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Legacy of bacterial meningitis in infancy

Many children continue to suffer functionally important deficits

Papers p 533

The global burden of childhood bacterial meningitis is substantial. A systematic review of 36 studies from the world's developing nations estimated that there are 126 000 cases of neonatal meningitis annually, with over 50 000 deaths.[1] In these countries the major neonatal pathogens are Gram negative bacilli, such as *Escherichia coli* and *Klebsiella* species. A further recent review of almost 30 000 children and adults in 50 studies from 25 African countries found *Streptococcus pneumoniae* and *Haemophilus influenzae* type b to be the commonest causes of bacterial meningitis, with *Neisseria meningitidis* ranked third.[2] Annually there are 400 000 cases alone of *H influenzae* b meningitis in the developing world: 80% are in infants, nearly 30% die, and another 30% have major impairments.[3] Experience in the developed world suggests that even if mortality can be greatly reduced, the burden of continuing morbidity from meningitis in infancy remains high.

After the introduction of conjugate *H influenzae* b vaccines the United States has seen a 73% reduction in the incidence of paediatric bacterial meningitis, with fewer than 3000 cases each year.[4] A meta-analysis of 1602 prospectively enrolled children with bacterial meningitis from 19 studies in Europe and North America found that 4.5% died, but at least one major adverse outcome was present (severe intellectual disability, spasticity, paresis, seizures, deafness) in 16.4% of survivors.[5] The assessments were, however, limited to neurological examinations and tests of general intellectual function or hearing acuity, with review restricted to less than two years' follow up. The long term effects may thus have been underestimated, as many cognitive skills are undeveloped at the time of meningitis, and functionally important deficits may not emerge until after the child starts school.

There are few reports of the long term complications of bacterial meningitis. A Canadian study of 97 survivors of *H influenzae* b meningitis identified by chart review found that those suffering acute neurological complications (seizures, coma, focal neurological deficits, hearing loss) had poorer school performance and more behaviour difficulties than their siblings.[6] These findings were extended by a prospective cohort study from Melbourne, where 130 school aged children were assessed seven and 12 years after meningitis.[7 8] Though they achieved average scores on measures of intelligence, learning, and high level neuropsychological skills, after adjusting for sociodemographic variables these scores were consistently below those of age and grade matched controls. Only 53% of children experiencing acute neurological complications were judged as normal, while those presenting during infancy performed especially poorly on language and reading measures and complex learning tasks.[9] There were also increased behaviour problems over time, possibly from academic difficulties and low self esteem.[8] Twelve years after meningitis, 38% of patients had either major neurological, auditory, or intellectual impairments or functionally important behaviour or learning disorders impeding their academic performance. In comparison, 11% of controls had minor functional disabilities. Similar findings of cognitive and behaviour impairment have recently been observed in another prospective cohort study in which 115 survivors of meningococcal disease from Liverpool were compared 10 years after their illness with age and sex matched controls.[10]

In this week's issue Bedford et al (p 533) report the results from a questionnaire survey of parents and general practitioners about 1717 children aged 5 years who had had meningitis during infancy, together with matched controls. The children were originally identified by a prospective national study of infantile meningitis in England and Wales in 1985-7. Those who had had meningitis were at significantly greater risk of disability across all health, developmental, and behavioural categories tested, but especially in the domains of learning and neuromotor function. At greatest risk were neonates and those infected by *S pneumoniae* and Gram negative bacilli. Of concern, 2% who survived their original illness had died by the age of 5 and at least half of these deaths seemed attributable to complications of meningitis.

The strengths of this study include its prospective design, recruitment restricted to infants within a national population base, large numbers affected by different pathogens, and high retention rates. This provides future opportunities for comprehensive neuropsychometric assessments during school years and into adolescence and adulthood. Outcomes that may be clarified include the long term complications of neonatal meningitis, effects of pathogens other than *H influenzae* b, and whether higher cognitive functions, like some lower order skills, improve with maturation.[8] This should also help in understanding critical phases of postnatal brain development.

Bacterial meningitis exacts a large physical, social, and economic toll on the world's children. This is especially true in developing countries, where greater rates

BMJ 2001;323:523–4

of adverse outcomes are superimposed on poverty, other severe illness, and illiteracy.[11] Furthermore, despite advances in antibiotic treatment, the morbidity from meningitis has not improved and a role for routine steroid administration is unproved. Strategies required to reduce neonatal meningitis include improved antenatal care, aseptic techniques during labour and delivery, and promotion of breast feeding and domestic hygiene. For older children vaccination remains the only realistic hope for improvement. As disease is greatest in the young, conjugate vaccines are necessary, first with *H influenzae* b and eventually for pneumococcal and meningococcal infections. Cost is the greatest obstacle. It is sobering to consider that although conjugate *H influenzae* b immunisation leads to a 90% reduction of invasive disease, this has resulted in only a 6% decrease in cases of *H influenzae* b meningitis globally.[3] Bulk purchasing and decreased numbers of vaccine doses may help to address this disparity.[3 12] Meanwhile, even in countries able to afford conjugate vaccines there are many survivors of meningitis, most of whom are considered by their parents and peers to be normal. Nevertheless, they are at moderate risk of developmental problems associated with learning and behaviour difficulties. Doctors need not only to check vision and hearing after bacterial meningitis but also to ensure that caregivers and schoolteachers are aware of possible language deficits and problems understanding language based material. Simple educational interventions may help compensate for these deficits, improving academic performance, behaviour, and self esteem.

