GUIDELINES

Management of invasive meningococcal disease in children and young people: summary of SIGN guidelines

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Why read this summary?

Despite the successful introduction of immunisation with meningococcal group C conjugate vaccine in 1999,¹ invasive meningococcal disease continues to cause substantial morbidity and mortality.² Most deaths occur in the first 24 hours, often before specialist care starts. The challenge therefore is to identify those patients who will progress rapidly from non-specific early presentation to life threatening disease.³

Major changes to the organisation of health care in the United Kingdom, particularly in the provision of resuscitation and paediatric intensive care, have been associated with dramatically improved outcomes over recent decades.^{4,5} However, lack of high quality evidence to inform changes in clinical practice has been a particular challenge in developing this evidence based guideline. This article summarises the most recent guidance from the Scottish Intercollegiate Guidelines Network (SIGN) on the management of invasive meningococcal disease in children and young people.⁶

Recommendations

SIGN recommendations are based on systematic reviews of best available evidence. The strength of the evidence is graded as A, B, C, or D (fig 1), but the grading does not reflect the clinical importance of the recommendations. Recommended best practice ("good practice points"), based on the clinical experience of the guideline development group, is also indicated (as GPP).

Signs and symptoms

Invasive meningococcal disease has an early, non-specific stage with signs such as fever, lethargy, irritability, nausea, and poor feeding. These signs are commonly found in children with self limiting viral illnesses, so a confident differential diagnosis at an early stage is very difficult. Observational studies have associated leg pain, cold extremities, and abnormal skin colour with developing invasive meningococcal disease.⁷ This non-specific early stage commonly lasts for several hours before invasive meningococcal

disease progresses rapidly to three general disease patterns⁸:

- Clinical meningitis—This is characterised by fever, lethargy, vomiting, headache, photophobia, neck stiffness, and positive Kernig's sign (pain after the patient's hip is flexed 90° and the knee extended) and Brudzinski's sign (flexing the patient's neck causes flexion of the patient's hips and knees). Petechiae or purpura may also be present. Some infants and young children with meningitis display less specific features, such as poor feeding, irritability, a high pitched cry, and a full fontanelle.
- Meningococcal septicaemia—Occurring in about 20% of cases, this is characterised by fever, petechiae, purpura, and shock. This presentation is associated with poorer outcome.
- A mixed picture of septicaemia and meningitis.

Early assessment and treatment

Figure 2 and the list below outline the assessment and diagnosis of meningococcal disease in children and young people. The following points are important.

- Do not automatically exclude meningococcal disease as a potential diagnosis if young children present with non-specific symptoms such as fever, lethargy, poor feeding, nausea, vomiting, or irritability in the first four to six hours of illness (D).
- Reassess children with non-specific symptoms at initial presentation, in whom meningococcal disease cannot be excluded, within four to six hours (GPP).
- Advise carers to seek further clinical advice if the child's condition deteriorates (for example, a rash develops) before planned reassessment. Take account of local arrangements for health care.
- Consider diagnosis of invasive meningococcal disease in an ill child with the following features: fever; extremity pain; cold hands and feet; skin mottling; headache; neck stiffness; altered mental state; petechial rash (D).
- In children with symptoms or signs that are highly suggestive of meningococcal disease, do not delay treatment by interval assessment or pending

This is one of a series of BMJ summaries of new guidelines, which are based on the best available evidence; they highlight important recommendations for clinical practice, especially where uncertainty or controversy exists. Further information about the guidance, further references, and a list of members of the guideline development group are in the full version on bmj.com.

investigations (D). Administer parenteral antibiotics (out of hospital, intramuscular benzylpenicillin is widely used)⁹ and arrange urgent hospital assessment (D).

- A generalised petechial rash, beyond the distribution of the superior vena cava, or a purpuric rash in any location, in an ill child is strongly suggestive of meningococcal septicaemia—urgently treat and refer to hospital (D).

Hospital care

The absence of senior specialist input from paediatrics, anaesthesia, and intensive care—including the absence of consultant supervision during the first 24 hours in hospital—has been associated with increased mortality.¹⁰

- After arrival at hospital, children with suspected invasive meningococcal disease should be reviewed and treated promptly by a senior and experienced clinician (D).
- Discuss management of children with progressive invasive meningococcal disease with staff in the paediatric intensive care unit at an early stage (D).

