• Abdominal pain
• Alcohol poisoning
• Analgesia
• Anaphylaxis
• Antibiotics
• APLS - recognition and assessment of the sick child
• Apparent life threatening events (ALTE)
• Arthritis
• Asthma – acute management
• Bites
• Blood and platelet transfusions
• Bronchiolitis
• Cervical lymphadenopathy
• Child protection
• Constipation
• Croup
• Cyanotic congenital heart disease
• Cystic fibrosis
• Diabetes and fasting
• Diabetes new (non-ketotic)
• Diabetic ketoacidosis
• Diarrhoea and vomiting
• ECG interpretation
• Endocarditis prophylaxis
• Epilepsy
• Facial palsy
• Failure to thrive
• Febrile neutropenia
• Fever
• Glasgow coma score
• Glomerulonephritis
• Haemolytic uraemic syndrome
• Haemophilia
• Heart failure and weak pulses
• Henoch-Schönlein purpura
• Hepatitis
• HIV and hepatitis B post-exposure prophylaxis (PEP)
• HIV infection testing
• Hypertension
• Hypoglycaemia
• Immune thrombocytopenic purpura (ITP)
• Immunodeficiency
• Intraosseous infusion
• Iron poisoning
• IV Fluid therapy
• Jaundice
• Kawasaki disease
• Ketone monitoring
• Limping child
• Long line insertion
• Malaria
• Meningitis
• Nephrotic syndrome
• Notifiable infectious diseases and food poisoning
• Nutritional first line advice
• Orbital cellulitis
• Osteomyelitis and septic arthritis
• Pain assessment
• Paracetamol poisoning
• Petechial/purpuric rashes
• Pleural effusion
• Pneumonia
• Pneumothorax
• Poisoning and drug overdose
• Post GA monitoring ex-premature infants
• Pre-op fasting
• Renal calculi
• Renal failure
• Renal investigations
• Salicylate poisoning
• Sedation
• Septicaemia (including meningococcal)
• Status epilepticus
• Steroid dependence
• Tachycardia and bradycardia
• Tricyclic poisoning
• Tuberculosis
• Urinary tract infection
• **Vitamin D deficiency**
**ABDOMINAL PAIN IN CHILDHOOD**

**Supporting information**

**What is the value of the abdominal x-ray in the diagnosis of acute abdominal pain?**

Ultrasonography has been recommended by US sources as the most useful diagnostic tool in this situation for some years, principally for its precision and avoidance of the use of ionising radiation (Sivit, 2004; Sivit, 1997). Abdominal x-ray is advised primarily when small bowel obstruction or perforation is suspected (Sivit, 1997). European sources have tended to be more conservative, advocating that ultrasonography (and to a lesser extent CT) be reserved for equivocal cases (van den Broek, 2004). Others, however, agree with the US view that that ultrasonography is more likely to reveal the underlying cause of pain than plain film radiography (Hayes, 2004; Rosendahl, 2004).

It has been suggested that chest x-ray should always be performed before abdominal x-ray, as pneumonia is frequently the cause of abdominal pain and vomiting in children with less than obvious signs of pulmonary disease (John, 1999).

A study in 2,427 children with suspected acute appendicitis (Even-Bendahan, 2003) found that ultrasound diagnosis halved the misdiagnosis rate from 13.2% to 6.5%, saving unnecessary surgery and identifying other conditions that mimic appendicitis. Abdominal x-ray was not advised in this study.

A retrospective review of 449 patient records of children having abdominal radiography (Rovira, 2005) found that the results were helpful in the diagnosis of less than half the cases that needed surgical intervention. The authors concluded that "Plain abdominal radiograph is of little value in the diagnosis of acute abdominal pain in children".


**Evidence Level: V**

**How specific is abdominal pain in the diagnosis of appendicitis?**

A number of scoring systems have been developed in an attempt to improve the diagnosis of appendicitis (Bailey, 2007; Kharbanda, 2005; Samuel, 2002; Alvarado, 1986). Common to all of them is the localisation of tenderness to the right lower quadrant, migration of pain, and rebound tenderness/pain with percussion (all P<0.001).

Inclusion of these three pain-related signs resulted in a specificity of 0.72-0.92.


Evidence Level: V

Does the administration of analgesia impede diagnosis?
A randomised, double-blind, placebo-controlled trial in 108 children (Green, 2005) allocated 52 to receive iv morphine and 56 to receive a placebo saline solution. The reduction in the mean pain score was significantly greater in the morphine group (2.2 vs 1.2 cm) and the clinical staff reported that confidence in their diagnosis was not affected by the administration of morphine.
Another randomised, placebo-controlled trial in 90 children (Bailey, 2007) found that the use of morphine (0.1 mg/kg) did not delay the decision to perform surgery, but also was no more effective than placebo at diminishing pain 30 minutes after administration.


Evidence Level: II

Last amended November 2007
At what rate does serum ethanol decline in the paediatric age range?
In a study in 39 patients from 6 weeks to 17 years (mean 14.6 years of age (Simon, 1994),
initial serum ethanol levels ranged from 13.7 to 84.2 mmol/L (63-388 mg/dL) and the mean
serum ethanol clearance rate was 4.0 mmol/L/hr (18.6 mg/dL/hr), consistent with clearance
rates previously reported for adults. The authors concluded that there was no age-related
difference in serum ethanol clearance rates.

