



Early Management of Suspected Bacterial Meningitis and Meningococcal Septicaemia in Adults

R. S. Heyderman*, H. P. Lambert, I. O'Sullivan, J. M. Stuart, B. L. Taylor and R. A. Wall on behalf of The British Infection Society

Bacterial meningitis and meningococcal septicaemia are important causes of preventable morbidity and mortality in the UK. Around 900 cases of adult bacterial meningitis are reported each year, primarily caused by *Neisseria meningitidis* and *Streptococcus pneumoniae*. In addition, almost 500 adult cases of meningococcal septicaemia without meningitis are reported annually. The introduction of a meningococcal serogroup C conjugate vaccine to the UK national immunisation programme has had a dramatic impact on the number of cases of serogroup C disease *N. meningitidis* [1,2]. However, the serogroup B meningococcus is the commonest cause of bacterial meningitis in the UK and the annual numbers of serogroup B-related cases of meningococcal septicaemia have been rising recently (PHLS data). The serogroup C conjugate vaccine does not protect against serogroup B disease, and despite numerous efforts to exploit known alternative meningococcal antigens and novel antigens discovered as a result of the serogroup B genome sequencing project and immunological screening-based techniques [3–5], a specific vaccine is unlikely to be widely available in the near future. Although conjugate pneumococcal vaccines appear potent in children [6], their efficacy in preventing meningitis in older adults is unproven. It is important to recognise that any new childhood vaccination programme will not lead to a reduction in the incidence of adult disease in the short term (the extent will depend on age groups immunised and herd immunity). This may lead to an upward shift in age distribution of bacterial meningitis and meningococcal septicaemia. Clinicians will therefore need to

remain vigilant for the possibility of cases of meningitis and septicaemia.

Potential improvements in the way we identify and manage patients who may have meningitis or septicaemia have been identified for all levels of healthcare [7]. These range from awareness of the disease in the community through to the interface with primary care and emergency departments to the management by specialist paediatricians and physicians [8–12]. Such studies have focused largely on meningitis and septicaemia in childhood where the majority of cases occur. In paediatric practice, the formulation of management algorithms [13,14], targeted postgraduate training and a greater willingness to refer critically ill patients to specialist centres is thought to have had a significant impact on mortality, particularly amongst septicaemic cases [15,16]. In contrast, the mortality amongst otherwise fit young adults remains higher than amongst younger children [2,7]. Clinical management appears to vary considerably between centres.

To address this issue, in 1999 the British Infection Society (BIS) published consensus guidelines for the management of acute bacterial meningitis in immunocompetent adults [17]. Most adults with bacterial meningitis or meningococcal septicaemia present to clinicians with little experience of these conditions. Early recognition, stabilisation and institution of specific therapeutic measures are crucial to patient outcome. Although characteristic features such as fever, headache, vomiting, signs of meningeal irritation, shock, with or without a petechial rash, are easy to recognise, in the early stages, the clinical features of meningitis or meningococcal septicaemia are often non-specific and require a high index of suspicion [18,19]. Depending on whether septicaemia or meningitis predominates, the major clinical management problems may differ considerably and although patients with these conditions may appear relatively well at presentation, they may deteriorate rapidly even after commencing appropriate

*Please address all correspondence to: R. S. Heyderman, Department of Pathology and Microbiology, School of Medical Sciences, University of Bristol, University Walk, Bristol, BS8 1TD, UK. Tel.: +44 (0) 117 928 2567; Fax: +44 (0) 117 929 9162; E-mail address: r.heyderman@bristol.ac.uk (R. S. Heyderman).

antibiotics. Decisions on which and when interventions should be performed can be extremely difficult and often require early involvement of the critical care team. We have therefore formulated a management algorithm for use in emergency departments, medical admission units and medical wards which are based on the BIS consensus guidelines. The algorithm focuses specifically on minimising delays in diagnosis and administration of antibiotics, appropriate use of monitoring, investigations, critical care facilities and management of the complications of the disease, primarily shock and raised intracranial pressure. There is a strong emphasis on seeking senior advice in the context of these complications and important warning signs (see algorithm). We have also clarified when a lumbar puncture (LP) can be used safely. In recent years there has been a dramatic move away from performing LPs in patients presenting with suspected meningitis [20]. Indeed it is essential to be aware of the specific and well accepted contraindications to LP in patients with meningitis (see algorithm). In the absence of contraindications, information gained from LP may optimise management. If a LP can be performed and IV antibiotics administered within 30 min of initial assessment without compromising patient safety, a significant therapeutic delay will be avoided. LP provides confirmation of the diagnosis, yields vital data regarding aetiology and antibiotic sensitivities and provides important prognostic information [7]. Although not ideal [21], in the event that antibiotic therapy precedes LP or that LP is deferred until the patient has been stabilised, the procedure may remain diagnostic [22]. This algorithm emphasises that a CT brain scan should only be used when appropriate and that if there are no clinical contraindications to LP, a CT scan is not necessary beforehand [23]. Clinically significant raised ICP cannot be ruled out by brain CT and it is hazardous to transport patients to a CT scanner until they have been adequately stabilised [18,23,24]. A CT scan may be useful in identifying dural defects predisposing to meningitis.

