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Meningococcal disease

Emergency management of meningococcal disease: eight years on

Andrew J Pollard, Simon Nadel, Nelly Ninis, Saul N Faust, Michael Levin

Application of the new edition of the meningococcal treatment algorithm may help in the early management of critically ill patients

In 1999, our personal practice article, “Emergency management of meningococcal disease” was published in this journal and, although the journal considered publishing such personal practice statements to be unfashionable, it was mostly well received and has since been cited over 60 times.

In the original article, we proposed an algorithm for identifying management priorities in treating patients with meningococcal disease, on the basis of our experiences of 425 cases and on the available published evidence wherever possible. During, the past 8 years, over 51 000 copies of the algorithm have been disseminated to accident and emergency departments, intensive care units and paediatric units in the UK and elsewhere by the charity Meningitis Research Foundation. The algorithm has also appeared in several other articles, book chapters and a handbook for junior doctors (35 000 copies distributed and now available at http://www.meningitis.org). It has now been revised for the fifth time and the updated version is included with this perspective (fig 1). Furthermore, a version of the algorithm modified for the management of adults with meningococcal disease has been published and an interactive tool designed for education of junior doctors (see http://www.meningitis.org).

Several changes have been made since the 1999 edition of the algorithm was published. We still advocate the use of 4.5% human albumin solution as the fluid for volume resuscitation during meningococcal disease in view of the low mortality that we have observed when using this fluid. The safety of the use of albumin solution in adults has been confirmed in a recent large study, in which there was also a trend towards decreased mortality in a subgroup analysis of those with septic shock. Unfortunately, no data on the safety or efficacy of either albumin or saline exist specifically for children with meningococcal disease and further data are required before a definitive new recommendation about the use of any resuscitation fluid could be made. However, albumin solution is no longer freely available in the emergency department at some hospitals as a resuscitation fluid, so, although we remain in favour of albumin by extrapolation from the above evidence, the algorithm now specifies the use of crystalloid or alternative colloid solution when albumin is not available. We have also changed the point at which elective tracheal intubation is recommended, in recognition of recent guidelines for haemodynamic support of paediatric patients in septic shock and suggest that intubation be performed if there is persistent shock after 40–60 mls/kg of volume resuscitation have been administered, rather than the slightly more conservative 40 mls/kg figure recommended previously. However, if features of respiratory decompensation are present, emergency intubation should be undertaken immediately.

Both cuffed and uncuffed endotracheal tubes (ETTs) can be associated with tracheal injury if incorrectly used, but the use of the appropriate sized and positioned low-pressure cuffed ETTs is increasingly advocated in paediatric practice because of their advantages. Because of the potential difficulty caused in delivering sufficient tidal volume and pressure when there is a large leak around an uncuffed ETT, in meningococcal sepsis we now advise the use of a modern low-pressure cuffed ETT, when these are available, to facilitate delivery of effective ventilatory pressures. The aim of this is to reduce the need for additional airway manoeuvres in children who develop pulmonary oedema. Conversely, therefore, if a cuffed tube is not immediately available, we use an uncuffed ETT and do not advocate changing to a cuffed ETT if the airway is being successfully managed. We have also brought the seizure management recommendations in line with current paediatric guidelines and generally revised the design.

Although the approach that we have used is generally in keeping with the standard approach to the sick child, there are two areas of particular controversy: whether to undertake a lumbar puncture (LP); and the use of adjunctive therapies. We advise a cautious approach to lumbar puncture in children with meningococcal disease because of the risk of decompensation in those in shock, the possibility of coagulopathy associated with meningococcaemia and our experience of deterioration and even cerebral herniation in patients where LP had been undertaken in severe meningococcal meningitis with unrecognised raised intracranial pressure. Although the avoidance of LP in children with cardiovascular instability is widely accepted, opinions are more varied about performing LP in meningitis. Infectious Disease Society of America (IDSA) guidelines recommend LP, even in the presence of focal neurology, as long as a CT brain scan is normal. Furthermore, LP is widely performed in a tropical paediatric setting in the presence of focal neurology and without brain imaging. Nevertheless, clinical deterioration, temporally associated with LP, leaves us cautious in our approach to the use of LP in severe meningococcal disease and we concur that the CT scan does not reliably predict intracranial pressure. Furthermore, in patients with a purpuric rash, which is only rarely seen with causes of meningitis other than meningococcus, the results of the LP are unlikely to influence management. That said, we are eager to undertake LP in all patients with bacterial meningitis who do not have typical features of meningococcal disease, in the absence of recognised contraindications, in view of the importance of obtaining a microbiological diagnosis, particularly where antimicrobial-resistant pneumococci are prevalent and present an alternative aetiological diagnosis.