Simon HK, Cox JM, Sucov A, et al. Serum ethanol clearance in intoxicated children and
adolescents presenting to the ED. Acad Emerg Med 1994;1:520-4

Evidence Level: IV

Last amended March 2011
Diclofenac is a suitable alternative to ibuprofen or codeine in the treatment of moderate pain?

A Cochrane systematic review of 86 studies (Standing, 2009) found that, compared with placebo/no treatment, diclofenac significantly reduced need for post-operative rescue analgesia (RR 0.6; NNT 3.6; 95% CI 2.5 to 6.3). Compared with any other non-NSAID, patients receiving diclofenac suffered less nausea or vomiting, or both (RR 0.6; NNT 7.7 [5.3 to 14.3]). There appeared to be no increase in bleeding requiring surgical intervention in patients receiving diclofenac in the peri-operative period. Serious diclofenac adverse reactions occurred in fewer than 0.24% of children treated for acute pain. The authors concluded that “Diclofenac is an effective analgesic for perioperative acute pain in children.”


Evidence Level: I

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:

NICE. Anaphylaxis: Assessment to confirm an anaphylactic episode and the decision to refer after emergency treatment for a suspected anaphylactic episode. London: NICE, 2011


Last amended November 2012
The oral route of administration is preferred where possible?
A Cochrane systematic review of 2 studies (Rojas-Reyes, 2006) concluded that: “Oral therapy appears to be an effective and safe alternative to parenteral antibiotics in hospitalised children with severe pneumonia who do not have any serious signs or symptoms.” In the 2 studies under consideration, Campbell 1988 compared oral co-trimoxazole versus intramuscular procaine penicillin followed by oral ampicillin in 134 children. At the seventh day of follow up, treatment failure occurred in 6/66 (9.1%) in the oral co-trimoxazole group and 7/68 (10.2%) in the combined-treatment group. The risk difference was -0.01% (95% CI -0.11 to 0.09). The APPIS Group 2004 evaluated 1702 patients comparing oral amoxicillin versus intravenous penicillin for two days followed by oral amoxicillin. After 48 hours, treatment failure occurred in 161/845 (19%) in the amoxicillin group and 167/857 (19%) in the parenteral penicillin group. The risk difference was -0.4% (95% CI -4.2 to 3.3). The authors reported similar recovery in both groups at 5 and 14 days.


Evidence Level: I

What constitutes an appropriate regimen for community acquired pneumonia (CAP)?
A Cochrane systematic review of 27 studies in a total of 11,928 children (Kabra, 2010) compared multiple antibiotics with each other but not with placebo. For ambulatory treatment of non-severe CAP, amoxicillin compared with co-trimoxazole had similar failure rates (OR 0.92; 95% CI 0.58 to 1.47) and cure rates (OR 1.12; 95% CI 0.61 to 2.03). (Three studies involved 3952 children). In children hospitalised with severe CAP, oral amoxicillin compared with injectable penicillin or ampicillin had similar failure rates (OR 0.95; 95% CI 0.78 to 1.15). (Three studies involved 3942 children). Relapse rates were similar in the two groups (OR 1.28; 95% CI 0.34 to 4.82). In very severe CAP, death rates were higher in children receiving chloramphenicol compared to those receiving penicillin/ampicillin plus gentamicin (OR 1.25; 95% CI 0.76 to 2.07). (One study involved 1116 children).

The authors concluded that: “For treatment of ambulatory patients with CAP, amoxicillin is an alternative to co-trimoxazole. With limited data on other antibiotics, co-amoxiclavulanic acid and cefpodoxime may be alternative second-line drugs. For severe pneumonia without hypoxia, oral amoxicillin may be an alternative to injectable penicillin in hospitalised children; however, for ambulatory treatment of such patients with oral antibiotics, more studies in community settings are required. For children hospitalised with severe and very severe CAP, penicillin/ampicillin plus gentamicin is superior to chloramphenicol. The other alternative drugs for such patients are ceftriaxone, levofloxacin, co-amoxiclavulanic acid and cefuroxime. Until more studies are available, these can be used as a second-line therapy.


Evidence Level: I
The weight of children aged 1-10 yr is best estimated by using the formula “Weight (kg) = 3 x (age in yrs + 7)”?

A retrospective study in 17,244 children aged 1-10 yr (Luscombe, 2007) studied the weight difference between measured weight and expected weight, estimated using the formula “Weight (kg) = 2 x (age in yrs + 4)”, which was the accepted method at the time. This was found to underestimate true weight by a mean of 18.8% (95% CI 18.42% – 19.18%). The authors tested 10 new formulae, of which “Weight (kg) = 3 x (age in yrs + 7)” proved the most accurate, with a mean underestimate of 2.48% (95% CI 2.17% – 2.79%).