Confirming the diagnosis

- To confirm the diagnosis in all children with suspected invasive meningococcal disease, take blood for culture (D) and polymerase chain reaction (C) as soon as possible after admission to hospital; however, this should not delay treatment.⁹

The grade of recommendation relates to the strength of the supporting evidence on which the evidence is based. It does not reflect the clinical importance of the recommendation

A • At least one high quality meta-analysis, systematic review of randomised controlled trials, or randomised controlled trial with a very low risk of bias and directly applicable to the target population; or

• A body of evidence consisting principally of well conducted meta-analyses, systematic reviews of randomised controlled trials, or randomised controlled trials with a low risk of bias directly applicable to the target population, and demonstrating overall consistency of results

B • A body of evidence including studies rated as high quality systematic reviews of case-control or cohort studies, and high quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target population, and with overall consistency of results; or

• Extrapolated evidence from studies described in A

C • A body of evidence including well conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target population and with overall consistency of results; or

• Extrapolated evidence from studies described in B

D • Non-analytic studies, such as case reports, case series, expert opinion; or

• Extrapolated evidence from studies described in C

Good Practice Points (GPP)

☒ Recommended best practice based on the clinical experience of the guideline development group

- In patients with suspected invasive meningococcal disease and features of septicaemia, lumbar puncture is not recommended in the initial assessment. It may be considered later if there is diagnostic uncertainty and unsatisfactory clinical progress and if there are no contraindications such as coagulopathy, low platelets, cardiovascular instability, or neurological concerns (GPP).
- In patients with clinical meningitis without features of septicaemia (purpura), do lumbar puncture if there are no contraindications (D).

Treatment

Intravenous fluids—Consensus exists for the use of early, aggressive intravenous fluid therapy in adults and children diagnosed with invasive meningococcal disease in whom there are signs of shock.

- If signs of shock are present, administer a rapid infusion of intravenous fluids as isotonic crystalloid or colloid solution up to 60 ml/kg, given as three boluses of 20 ml/kg, with reassessment after each bolus (B).
- Fluid resuscitation in excess of 60 ml/kg (B), plus inotropic support (D), is often required.
- Evidence of circulatory failure and the need for repeated intravenous fluid boluses should prompt early consultation with intensive care as inotropic and ventilatory support may be required (GPP).

Antibiotics—Administer as follows:

- Administer intravenous cefotaxime as initial treatment for previously well children aged over 3 months and diagnosed with invasive meningococcal disease (B).
- Once daily ceftriaxone monotherapy may be substituted if parenteral agents containing calcium (such as intravenous calcium, parenteral nutrition, or Hartmann's solution) have not been used in the preceding 48 hours (GPP). This is a precaution following reports of fatal interactions in neonates.
- When parenteral antibiotics are indicated for infants aged less than 3 months, administer cefotaxime plus an antibiotic active against listeria (such as ampicillin or amoxicillin; GPP).
- In children with invasive meningococcal disease, antibiotic treatment should last seven days, assuming satisfactory clinical progress (GPP).

Corticosteroids—Administer as follows:

- Steroids are not recommended for treating children with meningococcal septicaemia (B) except in the case of inotrope-resistant shock.
- In children starting empirical treatment for bacterial meningitis of unknown aetiology (A) or in children with confirmed meningococcal meningitis (B), administer parenteral dexamethasone (0.15 mg/kg every six hours) with, or within 24 hours of, the first antibiotic dose, and continue for four days.

Intensive care—Take the following action:

- For patients who continue to deteriorate despite appropriate supportive treatment, arrange transfer to paediatric intensive care (D).

Fig 1 | Explanation of SIGN grades of recommendations

- For children with fluid-resistant shock, consider early ventilatory support after inotropes are started (GPP).
- Before and during intubation, consider volume loading. Use anaesthetic agents that maintain cardiovascular stability (D).
- In children with refractory hypotension (inotrope-resistant shock) intravenous vasopressin and steroid dose titration are appropriate rescue strategies (GPP).
- For children with inotrope-dependent septic shock, severe metabolic acidosis, acute or impending renal failure, and complex or problematic fluid balance, consider continuous venovenous haemofiltration (GPP).

Prevention of secondary transmission

Liaise with the local public health department to ensure appropriate public health actions.

- Chemoprophylaxis with some antibiotics (ciprofloxacin, rifampicin, minocycline, ampicillin) has been found to be effective. Offer prophylaxis to those who have had prolonged close contact in a household setting with a child with meningococcal disease during the seven days before onset of illness (C). Close contacts are defined as those living or sleeping in the same household (including extended household); pupils in the same dormitory; boyfriends and girlfriends; and university students sharing a kitchen in a hall of residence.⁹

- In isolated cases of meningococcal disease, prophylaxis is not indicated for pupils in the same nursery, school, or class as a child diagnosed with meningococcal disease, unless they are a close contact (D).
- Before discharge from hospital, offer meningococcal C vaccine (D).

Follow-up care

Consider the following potential morbidities (C), depending on the individual case severity, and manage accordingly.