There are reasonable data to support the use of steroids, given with the first dose of antibiotics, to reduce the incidence of neurological sequelae caused by Haemophilus influenzae type b and pneumococcal meningitis in children and in adults, but there are no adequately powered studies to provide a definitive view in the context of meningococcal meningitis. The conclusion of a Cochrane systematic review on the use of steroids in bacterial meningitis strongly supports their use in both adults and children, irrespective of microbial aetiology. Although limited data were available for meningococcal meningitis, there was a trend towards a reduction in mortality for patients treated with steroids with this disease, mirroring the marked effects on mortality seen for Haemophilus and pneumococcal meningitis. Conversely, a study by Molyneux et al in Malawi showed no benefit of steroids in meningitis in a developing country context, creating...
Early Management of Meningococcal Disease in Children*

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<th>RECOGNITION</th>
<th>Recognition algorithm for meningococcal disease in children.</th>
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- Call consultant in A&E, Paediatrics, Anaesthesia or Intensive Care.
- Rigid initial assessment, looking for features of early shock (reduced ICP).
- Do not attempt lumbar puncture.
- IV Ceftriaxone (50mg/kg) or Ceftriaxone (50mg/kg).

- **RAISED INTRACRANIAL PRESSURE**: Decreasing or fluctuating level of consciousness.
- Hypertension and relative bradycardia.
- Unequal, dilated or poorly reacting pupils.
- Focal neurological signs.
- Abnormal posturing or reflexes.
- Papilloedema (late sign).

- **AIBC and Oxygen (10 l/min), bedside glucose**.
- Insert 2 large-bore cannula (or intra-osseous)

**VOLUME RESUSCITATION**
Balances of 20mL/kg of colloid (preferably 6% albumin) or crystalloids solutions over 5-10 minutes and review.
Repeat fluid bolus if necessary over 5-10 minutes.
Observe closely for response/deterioration.
Do not attempt lumbar puncture.

- After 40 mL to 60 mL bolus fluid resuscitation,

**STILL SIGNS OF SHOCK?**

- **WILL REQUIRE ELECTIVE INTUBATION AND VENTILATION**
Call anaesthetist and contact PICU.
- Continue boluses of 10-20 mL/kg of colloid or crystalloids with review.
- Start peripheral vasoconstrictors (Dopamine, Dobutamine).
- Nasogastric tube and urinary catheter.
- ET tube (cuffed if possible) and CXR.
- Anticipate pulmonary oedema (ensure PEEP).
- Central venous access.
- Start adrenaline infusion (central) if continuing need for volume resuscitation and periportal vasoconstrictors.

- Antidote, monitor and correct:
  - Hypoglycaemia.
  - Acidosis.
  - Hypokalaemia.
  - Hypomagnesaemia.
  - Hypocalcaemia.
  - Anaemia.
  - Coagulopathy (fresh frozen plasma: 10 mL/kg).
  - Raised intracranial pressure.

Transfer to Intensive Care
Further uncertainty about the data surrounding the use of steroids in different clinical settings. However, in view of the frequent late presentation of meningitis in less developed countries, and the different spectrum of pathogens, these data may not be relevant in the context of meningococcal disease in developed countries where there is ready access to healthcare. We continue to support the use of steroids in meningococcal meningitis in the UK, but acknowledge that opinion varies among experts on this issue. By contrast, high-dose steroids should be avoided in septic shock, but impaired adrenal gland responsiveness and diminished glucocorticoid production are often present in both adults and children with refractory septic shock, which may be aided by low-dose, replacement hydrocortisone. Further paediatric studies are needed before corticosteroid use in paediatric sepsis becomes standard practice as there is significant potential for these drugs to cause serious harm as well as benefit.

It is difficult to evaluate the direct effect of publication of this algorithm and provision of educational materials to junior doctors, on widespread paediatric practice or on the outcome of the disease. The recently published Royal College of Paediatrics and Child Health Study on the hospital management of meningococcal disease evaluated the effect of departure from the recommendations in the algorithm on outcome and found an increased risk of a fatal outcome in such cases. Although our approach has been widely disseminated through various media, we have proposed the same aggressive approach to management of the critically ill child that has become standard paediatric life support training. Data from St Mary's and from Liverpool indicate that there has been a decrease in the patient death rate associated with severe meningococcal disease over time, which we believe reflects improved early recognition and management of shock, driven by changes in clinical practice after arrival of the patient at the hospital.