Evidence Level: III

Last amended July 2010
APPARENT LIFE THREATENING EVENT (ALTE)  
Supporting information

This guideline and supporting information has been prepared with reference to the following:


http://www.springerlink.com/content/4kwI8acxhnyvxpnf/fulltext.pdf

What are the most common causes of ALTEs?
A systematic review of 8 studies involving 643 infants aged 0-13 months (McGovern, 2004) found 728 diagnoses assigned overall. Some infants had multiple diagnoses. The most common diagnoses were gastro-oesophageal reflux (n = 227), seizure (n = 83), lower respiratory tract infection (n = 58), and "unknown" (n = 169). Five deaths were noted in total.


Evidence Level: I

Skeletal survey is indicated in the further investigation of cases involving possible abuse?
A retrospective, descriptive study of 703 skeletal surveys (Duffy, 2011) found a total of 10.8% of the surveys yielded positive results. Children <6 months of age, children with an apparent life-threatening event or seizure, and children with suspected abusive head trauma had the highest rates of positive results. Of children with positive results, 79% had >=1 healing fracture. The authors concluded that, as 50% of the positive results directly influenced a diagnosis of abuse, broader use of these surveys may be justified.


Evidence Level: IV

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:


In suspected juvenile idiopathic arthritis (JIA), chronic anterior uveitis can be asymptomatic initially but may progress to irreversible loss of vision if referral is delayed? “Uveitis, which occurs in 5-20% of (jia) patients, most commonly in the oligoarticular subtype, can be asymptomatic and can lead to cataracts and even blindness” (Foster, 2003).

Foster CS. Diagnosis and treatment of juvenile idiopathic arthritis-associated uveitis. Curr Opin. Ophthalmol 2003;14:395-8

Evidence Level: V
Routine arterial blood gas (ABG) testing does not alter the initial management and thus is inappropriate?
A prospective study in 89 acute severe asthma patients (Carruthers, 1995) found that when oxygen saturation was \( \geq 92\% \) (72 patients), 3 (4.2\%) had respiratory failure. In the 82 patients with a saturation of \( \geq 90\% \), 6 (7.3\%) had respiratory failure. The authors concluded that an oxygen saturation of \( > 92\% \) gave sufficient indication that respiratory failure was unlikely and that ABG measurement was therefore unnecessary.

SIGN guidelines also acknowledge that ABG measurement is only necessary in those patients with oxygen saturation \(< 92\% \) (See above).

Carruthers DM, Harrison BD. Arterial blood gas analysis or oxygen saturation in the assessment of acute asthma? Thorax 1995;50:186-8

Evidence Level: IV

Nebulised treatment should not be given routinely if the child is breathless, without trying inhalers first?
A comparative study (Boyd, 2005) looked at two sequential three-month periods. During the first period, nebulised therapy was given routinely and in the second period, treatment was with pressurised metered dose inhalers with spacers. Admission rates fell significantly from 31\% to 20.6\% during the second period, although no significant change in total hospital or emergency department times were recorded.


Evidence Level: IV

What are the appropriate doses and mode of administration for intravenous salbutamol, if there is no response to nebulised salbutamol?
The evidence for intravenous salbutamol is uncertain. A Cochrane review of 15 trials involving 584 patients (Travers, 2001) concluded that: "There is no evidence to support the use of IV beta2-agonists in patients with severe acute asthma. These drugs should be given by inhalation. No subgroups were identified in which the IV route should be considered." The SIGN asthma guideline (See above), referencing the Cochrane review, states: "The role of intravenous beta2 agonists in addition to nebulised treatment remains unclear. One study has shown that an IV bolus of salbutamol given in addition to near maximal doses of nebulised salbutamol results in clinically significant benefits". On the strength of this trial (Browne, 2002), SIGN recommends that: "The early addition of a bolus dose of intravenous salbutamol (15 mcg/kg) can be an effective adjunct to treatment in severe cases" (Category B recommendation), with the stipulation that such treatment should only be given within a PICU environment.
The recommended bolus dose of 15 mcg/kg, given over 10-20 minutes, is also used in the other two identified RCTs on this topic (Roberts, 2003; Browne 1997), one of which was an earlier study by Browne.
A review of evidence on this subject (Tobin, 2005) warns that intravenous salbutamol “has metabolic effects that may worsen respiratory function…and should not be given…outside of clinical trials.”

No recent recommendations for continuous infusion, or for mode of administration were identified.

The SIGN guideline also states that continuous nebulised salbutamol has no advantage over doses repeated every 20-30 minutes.


**Evidence Level: I**

**Corticosteroids can help to prevent recurrent episodes?**

A Cochrane review of 6 trials involving 374 children and adults (Rowe, 2007) found that a short course of corticosteroids significantly reduced the number of relapses without any apparent increase in side effects. Results in the first week after discharge were RR 0.38; 95% CI 0.2 – 0.74. This effect was maintained over the first 21 days following discharge (RR 0.47; 95% CI 0.25 – 0.89; NNT = 10).


**Evidence Level: I**

**Is magnesium sulphate of use?**

A systematic review and meta-analysis of 24 studies in 1,669 adults and children (Mohammed, 2007) found that intravenous (but not nebulised) magnesium had a significant effect on respiratory function in children (but not adults): SMD 0.25, 95% CI 0.80 – 3.08. There was also a significant reduction in hospital admission, again in children but not adults: RR 0.70, 95% CI 0.54 – 0.90.


