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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

of selection bias (the sickest children might die before reaching one of these units), but the recent dramatic improvement in outcome in paediatric intensive care units¹ implies that it is the result of improved care and that early referral to such a unit would be likely to improve mortality.

Hospital treatment

The SIGN guidelines emphasise the need for vigorous fluid resuscitation and early intubation, for which there is no good evidence but strong consensus. For fluid-resistant shock, inotropes are recommended on the basis of case-control findings of an association between inadequate inotropes and worse outcome.⁵ The SIGN recommendation to use a third generation cephalosporin to treat meningococcal infection, rather than the narrower spectrum antibiotic benzylpenicillin, is not explained but is unlikely to affect outcome.

The SIGN guidelines represent a laudable attempt to improve management. We lack high level evidence on which interventions are most likely to improve outcome, and future randomised controlled trials of interventions would be invaluable. Apart from primary prevention, major advances in improving the outcome of childhood meningococcal infection in the UK seem

most likely to follow system changes to improve supervision of junior doctors in emergency departments, good access to experienced paediatricians, and early referral to specialist centres.⁵

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LESSON OF THE WEEK

Unrecognised severe vitamin D deficiency

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Vitamin D deficiency remains common and may mimic other musculoskeletal disorders or mental health problems

Since Glisson gave the first authoritative description of rickets in 1650 and McCollum and coworkers described its cause as vitamin D deficiency in 1922,¹ clinical descriptions of hypovitaminosis D have become more variable, making the condition less recognisable.² At the same time, the condition remains highly prevalent world wide, yet is preventable.³ We present two cases of longstanding undiagnosed severe vitamin D deficiency with important clinical consequences.

Case reports

Case 1

A 53 year old woman of Pakistani origin underwent mastectomy for invasive ductal carcinoma of the right breast with adjuvant radiotherapy and tamoxifen treatment. Over the next two years she presented at her follow-up appointments with migratory musculoskeletal pains, including pain in the right arm, loin, right posterior chest with bony tenderness and whole

body discomfort. A chest x ray showed an irregularity of the upper cortex of the right posterolateral seventh rib. An isotope bone scan showed multiple areas of increased radionuclide uptake in the ribs and left sacroiliac joint. We made a working diagnosis of metastatic bone disease and started the aromatase inhibitor anastrozole and the oral bisphosphonate sodium clodronate.

Over the next six months her pains worsened, and areas of tenderness in the arms, legs, ribs, and left sacroiliac joint were poorly controlled by cocodamol. A repeat bone scan showed no change (fig 1). A poor prognosis was given and combination chemotherapy (adriamycin, taxotene) was planned, but first she took a six week summer trip to Pakistan to visit family. On her return to the United Kingdom, her symptoms had completely resolved. A whole body computed tomography scan showed a pelvic stress fracture but no evidence of visceral metastasis. Chemotherapy was delayed.

Her symptoms relapsed during winter and spring. When pain in the left lateral ribs and right hip worsened, she was switched to a second line aromatase inhibitor, exemestane. She was also given an intravenous infusion of the aminobisphosphonate pamidronate 90 mg, after which she acutely developed distal