Despite this improvement in outcome during the 1990s, there is no reason to be complacent about our medical management of children with this disease. A recently published nationwide UK survey of meningococcal deaths undertaken in the late 1990s identified suboptimal healthcare delivery as an important factor contributing to poor outcomes from the disease. In developing our algorithm, we recognise the difficulty in getting the patient to the starting point of the algorithm, particularly in the early stages of the illness where the clinical features are similar to those of a viral illness and signs of shock may be subtle and the rash atypical. Attempts to clarify the early signs of meningococcal disease (leg pain, cold hands and feet, and abnormal skin colour are typical signs of shock rather than of meningitis), before more recognisable features of the illness become evident, may further improve early referral to hospital by parents and general practitioners, and some have advocated the use of the Glasgow Meningococcal Septicaemia Prognostic Score in the evaluation of children with suspected meningococcal disease to aid in the recognition of signs of the disease.

Another problem for doctors in the front line is recognition of early shock. Efforts must continue to provide further evidence and education on normal values for heart rate and respiratory rate in children, to ensure that all doctors charged with the care of children are adequately trained in recognition of the sick child. When detected, tachycardia and tachypnoea are easily dismissed as the doctor may attribute these findings to fever from a viral infection (a rise of 9.5 beats/min and 2.5 breaths/min per 1°C rise in temperature occurs22–24) or the young child’s fear of the stranger. There are no evidence-based values available for abnormal vital signs, and we have used normal values in our algorithm. Consensus guidelines for defining paediatric sepsis have been published recently, which include values for tachycardia and tachypnoea produced by an expert panel, which if validated, may prove to be useful. Important signs of shock, such as cool peripheries, may be attributed to environmental temperature or assumed to reflect vasoconstriction as the temperature rises in fever and should not be overlooked. Although poor peripheral perfusion is associated with shock, parents of healthy young infants commonly express concern about the presence of cold peripheries, indicating the difficulty in using parental perceptions of peripheral temperature in the assessment of perfusion. Repeated observation of vital signs provides the possibility of excluding these confounders, since the symptoms and signs of meningococcal disease evolve progressively within a 24 h timespan. Those assessing children in emergency departments should be aware of this evolution, and that reassessment may be needed in only a few hours if new symptoms appear. Unfortunately, pressure to move patients rapidly through the emergency departments undermines our ability to provide such opportunities for observation and review.

Introduction of the serogroup C meningococcal conjugate vaccines in 1999 resulted in a significant reduction in meningococcal disease rates (fig 2), by virtually eliminating serogroup C-invasive disease and nasopharyngeal carriage. However, serogroup B and, to lesser extent, groups Y and W135 meningococci, continue to cause more than 1400 laboratory-confirmed cases of the disease each year. A further 425 children with meningococcal disease have been admitted to the paediatric intensive care unit at St Mary’s, London, UK since our algorithm was published in 1999.

A vaccine with immunogenicity against A, C, Y and W135 meningococci was launched in the US last year and is now recommended for all children aged >11 years in that country, and it is likely that quadrivalent ACYW meningococcal conjugate vaccines will also be available in the European Union before too long. However, without a serogroup B meningococcal vaccine, we are unlikely to see a further large reduction in the number of patients in the UK in the next decade.
For any doctor meningococcal disease remains a rarity, and expertise in its recognition is not common among those in the front line. However, careful assessment of all children with abnormal vital signs may lead to earlier recognition of meningococcal sepsis and application of the new edition of the meningococcal treatment algorithm described here may help in the early management of critically ill patients with meningococcal disease. We hope and believe that this approach to management of children with meningococcal disease is making a difference.

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Childhood pneumonia

Dealing with childhood pneumonia in developing countries: how can we make a difference?
Zulfiqar A Bhatta

Perspective on the paper by Hazir et al (see page 291)

The past few years have seen renewed attention focused on the persistent burden of childhood mortality globally. Of the 10.6 million deaths of children under 5 every year, the vast majority occur in a mere 42 countries of the developing world. It is also apparent that despite advances in understanding the pathophysiology and significance of the major causes of child death, most of the known killers such as diarrhoeal disorders and acute respiratory infections (ARI) still continue to take a heavy toll.1 Most of the deaths from ARI are due to pneumonia. The annual incidence of pneumonia is estimated at 151 million new cases per year, of which 11–20 million (7–13%) cases are severe enough to require hospitalisation.2 Serious neonatal infections account for 30–50% of neonatal mortality in different regions and it is difficult to disentangle sepsis and deaths from pneumonia. With the inclusion of neonatal pneumonia, recent estimates indicate that pneumonia is the single largest contributor to child mortality, accounting for almost 28–34% of all under-5 deaths globally.3 It is also important to note that in contrast to diarrhoeal deaths where mortality rates have reduced dramatically, despite the introduction of a global programme for the control of ARI almost 15 years ago, there has been little change in overall burden of deaths from pneumonia. Figure 1 shows estimates of deaths of children under 5 from pneumonia, and although recent figures represent improvements in estimates rather than increasing trends, it is evident that the global burden of deaths

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