**Evidence Level: I**

_Last amended January 2012_
This guideline and supporting information has been prepared with reference to the following:

HEALTH PROTECTION AGENCY NORTH WEST. Guidance for the management of human bite injuries. Guidance for healthcare professionals on dealing with injuries where teeth break the skin. 2010

http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1194947350692

**Antibiotic prophylaxis is indicated after bites from humans or other mammals?**

A Cochrane systematic review of 8 studies (Medeiros, 2001) found that the use of prophylactic antibiotics was associated with a statistically significant reduction in the rate of infection after bites by humans. Prophylactic antibiotics did not appear to reduce the rate of infection after bites by cats or dogs. Wound type, e.g. laceration or puncture, did not appear to influence the effectiveness of the prophylactic antibiotic. Prophylactic antibiotics were associated with a statistically significant reduction in the rate of infection in hand bites (OR 0.10, 95% CI 0.01 to 0.86; NNT = 4, 95% CI 2 to 50).


**Evidence Level: I**

Last amended November 2012
The stated thresholds for transfusion are appropriate?
A questionnaire of case scenarios sent to members of the European Society of Pediatric and Neonatal Intensive Care (Nahum, 2004) was completed by 134 of 258 members (51.9%). The suggested blood transfusion thresholds for case scenario 1 (post-orthopaedic surgery child) ranged from <7.0 g/dl to 11 g/dl. A total of 57.3% suggested 7 g/dl, 33.6% suggested 8 g/dl, and 6.9% suggested 9 g/dl as a haemoglobin threshold for transfusion (mean, 7.54 +/- 0.75). For case scenarios 2 to 4, the suggested haemoglobin thresholds were 7 g/dl to 12 g/dl. For case scenario 2 (a child with acute respiratory distress syndrome), 22.4% suggested 8 g/dl, 15.7% suggested 9 g/dl, and 41% suggested 10 g/dl as a haemoglobin threshold for transfusion (mean, 9.40 +/- 1.27 g/dl). For case scenario 3 (a post-cardiac surgery infant), 20.1% suggested 7 g/dl, 24.6% suggested 8 g/dl, 21.6% suggested 9 g/dl, and 23.9% suggested 10 g/dl as a haemoglobin threshold for transfusion (mean, 8.72 +/- 1.24 g/dl). For case scenario 4 (a child with septic shock), 23.1% suggested 8 g/dl, 16.4% suggested 9 g/dl, and 41% suggested 10 g/dl as a haemoglobin threshold for transfusion (mean, 9.45 +/- 1.24 g/dl). The threshold for transfusion was not statistically different (P >.05) between the physicians according to their subspecialty, years of experience, or country of origin. The suggested volume of transfused blood was 10 to 15 ml/kg in 427 responses (82.6%) and 20 ml/kg in 89 responses (17.2%). Of the 106 (79.1%) physicians who detailed their considerations for elevating the threshold for transfusion, 82 (77.3%) gave a general nonspecific indication, 47 (44.3%) stated haemodynamic instability and shock, and 40 (37.7%), ongoing bleeding. The authors concluded that haemoglobin threshold for blood transfusion and transfusion volume varied among European paediatric intensive care physicians, for the same patient. This reflected the lack of clinical trial evidence to support more rigid interpretation of what should be an appropriate threshold for transfusion.


Evidence Level: V

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:


http://www.sign.ac.uk/pdf/sign91.pdf

Drug treatments and physiotherapy are ineffective (in the acute phase) in immunocompetent patients and should not be used?
A Cochrane review (Perrota, 2005) of 3 RCTs found that chest physiotherapy using vibration and percussion techniques did not reduce length of hospital stay or oxygen requirement, or improve the severity clinical score. Chest physiotherapy using forced inspiratory techniques remains to be evaluated by clinical research.
A Cochrane review of 8 trials in 394 children (Kellner, 1999) found that bronchodilators produced no improvement in measures of oxygenation, rate of hospitalisation (18% vs 26%, OR 0.70, 95% CI 0.36-1.35) or duration of hospitalisation (weighted mean difference 0.12, 95% CI -0.3 - 0.5).
A Cochrane review on the usefulness of antibiotics for bronchiolitis is currently in progress (Fonseka, 2005). A prospective randomised study in 136 children (Frisi, 1984) found no benefit from antibiotic treatment.
A Cochrane review on 13 RCTs in 1198 children (Patel, 2004) found no benefits in terms of length of stay or clinical score in patients treated with glucocorticoids compared with placebo.
A Cochrane review of 5 RCTs in 374 infants (Blom, 2007) found no effect of inhaled corticosteroids in the prevention of wheezing following an episode of bronchiolitis.
A Cochrane review of 4 trials involving 254 infants with acute viral bronchiolitis found that patients treated with nebulized 3% saline had a significantly shorter mean length of hospital stay compared to those treated with nebulized 0.9% saline (mean difference (MD) -0.94 days, 95% CI -1.48 to -0.40, P = 0.0006). The 3% saline group also had a significantly lower post-inhalation clinical score than the 0.9% saline group in the first three days of treatment (day 1: MD -0.75, 95% CI -1.38 to -0.12, P = 0.02; day 2: MD -1.18, 95% CI -1.97 to -0.39, P = 0.003; day 3: MD -1.28, 95% CI -2.57 to 0.00, P = 0.05).
A randomised controlled trial in 600 children aged 2 – 12 months (Cornell, 2007) found that a single dose of oral dexamethasone (1 mg/kg) did not significantly alter hospital admission, respiratory status after 4 hours, or later outcomes.
A randomised controlled trial in 703 children up to 18 months of age (Walsh, 2008) compared 352 given nebulised albuterol to 351 given nebulised adrenaline. A total of 173 in the albuterol group and 160 in the adrenaline group were successfully discharged (defined as needing no further treatment and not re-admitted within 72 hrs).
A systematic review and meta-analysis of 48 trials in a total of 4897 patients (Hartling, 2011) found that only adrenaline (epinephrine) reduced admissions on day 1 (compared with placebo: pooled RR 0.67, 95% CI 0.50 to 0.89; NNT 15, 95% CI 10 to 45 for a baseline risk of 20%; 920 patients). Unadjusted results from a single large trial with low risk of bias showed that combined dexamethasone and adrenaline reduced admissions on day 7 (RR 0.65, 0.44 to 0.95; NNT 11, 7 to 76 for a baseline risk of 26%; 400 patients). A mixed treatment comparison supported adrenaline alone or combined with steroids as the preferred treatments for outpatients (probability of being the best treatment based on admissions at day 1 were 45% and 39%, respectively). The incidence of reported harms did not differ. Crucially, none of the interventions examined showed clear efficacy for length of stay among inpatients and the authors called for further research in this area.
A Cochrane review of 5 studies in a total of 543 children (Spurling, 2011) found “minimal evidence to support the use of antibiotics in bronchiolitis.”