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1 Stoll BJ. The global impact of neonatal infection. *Clin Perinatol* 1997;24:1-21.
2 Peltola H. Burden of meningitis and other severe bacterial infections of children in Africa: implications for prevention. *Clin Infect Dis* 2001;31:64-75.
3 Peltola H. Worldwide *Haemophilus influenzae* type B disease at the beginning of the 21st century: global analysis of the disease burden 25 years after the use of the polysaccharide vaccine and a decade after the advent of conjugates. *Clin Microbiol Rev* 2000;13:302-17.
4 Schuchat A, Robinson K, Wenger JD, Harrison LH, Farley M, Reingold AL, et al. Bacterial meningitis in the United States in 1995. *N Engl J Med* 1997;337:970-6.
5 Baraff LJ, Lee SI, Schriger DL. Outcome of bacterial meningitis in children: a meta-analysis. *Pediatr Infect Dis J* 1993;12:389-94.
6 Taylor HG, Mills EL, Ciampi A, du Berger R, Watters GV, Gold R, et al. The sequelae of *Haemophilus influenzae* meningitis in school-age children. *N Engl J Med* 1990;323:1657-63.
7 Grimwood K, Anderson VA, Bond L, Catroppa C, Hore R, Keir EH, et al. Adverse outcomes of bacterial meningitis in school-age survivors. *Pediatrics* 1995;95:646-56.
8 Grimwood K, Anderson P, Anderson V, Tan L, Nolan T. Twelve year outcomes following bacterial meningitis: further evidence for persisting effects. *Arch Dis Child* 2000;83:111-6.
9 Anderson V, Bond L, Catroppa C, Grimwood K, Keir E, Nolan T. Childhood bacterial meningitis: impact of age at illness and acute medical complications on long term outcome. *JINS* 1997;3:147-58.
10 Fellick JM, Sills JA, Marzouk O, Hart CA, Cooke RWI, Thomson APJ. Neurodevelopmental outcome in meningococcal disease: a case-control study. *Arch Dis Child* 2001;85:6-11.
11 D'Angio CT, Froehlke RG, Plank GA, Meehan DJ, Aguilar CM, Lande MB, et al. Long-term outcome of *Haemophilus influenzae* meningitis in Navajo Indian children. *Arch Pediatr Adolesc Med* 1995;149:1001-8.
12 Heath PT, Booy R, Azzopardi HJ, Slack MPE, Bowen-Morris J, Griffiths H, et al. Antibody concentration and clinical protection after Hib conjugate vaccination in the United Kingdom. *JAMA* 2000;284:2334-40.

Telemedicine in developing countries

May have more impact than in developed countries

Clinical review p 557

The advent of modern communication technology has unleashed a new wave of opportunities and threats to the delivery of health services.[1] Telemedicine, a broad umbrella term for delivery of medical care at a distance, has reached around the world, and now health professionals can communicate faster, more widely, and more directly with clients and colleagues, no matter where they are.[2] Telemedicine may in fact have a more profound impact on developing countries than on developed ones.

Satellite stations in Uzbekistan, wireless connections in Cambodia, and microwave transmission in Kosova have shown that the low bandwidth internet can reach into remote areas, some of them with troubled political situations and uncertain economic environments. It has been more difficult and costly to implement broad bandwidth applications in these locations. Nevertheless, with the internet come email, websites, chatlines, multimedia presentations, and occasional opportunities for synchronous communication via internet phones and videoconferencing. Each of these communication vehicles provides an opportunity for medical education and medical care, not to mention collegial support.[3] Of course, they also provide the threat of mischief occurring within the health community, with breaches of security, inappropriate use of equipment, and engagement of terrorist tactics to reach political ends. For example, malicious hackers have been known to electronically deface websites. Threatening messages have been sent to health providers by opposing forces in some conflicts. Lack of systems support may lead to higher levels of virus and worm infections of electronic patient data.

Many physicians who travel to developing countries now take their laptops with them, or check in to internet cafes to maintain their medical contacts.[4] Although connections are sometimes unreliable, and often the practitioner needs more than a passing knowledge of communication protocols, modems, and software, it is remarkable how many locations are accessible via the internet. This connectivity allows greater flexibility in consultation, whether it is on health policy for hospitals or unique therapy for rare autoimmune diseases. For example, I have recently communicated with a visiting health professional in Cambodia who suspected a case of Henoch-Schönlein purpura (vasculitis) and sent a complete case history plus digital photographs of the lesions. The patient, living in a hill community, improved dramatically on prednisone after languishing for weeks with an undiagnosed illness. Another example of the value of the internet was the implementation of educational

BMJ 2001;323:524–5