REVIEW

Bacterial meningitis in developing countries

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INTRODUCTION

Bacterial meningitis remains a major cause of mortality and morbidity in the developing world, despite the availability of effective antimicrobial therapy. There have been important recent developments in the diagnosis and management of meningitis, including the introduction of rapid diagnostic tests and the role of adjunct and pre-admission therapy. The introduction of the new HIB vaccine has further important implications for the management and prevention of meningitis. In this article we will be discussing what is known about the disease in developing countries, and what the impact and relevance of these developments will be to medical practice.

THE NATURE OF THE PROBLEM

It is difficult to obtain a true picture of the extent of the problem due to the lack of accurate epidemiological data from the developing world[1]. Approximately one in 250 children in Dakar, Senegal develops bacterial meningitis in the first 5 years of life, with an average incidence of 50 cases per 100 000 population[2]. A similarly high incidence of 46 cases per 100 000 population has been found in Brazil, indicating incidence rates 10-fold higher than in the US or Europe[3]. In India bacterial meningitis constitutes 1.5% of admissions to paediatric wards[4].

A common feature in countries throughout the world, is the type of pathogens responsible for the large majority of cases[5]. *Haemophilus influenzae, Streptococcus pneumoniae* and *Neisseria meningitidis* account for over 75% of all cases of bacterial meningitis, the rest comprising of a variety of organisms including Gram-negative enteric bacteria, *Staphylococcus aureus* and *Listeria monocytogenes*. Whereas *H. influenzae* is the commonest aetiological organism in the USA, and meningococcus the commonest in the UK, *S. pneumoniae* is the commonest causative organism in many developing countries, particularly in Africa, outside the meningitis belt[5–7]. The meningitis belt includes the sub-Saharan region from Eastern Sengal through to Somalia in the West. Periodic epidemics of meningococcus, usually serotype A, sweep through this belt every 8 to 12 years.

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OUTCOMES

The most worrying feature of bacterial meningitis in developing countries is the high mortality rates for this treatable disease. Overall case fatality rates varying from 33% to 44% have been reported, rising to over 60% in adult groups[3,5–7]. *S. pneumoniae* accounts for the highest mortality, and this pattern is consistent worldwide[8]. Adverse socioeconomic conditions, poor nutritional states and delays in treatment undoubtedly contribute to this high mortality, in addition to the high proportion of cases due to *S. pneumoniae*.

Although there has been a significant fall in case fatality rates in industrialized countries, the rate of occurrence of neurological sequelae following bacterial meningitis has remained constant[9]. Sequelae rates of 22–26% of survivors have been found in African studies[7,10], mostly of a neurological nature:

(i) Dizziness
(ii) Headache
(iii) Gait ataxia
(iv) Mental retardation
(v) Epileptic fits
(vi) Hearing deficits
(vii) Hemiparesis/hemiplegia
(viii) Paraparesis/paraplegia
(ix) Hydrocephalus

The incidence and nature of the sequelae are an important consideration in developing countries, where rehabilitation and support services may be limited or virtually non-existent, and the burden of handicap is therefore great.

PREDISPOSING FACTORS

A number of factors increase the risk of infection, and the rate of spread of bacterial meningitis: race; age; overcrowding; malnutrition; drought; and predisposing disease.

The higher incidence rates in developing countries is reflected to a much lesser degree in ethnic groups in industrialized countries, with rates higher among Africans than Caucasians in the USA, and in aboriginal populations in Australia[5]. It is probable that this is due in part to a racial genetic predisposition rather than solely socioeconomic factors such as living conditions, income and educational status[11].

The spread of all three major causative organisms for meningitis is favoured by overcrowding, for example in refugee camps, and malnutrition reduces host defences to infection[1]. An increase in incidence has been observed during drought and is probably related to a combination of the above factors[7].

The highest incidence of bacterial meningitis is in the very young and the old (>60 years)[5], probably related to levels of host immunity.