Perrotta C, Ortiz Z, Roque M. Chest physiotherapy for acute bronchiolitis in paediatric patients between 0 and 24 months old. The Cochrane Database of Systematic Reviews 2005, Issue 2. Art. No.: CD004873


Evidence Level: I (for no effect of treatment with the exception of nebulised saline)

Last amended October 2011
Lymph nodes > 3 cm diameter are highly suggestive of neoplasia?
A study of 43 children undergoing lymph node biopsy for cervical lymphadenopathy (Vargas-Vallejo, 2007) found malignant disease in 23 cases. The most significant predictors of malignancy were bilateral nodes, disease progression shorter than 6 months, and lymph nodes > 3cm in diameter.


Evidence Level: IV

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:

NICE. When to suspect child maltreatment. London: NICE, 2009


What proportion of medical assessments provide evidence of abuse?
A review of 4549 child protection referrals between January 2002 and March 2006 (Kirk, 2010) found that 848 (19%) proceeded to a medical examination and 742 (88%) case notes were reviewed. Of the medical examinations, 383 (52%) were for alleged physical abuse, 267 (36%) for sexual abuse and 20 (3%) for neglect. 258 (67%) of the physical abuse cases were considered to have diagnostic or supportive findings as compared to 61 (23%) of the sexual abuse cases (chi2=146.31, p<0.001). In diagnostic or supportive examinations or where other potentially abusive concerns were identified, 366 (73%) proceeded to further multi-agency investigation and 190 (41%) to case conference. 131 (69%) of these resulted in the registration of the child on the child protection register. Other health concerns were identified in 121 (31%) of physical and 168 (63%) of sexual abuse cases. Overall, 465 (63%) out of 742 examinations showed signs diagnostic or supportive of alleged abuse or highlighted other abusive concerns.


Evidence Level: IV

Is an intact hymen evidence for the absence of sexual abuse?
A retrospective chart review of 506 girls aged 5 -17 who gave a history of non-acute, penetrative genital abuse (Anderst, 2009) found that 87% of victims providing a history of >10 penetrative events had no definitive evidence of penetration.


Evidence Level: IV

Last amended March 2011
Abdominal x-rays are of use as a diagnostic tool in constipation?

Radiographic assessment of 33 constipated and 67 control children (Leech, 1999) using a scoring system from 0 (no stool) to 5 (gross faecal loading with bowel dilatation) found that assessment of faecal loading was subjective and varied considerably between observers. Consistency was good if a single observer scored all radiographs, however. The authors concluded that, to limit exposure to radiation, radiography should not be routine, but should be reserved for the investigation of intractable constipation and that the same observer should score all radiographs. This accords with advice from the Royal College of Radiologists (RCR, 1998). Of the two earlier studies (Blethyn, 1995; Barr, 1979) using this technique in children, the former found more inter- and intra-observer correlation than did the latter, although both commended its usefulness.

A study in adults, using a similar scoring system (Starreveld, 1990), found “significant correlation” between the radiograph scores and frequency of defaecation, faecal consistency and stool weight.

Abdominal x-ray may also be used in conjunction with radio-opaque markers to identify segments of colon with impaired motility (Fotter, 1998; Zaslavsky, 1998).

A systematic review of 6 studies (Reuchlin-Vroklage, 2005) found conflicting evidence for an association between a clinical and a radiological diagnosis of constipation. The likelihood ratio (LR) in 2 high-quality studies was close to 1 (LR, 1.2; 95% confidence interval [CI], 1.0-1.4; and LR, 1.0; 95% CI, 0.5-1.6). More and better quality studies were called for.