When considering bacterial meningitis and meningococcal septicaemia, it is helpful to understand the essential pathogenic processes that mediate these diseases. These aspects have been comprehensively reviewed elsewhere [25–28]. It is important to recognise that this algorithm does not address meningitis and septicaemia in the immunocompromised host or the management of possible viral meningitis/encephalitis. In both cases, while some of the basic principles apply, further specialist advice will be required. New treatments for shock and meningitis are continuously emerging [29–31] and as yet their place in routine management is uncertain. For example, corticosteroid therapy for

bacterial in adults remains contentious [7,18,32]. A large multi-centre European trial of dexamethasone for adults with bacterial meningitis has recently been reported in which dexamethasone treatment was associated with a reduction in the risk of death and disability but not deafness [31]. We have recommended dexamethasone with or just before the first dose of antibiotics for bacterial meningitis, particularly where pneumococcal disease is suspected (see algorithm). It is our intention to update the algorithm on a regular basis to accommodate new evidence and new practices as they arise.

Acknowledgments

We are grateful to the following for their invaluable discussion: Professor Jon Cohen, Dr David Dance, Dr Ardiana Gjini, Ms Linda Glennie, Dr Michael Jacobs, Dr Ed Kaczmarek, Dr Clifford Leen, Dr Michael McKendrick, Dr Simon Nadel, Dr Dilip Nathwani, Dr Alistair Thomson, Dr Philip Welsby, Dr Martin Wiselka. We are grateful for the support of the Meningitis Research Foundation.

The algorithm is available as a poster or leaflet from the BIS website (www.britisheinfectionssociety.org) and the Meningitis Research Foundation website (www.meningitis.org).

References

- Balmer P, Borrow R, Miller E. Impact of meningococcal C conjugate vaccine in the UK. *J Med Microbiol* 2002; **51**: 717–122.
- <http://www.phls.co.uk/facts/Mening/index.htm>
- Pizza M, Scarlato V, Masignani V, Giuliani MM, Arico B, Comanducci M et al. Identification of vaccine candidates against serogroup B meningococcus by whole-genome sequencing. *Science* 2000; **287**: 1816–1820.
- Grifantini R, Bartolini E, Muzzi A, Draghi M, Frigimelica E, Berger J et al. Previously unrecognized vaccine candidates against group B meningococcus identified by DNA microarrays. *Nat Biotechnol* 2002; **20**: 914–921.
- Kizil G, Todd I, Atta M, Borriello SP, Ait-Tahar K, Ala'Aldeen DA. Identification and characterization of TspA, a major CD4(+) T-cell- and B-cell-stimulating Neisseria-specific antigen. *Infect Immun* 1999; **67**: 3533–3541.
- Black S, Shinefield H, Fireman B, Lewis E, Ray P, Hansen JR et al. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. Northern California Kaiser Permanente Vaccine Study Center Group. *Pediatr Infect Dis J* 2000; **19**: 187–195.
- Heyderman RS, Klein NJ. Emergency management of meningitis. *J R Soc Med* 2000; **93**: 225–229.
- Strang JR, Pugh EJ. Meningococcal infections: reducing the case fatality rate by giving penicillin before admission to hospital. *BMJ* 1992; **305**: 141–143.
- Cartwright K, Reilly S, White D, Stuart J. Early treatment with parenteral penicillin in meningococcal disease. *BMJ* 1992; **305**: 143–147.
- Riordan FA, Thomson AP, Sills JA, Hart CA. Who spots the spots? Diagnosis and treatment of early meningococcal disease in children. *BMJ* 1996; **313**: 1255–1256.
- Nadel S, Britto J, Booy R, Maconochie I, Habibi P, Levin M. Avoidable deficiencies in the delivery of health care to children with meningococcal disease. *J Accid Emerg Med* 1998; **15**: 298–303.
- Granier S, Owen P, Pill R, Jacobson L. Recognising meningococcal disease in primary care: qualitative study of how general practitioners process clinical and contextual information. *BMJ* 1998; **316**: 276–279.