Susceptibility is increased by concurrent chronic or debilitating illness. Spread of infection to the meninges can occur either directly, via skull fractures or septic foci such as middle ear infections, or indirectly, secondary to septicaemia. Sickle cell disease is a particularly important factor in many developing countries, with the resultant hyposplenism predisposing to pneumococcal infection, including meningitis.

HIV AND MENINGITIS

Immunocompromised patients, such as those with lymphomas or on corticosteroids, are vulnerable to meningeal infections[11]. However, the relationship of AIDS and meningitis is less clear cut. There have been few reports of AIDS-related bacterial meningitis in the USA[12], and a recent study from Uganda found no association between HIV infection and meningococcal meningitis[13]. Stronger associations have been found between opportunistic infections, both viral (cytomegalovirus, herpes virus) and non-viral [tuberculosis (TB), *Toxoplasma gondii*, *Cryptococcus neoformans*]. However, further studies will be needed to investigate the association of HIV infection and bacterial meningitis[7,12].

DIAGNOSIS

The clinical features of meningitis are usually readily apparent except in neonates and young children. A lumbar puncture and analysis of the cerebrospinal fluid (CSF) should be performed on suspected cases unless there is suspicion of impending coning (decreasing consciousness or focal neurological signs). A turbid, yellowish CSF is highly suggestive of bacterial meningitis, and a CSF profile demonstrating >1000 leucocytes/mm^3 (with >75% neutrophils), CSF glucose of <1.9 mmol/l and protein of >1 g/l is virtually diagnostic. A Gram-stain, if positive, may indicate the causative organism, backed up with culture and sensitivity tests.

Even when facilities exist for all the above tests, in many cases no organism will be isolated, in part due to pre-admission antibiotic therapy. A correct diagnosis aids treatment and possible prevention of further spread, and serological tests including counter-immunoelectrophoresis, latex agglutination and coagglutination have been developed for rapid identification of bacterial antigens. However, the need for fairly sophisticated equipment has limited their use. A rapid enzyme immunoassay (EIA) test has been developed for use without sophisticated equipment, and appears to be both sensitive and specific[14]. The potential for use in developing countries is great; however, the cost at present would be prohibitive for general use.

TREATMENT

There has been good recent evidence of the benefit of early administration of parenteral penicillin prior to admission to hospital in patients with meningococcal disease[15]. The reduction in mortality far outweighs the inconvenience of reduced bacterial culture. Most health workers have access to parenteral penicillin, and could administer the required dose (Table 1) on initial suspicion of diagnosis, prior to referral to the nearest hospital. This is a simple measure with great potential benefit.

Standard antibiotic therapy for bacterial meningitis has consisted of penicillin in combination with chloramphenicol, to cover the three commonest causative organisms. However, chloramphenicol

Table 1. Pre-admission dosages of parenteral benzylpenicillin (preferably IV)

Age	*Dose*
Over 10 years	1200 mg
1–9 years	500 mg
Under 1 year	300 mg

alone is usually bactericidal for these organisms, and it has been shown to be as effective as the chloramphenicol/penicillin combination for treatment of children with bacterial meningitis[16,17]. The use of chloramphenicol alone is not only cheaper but more convenient: intramuscular administration is comparable with intravenous use, and can be given as a shorter course of therapy (2 or 3 days) followed by an oral course.

The use of adjunct therapy with corticosteroids in children is now commonplace in the USA and Europe. There has been encouraging evidence that the use of dexamethasone in children reduces mortality and sequelae from bacterial meningitis[18]; however, further studies are essential to judge the merit of its use. It appears reasonable to use dexamethasone, given early and in high dosage (0.15 mg/kg 6 hourly for 4 days), in those patients who are severely ill, although many doctors are using it more universally[19].

PREVENTION

Chemoprophylaxis is currently recommended for the index case prior to discharge and for household contacts. It should be given in cases of meningococcal meningitis and for meningitis from *H. influenzae* when young children are present in the household. The aim is to reduce nasopharygeal carriage and so prevent spread and progression of invasive disease. Rifampicin is effective for both (10 mg/kg twice daily for 2 days for meningococcal contacts, 20 mg/kg once daily for 4 days for haemophilus contacts, maximum 600 mg per dose) and although expensive, is generally available because of its use in TB treatment. There is concern that overuse may lead to rifampicin resistance in areas where TB is highly prevalent[1], and sulphonamides are often used as an alternative, being cheaper though less effective.