Evidence level: I
Studies of transit times are useful in the management of constipation?
In a study of physiologic testing for constipation in 104 patients (Halverson, 1998), the test results “added significant information” in half the cases, leading to a specific diagnosis. Transit times and defaecography were found to be the most useful, the others being manometry, balloon compliance, pudendal nerve latency and electromyography. Measuring total and segmental colonic transit times allows constipation caused by colonic dysfunction to be distinguished from that caused by distal obstruction (Zaslavsky, 1998). It may also provide evidence for the existence of slow-transit constipation in children as in adults (Benninga, 1996).

A study comparing transit times with Barr-scores (derived from abdominal radiographs) in 211 constipated children (Benninga, 1995) found transit times far more accurately distinguished children with constipation due to colonic inertia from those with encopresis/soiling or recurrent abdominal pain.

A study in 169 consecutive patients (de Lorijn, 2004) found that a colonic transit time of >100 hours to be associated with a poor outcome at one year, whilst transit times of < 100 hours were not predictive of outcome.

A diagnostic case-control study in 89 children by the same group (de Lorijin, 2006) found that the mean colonic transit time (CTT) was significantly longer in constipated children than in the control group (92 hours versus 37 hours; \( P < 0.0001 \)).

Other studies have also found transit times to be useful in the diagnosis and management of constipation (Benninga, 2004; Papadopoulou, 1994; Vattimo, 1993; Bautista, 1991; Vajro, 1988).


Halveron AL, Orkin BA. Which physiologic tests are useful in patients with constipation? Dis Colon Rectum 1998;41:735-9


Evidence level: IV
Osmotic or stimulant laxatives, Movicol, bowel cleansing preparations (eg Klean Prep), rectal enemas, combination therapy or prokinetic agents are of use in the management of constipation?

No studies have compared the relative efficacy of different laxatives or clean-out procedures (Brooks, 2000). Nor have any randomised trials on laxatives and enemas been conducted without the inclusion of a behavioural component (Brooks, 2000). If dietary interventions fail to relieve constipation, a stool softening or osmotic laxative such as lactulose should be tried first, and a stimulant laxative such as senna, bisacodyl or sodium picosulfate syrup next, if necessary (Anon, 2000; Baker, 1999).

Movicol and Klean Prep are both polyethylene glycol preparations that are not recommended for use in children, in the case of the former (n.b. Movicol Paediatric Plain is now available; it does not have UK marketing authorisation for use in faecal impaction in children under 5 years, or for chronic constipation in children under 2 years (NICE, 2010)), or not licensed for that use in the case of the latter (Anon, 2000). Both may be used if laxatives fail, however (Anon, 2000; Baker, 1999). A study in 74 children (Pashankar, 2003) treated for longer than 3 months (mean 8.4 months, range 3-30) with polyethylene glycol 3350 (PEG) found that symptoms improved significantly in all. In 31 children with encopresis, soiling ceased completely in 16 patients and decreased in all the others.

Two evidence-based reviews (Arora, 2005; Kinservik, 2004) found that low-dose (3350) PEG, with or without added electrolytes, was safe and effective both in the short and long term management of constipation in children.

A double blind, randomised trial in 100 patients aged between 6 months and 15 years (Voskuijl, 2004) compared PEG 3350 with lactulose. A significantly higher success rate (56% vs 29%) was found in the PEG group, which also reported fewer side effects.

A small study in 28 patients younger than 18 months of age (Michail, 2004) found that an initial dose of 0.88 g/kg/day, followed by a maintenance dose of 0.78 g/kg/day relieved constipation in 97.6% of them.

Small-volume sodium citrate enemas (micro-enemas) may also be tried (in preference to larger-volume phosphate enemas) (Anon, 2000).

If individual laxatives have failed, a combination (e.g. lactulose and senna) may be effective (Anon, 2000).

Anon. Managing constipation in children. Drug Ther Bull 2000;38:57-60


Evidence Level: V
What are the options for the management of faecal impaction?

A randomised prospective study comparing mineral oil and oral lavage solution in 26 patients with faecal impaction (Tolia, 1993) found that patients in the lavage group had more frequent bowel movements and better clearance of impacted faeces. Compliance was, however, poorer than with mineral oil, probably due to the larger volume of solution required (20 ml/kg/h for 4 hours on two consecutive days versus 2-8 tablespoons of mineral oil twice a day for two days).

If laxatives, alone or in combination, bowel-cleansing preparations and enemas have all failed, manual evacuation under general anaesthetic may be the only option (Anon, 2000). This procedure may, however, be the cause of iatrogenic structural injury to the anal sphincters, leading to faecal incontinence (Gattuso, 1996).

Pulsed-irrigation enhanced evacuation has been found simple, safe and effective in the management of faecal impaction (Gilger, 1994; Kokoszka, 1994) and removes the necessity for general anaesthesia.

A randomised trial in 90 children (male, n = 60; mean age: 7.5 +/- 2.8 years) compared enemas with high-dose oral polyethylene glycol (PEG) (Bekkali, 2009). Forty-six patients received enemas and 44 PEG. Successful disimpaction was achieved with enemas (80%) and PEG (68%; P = .28). Faecal incontinence and watery stools were reported more frequently with PEG (P < .01), but defecation frequency (P = .64), abdominal pain (P = .33), and behaviour scores were comparable between groups. Colonic transit time normalised equally (P = .85) in the 2 groups.