- 13 Pollard AJ, Britto J, Nadel S, DeMunter C, Habibi P, Levin M. Emergency management of meningococcal disease. *Arch Dis Child* 1999; **80**: 290–296.
- 14 Hodgetts TJ, Brett A, Castle N. The early management of meningococcal disease. *J Accid Emerg Med* 1998; **15**: 72–76.
- 15 Booy R, Habibi P, Nadel S, de Munter C, Britto J, Morrison A et al. Reduction in case fatality rate from meningococcal disease associated with improved healthcare delivery. *Arch Dis Child* 2001; **85**: 386–390.
- 16 Thorburn K, Baines P, Thomson A, Hart CA. Mortality in severe meningococcal disease. *Arch Dis Child* 2001; **85**: 382–385.
- 17 Begg N, Cartwright KA, Cohen J, Kaczmarek EB, Innes JA, Leen CL et al. Consensus statement on diagnosis, investigation, treatment and prevention of acute bacterial meningitis in immunocompetent adults. British Infection Society Working Party. *J Infect* 1999; **39**: 1–15.
- 18 Durand ML, Calderwood SB, Weber DJ, Miller SI, Southwick FS, Caviness VS Jr. et al. Acute bacterial meningitis in adults. A review of 493 episodes. *N Engl J Med* 1993; **328**: 21–28.
- 19 Sigurdardottir B, Bjornsson OM, Jonsdottir KE, Erlendsdottir H, Gudmundsson S. Acute bacterial meningitis in adults. A 20-year overview. *Arch Int Med* 1997; **157**: 425–430.
- 20 Kneen R, Solomon T, Appleton R. The role of lumbar puncture in suspected CNS infection—a disappearing skill? *Arch Dis Child* 2002; **87**: 181–183.
- 21 Kanegaye JT, Soliemanzadeh P, Bradley JS. Lumbar puncture in pediatric bacterial meningitis: defining the time interval for recovery of cerebrospinal fluid pathogens after parenteral antibiotic pretreatment. *Pediatrics* 2001; **108**: 1169–1174.
- 22 Blazer S, Berant M, Alon U. Bacterial meningitis. Effect of antibiotic treatment on cerebrospinal fluid. *Am J Clin Pathol* 1983; **80**: 386–387.
- 23 Hasbun R, Abrahams J, Jekel J, Quagliarello VJ. Computed tomography of the head before lumbar puncture in adults with suspected meningitis. *N Engl J Med* 2001; **345**: 1727–1733.
- 24 Heyderman RS, Robb SA, Kendall BE, Levin M. Does computed tomography have a role in the evaluation of complicated acute bacterial meningitis in childhood? *Dev Med Child Neurol* 1992; **34**: 870–875.
- 25 van Furth AM, Roord JJ, van Furth R. Roles of proinflammatory and anti-inflammatory cytokines in pathophysiology of bacterial meningitis and effect of adjunctive therapy. *Infect Immun* 1996; **64**: 4883–4890.
- 26 Meli DN, Christen S, Leib SL, Tauber MG. Current concepts in the pathogenesis of meningitis caused by *Streptococcus pneumoniae*. *Curr Opin Infect Dis* 2002; **15**: 253–257.
- 27 Rosenstein NE, Perkins BA, Stephens DS, Popovic T, Hughes JM. Meningococcal disease. *N Engl J Med* 2001; **344**: 1378–1388.
- 28 Brandtzaeg P, van Deuren M. Current concepts in the role of the host response in *Neisseria meningitidis* septic shock. *Curr Opin Infect Dis* 2002; **15**: 247–252.
- 29 Bernard GR, Vincent JL, Laterre PF, LaRosa SP, Dhainaut JF, Lopez-Rodriguez A et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. *N Engl J Med* 2001; **344**: 699–709.
- 30 Annane D, Sebille V, Charpentier C, Bollaert PE, Francois B, Korach JM et al. Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. *Jama* 2002; **288**: 862–871.
- 31 de Gans J, van de Beek D. Dexamethasone in adults with bacterial meningitis. *N Engl J Med* 2002; **347**: 1549–1556.
- 32 Tunkel AR, Scheld WM. Corticosteroids for everyone with meningitis? *N Engl J Med* 2002; **347**: 1613–1615.