Vaccines remain the most effective preventative measure, but restricted by cost for use in developing countries. One important factor is the marked difference in age distribution of meningitis in developing countries, the majority of cases being in infants. Children less than two years old have poor immunogenic responses to current vaccines against bacterial meningitis[20]. However, the recent development and introduction of conjugate vaccines for *H. influenzae* (HIB) has led to rapid reductions in the incidence of haemophilus meningitis in many European countries.

Vaccination would be recommended in high risk groups, such as for protection of local populations in the meningitis belt from epidemics of group A or C meningococcal disease, or the use of pneumococcal vaccine in patients with homozygous sickle cell disease[1].

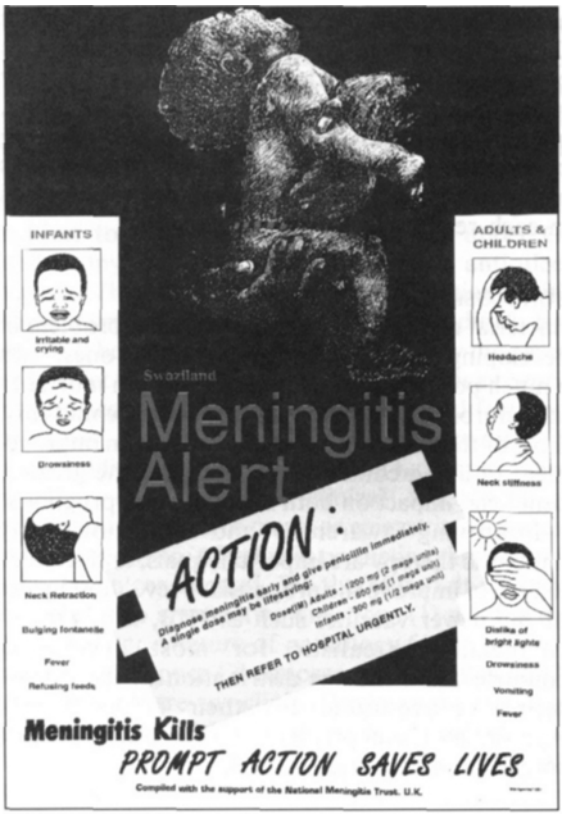

Figure 1. Meningitis alert poster

IMPROVING AWARENESS

Delay in the onset of antibiotic therapy has been associated with both increased mortality and morbidity[21]. More recent studies have found no correlation between duration of symptoms and fatality rates, but significant correlation with rates of sequelae[19,22]. This has important implications for rural populations where transport and access from rural centres to hospital is often limited. These factors and others such as initial use of traditional healing services may explain the delay in presentation that has been observed[7].

An important step in improving prognosis is to increase awareness in both health workers and the public, to encourage early hospital referral, and early antibiotic therapy. The authors attempted this while working as medical officers in Swaziland. Posters were designed and distributed to all

hospitals, health centres and outreach clinics (Figure 1). These demonstrated symptoms and signs of meningitis in both children and adults, together with an action plan of what should be done, including penicillin doses. A coordinated teaching programme for clinic and health centre nurses was also undertaken by clinic supervisors and doctors in each region.

CONCLUSION

Bacterial meningitis is a more common problem in developing countries than industrialized ones, with a much poorer outcome in terms of both mortality and morbidity. A variety of factors lie behind this, most of them socioeconomic in origin. An improvement in living conditions would have the greatest beneficial impact on both incidence and prognosis.

Improving awareness and achieving early antibiotic therapy are important goals, and steroids may help improve the prognosis. Prevention by use of the newer vaccines such as HIB, is at present financially unrealistic for most developing countries, and the age distribution of the disease seems unfavourable for their effective use. Appropriate chemoprophylaxis will, however, reduce spread on an individual level.

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