Anon. Managing constipation in children. Drug Ther Bull 2000;38:57-60


Evidence Level: III (lavage solution); V (Pulsed-irrigation enhanced evacuation)

What is the value of behavioural therapy/biofeedback in the treatment of constipation?

A randomised controlled trial in 192 children (van der Plas, 1996) compared 94 patients who received conventional treatment (laxatives and advice) with 98 who received the same treatment plus 5 biofeedback training sessions. After 6 weeks, 86% of the biofeedback group had achieved normal defaecation dynamics, compared with 52% of controls. This did not, however, affect the clinical outcome, follow-up after one year revealing that 59% of the control group had a defaecation frequency of 3 times a week or more with no laxatives, compared to 50% of the biofeedback group.

Very similar results were obtained in further trials in 49 (Sunic-Omejc, 2002), 29 (Nolan, 1998) and 253 children (Loening-Baucke, 1995). Despite the absence of proven long-term benefit, biofeedback could be used initially to achieve a faster response to other therapy (Nurko, 2000). Further research in this area is indicated (Bassotti, 2004). A small randomised study in 36 patients (Croffie, 2005) compared 24 patients given biofeedback in the laboratory to 12 who were also given home biofeedback. There were no significant differences between the two groups at 2 and 4 months follow-up. A Cochrane review of data from 8 studies (Brazzelli, 2005) found higher rates of persisting (up to 12 months) defaecation problems when biofeedback training was added to conventional treatment. The authors concluded that biofeedback could not be recommended for children with functional constipation.
Behavioural therapy has been shown to be a rapidly-effective and long-lasting treatment (Howe, 1992). Of 58 encopretic children placed on a regimen based on attempting to defaecate after a specific meal, 60% were completely continent after 5 months and a further 23% had only staining (Lowery, 1885). A prospective study of behavioural therapy in 27 children with Hirschsprung’s disease (van Kuyk, 2001) found that all outcome variables were significantly better in the 14 children of the treatment group compared to the 13 controls. The effect persisted at follow-up (mean 7 months).


Brazzelli M, Griffiths P. Behavioural and cognitive interventions with or without other treatments for the management of faecal incontinence in children. The Cochrane Database of Systematic Reviews 2006, Issue 2. Art. No.: CD002240


Evidence Level: I (for lack of long-term benefit from biofeedback); IV (for behavioural therapy)

Is rectal biopsy of use?
Rectal biopsy is generally requested to exclude the potentially fatal disorder, Hirschsprung’s disease and is the only test than can do so reliably (Baker, 1999). A retrospective review of 186 rectal biopsies from 141 children (Ghosh, 1998) compared the age at onset of symptoms with the diagnosis of Hirschsprung’s disease. 17 children (12%) had Hirschsprung’s disease and all of these experienced the first onset of constipation within the neonatal period. The authors concluded that, if the age at onset of constipation was after the neonatal period, rectal biopsy was unnecessary. The only other previous study to address this question (Landman, 1987) also found that the age of onset of constipation correlated with a positive diagnosis. A 5-year retrospective review of 70 patients referred for deep transanal rectal biopsy for intractable constipation (Simpson, 1996) found that a diagnosis was established in 30 of these, 17 of whom had subsequent surgical procedures to relieve the condition. The authors
concluded that the investigation was justified in constipation refractory to medical management. Retrospective analysis in 100 patients (Lewis, 2003) found that a history of delayed passage of meconium, abdominal distension, vomiting or the results of a contrast enema identified all patients with Hirschsprung’s and excluded the condition in approximately 36% of patients with idiopathic constipation. The authors concluded that it was not necessary to perform a rectal biopsy in children with constipation who displayed none of the key features.


Ghosh A, Griffiths DM. Rectal biopsy in the investigation of constipation. Arch Dis Child 1998;79:266-8


Evidence Level: IV

Last Amended March 2011
Glucocorticoids are of value in the treatment of croup?
A Cochrane review (Russell, 2011) of 38 studies in 4299 children found glucocorticoid treatment to be associated with an improvement in the Westley score at 6 hours with a weighted mean difference of -1.2 (95% CI -1.6 to -0.8) and at 12 hours -1.9 (95% CI -2.4 to -1.3). The improvement was no longer significant at 24 hours. Fewer return visits and readmissions occurred in patients treated with glucocorticoids (RR 0.50; 95% CI 0.36-0.70). Length of time spent in hospital or A&E was also significantly decreased (weighted mean difference 12 hours, 95% CI 5-19 hours). Use of epinephrine decreased for children treated with a glucocorticoid (risk difference 10%; 95% CI 1 to 20). The authors concluded that dexamethasone and budesonide were effective in relieving the symptoms of croup as early as 6 hours after treatment.


