the upper respiratory tract occurs. This is followed by bacterial invasion of the blood stream. If this infection is not controlled by the immune system, the blood-borne bacteria will then seed the meninges leading to an inflammation of the meninges and the intracranial structures. The brain parenchyma are inflamed and involvement of the blood vessel walls results in endothelial cell injury, vessel stenosis and thrombosis; secondary ischaemia and infarction may then occur. In the acute stage this inflammatory process may result in cerebral oedema and impaired cerebrospinal fluid flow leading to hydrocephalus <sup>8</sup>.

### Clinical features

Acute bacterial meningitis occurs when symptoms associated with the infection evolve rapidly over 1 to 24 hours. Clinically, older children can present with a variety of symptoms such as fever, general malaise, headache, neck stiffness and focal sensory and motor deficits. Seizures with fever, sometimes temperature instability and hypothermia, may be an important presenting feature of bacterial meningitis in infants, and a lumbar puncture should be considered <sup>9</sup>.

Signs of meningeal irritation such as neck stiffness, Kernig's and Brudzinski's signs, usually found in older children and adolescents, are often absent in young infants. Conversely, a bulging fontanelle and increased head circumference are common signs in this age group. Papilloedema is a late sign occurring in older children.

### Laboratory investigation

As soon as meningitis is suspected, basic information such as a complete blood count, serum electrolytes, renal function and also blood cultures should be obtained. The most important investigation is cerebrospinal fluid examination. A lumbar puncture is performed in all cases of suspected meningitis except in cases where papilloedema or focal signs are present, or when the child is deteriorating rapidly as in cases of meningococcal meningitis associated with septicaemia. In such cases, lumbar puncture may be omitted and the diagnosis based on clinical findings and blood cultures. Neuroimaging procedures (CT or MRI scans) may exclude space occupying lesion and demonstrate bone fractures which may have predisposed to the meningitis.

Usually bacterial meningitis is strongly suggested if the CSF contains a high proportion of polymorphonuclear leucocytes, a high protein and a low glucose concentration. This is, in general, a different picture from meningitis caused by other pathogens. In cases of partially treated bacterial meningitis, the results obtained may differ from the 'typical' picture mentioned above.

### Treatment

Until a few years ago, triple antibiotic therapy using Penicillin, Chloramphenicol and Sulphonamides was the standard treatment for bacterial meningitis. However, with bacteria becoming more resistant to antibiotics, third generation cephalosporins like ceftriaxone and cefotaxime are now preferred. These antibiotics penetrate the meninges effectively and quickly. Moreover, the use of third generation cephalosporins in acute bacterial meningitis appears to decrease the incidence of sequelae <sup>1</sup>. It is standard practice that as soon as meningococcal septicaemia (which may not necessarily be associated with meningitis) is suspected, an intravenous or intramuscular injection of Benzylpenicillin in high dose should be administered.

Several studies have been carried out in order to find other adjunctive therapies that significantly minimise sequelae. One such therapy is corticosteroids. The routine use of steroids with antibiotics in the treatment of bacterial meningitis remains controversial. Some studies have shown that adjunctive dexamethasone therapy improves the outcome of bacterial meningitis and recommend its use <sup>12,13</sup>. In contrast, a multicentre placebo controlled trial in the USA <sup>14</sup> concluded that dexamethasone did not significantly improve audiological, neurologic and developmental outcome in children with bacterial meningitis. Moreover, the injudicious use of corticosteroids in those with acute tuberculous meningitis can result in miliary spread of TB and death <sup>15</sup>.

Others <sup>16</sup> have investigated the possibility of giving oral Glycerol and/or IV dexamethasone to patients with bacterial meningitis <sup>16</sup>. They found that oral glycerol prevented neurologic sequelae in infants and children with bacterial meningitis more effectively than intravenous dexamethasone. The children who received oral glycerol showed less severe or profound bilateral hearing impairment than those who did not.

## Immunisation

Haemophilus influenzae type b vaccination has effectively decreased the incidence of H. influenzae meningitis<sup>1,2</sup>. This conjugate vaccine is given at the time of the standard triple vaccine. Work is currently being done on conjugate vaccines against pneumococci and meningococci.

## Antibiotic prophylaxis

Rifampicin is recommended for prophylaxis in contacts of meningococcal disease to eradicate nasopharyngeal carriage and decrease spread of the infection. In cases of Groups A and C meningococcal strains, the vaccination is recommended to at-risk individuals over 2-3 years of age.

Chemoprophylaxis is no longer recommended for contacts of patients with Haemophilus influenzae meningitis, in regions where Hib vaccination is implemented. Rifampicin prophylaxis is still given to all household contacts, if there are children under 4 years of age who have not been immunised completely or not at all.

No effective antibiotic prophylaxis is available for pneumococcal meningitis but Pneumovax can be given to contacts over 5 years of age<sup>1</sup>.

## Sequelae

The prognosis of bacterial meningitis remains rather unsatisfactory with an overall mortality of ten percent<sup>1</sup>. Long-term sequelae of meningitis result from direct inflammatory destruction of brain cells, vascular injury or secondary gliosis. Ten percent of survivors have sensorineural hearing loss, mainly due to cochlear damage. This occurs early on in the course of the disease and can lead to profound deafness<sup>10</sup>.

Seven percent of the surviving children have intractable epilepsy<sup>1</sup>. Neurological deficits such as hemiparesis, quadriplegia or blindness occur in four percent of children following bacterial meningitis<sup>10</sup>. Others may have attention deficits<sup>11</sup>, behavioural and learning difficulties and, less commonly, hydrocephalus.

## Conclusion

Acute bacterial meningitis is a curable disease and sequelae are significantly diminished if early diagnosis is made and prompt antibiotic therapy is implemented. Chemoprophylaxis is important especially in cases of meningococcal disease. Now that Hib vaccination is becoming widely available, it is expected that meningitis due to Haemophilus influenzae will continue to decrease.

Moreover, the development of effective vaccines against pneumococci and meningococci may further decrease the incidence of acute bacterial meningitis in children.

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