- Hearing loss.
- Neurological complications.
- Psychiatric, psychosocial and behavioural problems.
- Bone and joint complications (such as discrepancy in leg length), with awareness that these may not be apparent for many years after illness.
- Post-necrotic scarring with possible requirements for amputations and skin grafting.
- Renal impairment, particularly in those who required acute renal replacement therapy.
- Potential for post-traumatic stress disorder in both the children and their families.

Overcoming barriers

In primary care, the challenge is to discriminate the few children with early meningococcal disease from the many with self limiting viral illnesses. The recent guideline from the National Institute for Health and Clinical Excellence (NICE) may help in the preschool age group.¹¹ Postgraduate training programmes for primary care practitioners should include specific education in the recognition and early management of seriously ill children. In secondary care, such children should be reviewed by a senior paediatrician shortly after arrival in hospital. Patients needing intensive or high dependency care should receive support from a multidisciplinary team with input from anaesthetics and intensive care staff, ideally coordinated by a lead consultant in acute paediatrics. For critically ill children, there should be early dialogue with the regional paediatric intensive care unit, with a remit to advise on early management and provide a dedicated transfer team when necessary.

The interface between primary, secondary, and paediatric intensive care requires clearly defined lines of communication at senior level and would benefit from regular feedback and teaching (such as critical care outreach study days). Further improvements in outcome will depend on the quality of care at all three levels and, importantly, on the interface between them.

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Fig 2 | Assessment and diagnosis of invasive meningococcal disease in children and young people

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- 2 Health Protection Agency. *Enhanced surveillance of meningococcal disease national annual report: July 2002-June 2003*. London: HPA, 2003.
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- 5 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;85:386-90.
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Commentary: Controversies in SIGN guidance on management of invasive meningococcal disease in children and young people

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It is a moot point whether clinical practice guidelines are of more value if the evidence is strong, rather than weak. Guidelines based on strong evidence may simply reinforce existing knowledge. On the other hand, guidelines based on weak evidence may reassure the clinician, but be of questionable value to the patient. The authors of the guidelines from the Scottish Intercollegiate Guidelines Network (SIGN) claim to be the first to systematically scrutinise the literature to produce evidence based guidelines on recognition and management of meningococcal disease in children, while admitting elsewhere that their task was hampered by a lack of high quality evidence. Any guidelines are only of value if they improve care. With meningococcal infection this means improving mortality and morbidity, which are readily measurable.

A major controversy in childhood meningococcal infection is that the improvement in outcome in UK specialist centres (the case fatality rate at one paediatric intensive care unit fell from 23% in 1992 to 2% in 1997¹) has not been reflected in an overall fall in mortality nationally.^{2,3} The fall in mortality in paediatric intensive care units has been attributed to improved initial management at referring centres, improved transport using specialised mobile intensive care teams, and improved management in centralised units.¹

Why has national mortality not fallen? Interventions that may improve the outcome of children with meningococcal infection include earlier diagnosis and treatment, earlier referral to specialist centres, and improved management.

Early diagnosis and treatment

Diagnosis should be relatively straightforward if the child has fever and a classic non-blanching petechial or purpuric rash. However, as stated in the SIGN guidelines, children may present early with non-specific

symptoms, often to their general practitioner. Half of all children with meningococcal disease are sent home at first presentation, illustrating the importance of the SIGN recommendation for reassessment of children with non-specific febrile illness.⁴ Major diagnostic pitfalls include children with meningococcal infection who present with fever, diarrhoea, and/or vomiting but without rash, leading to a misdiagnosis of gastroenteritis, and children who present with a blanching rash, resulting in a misdiagnosis of viral infection.^{4,5}

A case-control study comparing hospital based care of children who died from meningococcal disease with survivors found three factors independently associated with an increased risk of death: failure to be looked after by a paediatrician, failure of sufficient supervision of junior staff, and failure of staff to administer adequate inotropes.⁵ An experienced clinician is better than any tests in assessing febrile children for serious illness.⁶ Better frontline recognition by nurses and doctors is essential to better national figures.

The guidelines recommend the use of antibiotics before admission to hospital, a practice that is widely advocated and makes good commonsense but lacks supportive evidence because a randomised controlled trial would be considered unethical, and observational studies are extremely subject to bias.

Specialist care

The SIGN guidelines recommend that children with suspected meningococcal infection should be reviewed and treated promptly by a senior and experienced clinician and that those with progressive invasive meningococcal disease should also be discussed early with staff from paediatric intensive care. However, the mortality from meningococcal infection in specialist paediatric intensive care units is now lower than the overall mortality in children.¹⁻³ This could be the result