Evidence Level: I

Nebulised adrenaline (epinephrine) is of value in the treatment of severe croup?
A Cochrane systematic review of 8 studies in a total of 225 children (Bjornson, 2011) found that nebulised epinephrine (NE) was associated with croup score improvement 30 minutes post-treatment (three RCTs, SMD -0.94; 95% CI -1.37 to -0.51; I(2) statistic = 0%). This effect was not significant two and six hours post-treatment. NE was associated with significantly shorter hospital stay than placebo (one RCT, mean difference -32.0 hours; 95% CI -59.1 to -4.9). Comparing racemic and L-epinephrine, no difference in croup score was found after 30 minutes (SMD 0.33; 95% CI -0.42 to 1.08). After two hours, L-epinephrine showed significant reduction compared with racemic epinephrine (one RCT, SMD 0.87; 95% CI 0.09 to 1.65). There was no significant difference in croup score between administration of NE via IPPB versus nebulisation alone at 30 minutes (one RCT, SMD -0.14; 95% CI -1.24 to 0.95) or two hours (SMD -0.72; 95% CI -1.86 to 0.42).


Evidence Level: I

Last amended April 2011
Cyanosis with mild or no respiratory distress indicates the likelihood of cardiac disease?

“Cyanosis in association with pulmonary or cardiac disease may be only mild or moderate in degree. Severe cyanosis usually indicates the presence of a cardiac problem” (Sahn, 1973).

Sahn DJ, Friedman WF. Difficulties in distinguishing cardiac from pulmonary disease in the neonate. Pediatr Clin N Am 1973;20:293-301

Evidence Level: V

Last amended June 2006
Tobramycin can be given tds or once daily?
A randomised trial in 244 children and adults (Smyth, 2005) found once or three-times daily doses of iv tobramycin (given with ceftazidime) to be equally effective in pulmonary exacerbations of CF. The authors concluded that “the once daily regimen might be less nephrotoxic in children”.
An open-label, randomised, multi-centre study in 88 patients aged >/= 6 months (Ratjen, 2010) found that treatment with tobramycin inhalation solution for 28 days resulted in 66% of patients remaining free of infection at 1 month following completion of treatment.


Evidence Level: II

Pancreatic enzyme supplements in doses > 10,000 units lipase/kg/day have the potential to cause colonic strictures?
A case-control study (FitzSimmons, 1997), looking at 29 patients with fibrosing colonopathy (FC) and 105 controls, found a RR of 10.9 (95% CI 1.6-71.8) of developing FC associated with a dose of pancreatic enzyme of 24,001-50,000 units of lipase/kg/day, as compared to a dose of < 24,001 units of lipase/kg/day. The RR associated with a dose of > 50,000 units/kg/day was 199.5 (95% CI 9.9 – 4026.0). The authors recommended that the daily dose of pancreatic enzymes should be < 10,000 units/kg/day for most patients.

Similar results have been reported from other studies (Freiman, 1996; Lancellotti, 1996; Smyth, 1995).


Evidence Level: IV

Dornase alfa is of use in exacerbations?
A Cochrane systematic review of 15 trials in a total of 2469 patients (Jones, 2010) found “evidence to show that therapy with dornase alfa over a one-month period is associated with an improvement in lung function in CF; results from a trial lasting six months also showed the
same effect. Therapy over a two-year period (based on one trial) significantly improved FEV₁ in children and there was a non-significant reduction in the risk of infective exacerbations."

Jones AP, Wallis C. Dornase alfa for cystic fibrosis. Cochrane Database of Systematic Reviews 2010, Issue 3. Art. No.: CD001127

Evidence Level: I

Vitamin A supplementation is of benefit?
A Cochrane systematic review (Bonifant, 2012) was unable to find any suitable evidence with which to address this issue. The authors concluded that: "Until further data are available, country or region specific guidelines on the use of vitamin A in people with cystic fibrosis should be followed."

Bonifant CM, Shevill E, Chang AB. Vitamin A supplementation for cystic fibrosis. Cochrane Database of Systematic Reviews 2012, Issue 8. Art. No.: CD006751

Evidence Level: I

Last amended October 2012
This guideline and supporting information has been prepared with reference to the following:

Royal College of Nursing. Perioperative fasting in adults and children: an RCN guideline for the multidisciplinary team. London: RCN, 2005


The principles of pre-procedural fasting in children with diabetes differ little from those which apply to healthy patients?
The RCN guidelines on this subject (see above) state that: “All higher risk patients (Includes those with obesity, diabetes and gastro-oesophageal reflux): Follow same fasting regime as healthy patients, unless contraindicated.” There is no evidence from randomised trials to inform decision-making in this area.

Evidence Level: V

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:

NICE. Type 1 diabetes: diagnosis and management of type 1 diabetes in children, young people and adults. 2004 (last amended 2010)


Suspected diabetes requires immediate referral?
The NICE guidelines referred to above state that: “Children and young people with suspected type 1 diabetes should be offered immediate (same day) referral to a multidisciplinary paediatric diabetes care team that has the competencies needed to confirm diagnosis and to provide immediate care.”

Evidence Level: V

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:

BSPED Recommended DKA Guidelines 2009
http://www.bsped.org.uk/professional/guidelines/docs/DKAGuideline.pdf


Fatalities are uncommon and are usually associated with cerebral oedema, hypokalaemia causing cardiac dysrhythmias, or coexisting infection, such as meningitis?
Of 55 deaths in a cohort of children diagnosed between 1950 and 1980 (Scibilia, 1986), DKA was the cause in 17 (85%) of the 20 deaths at disease onset, and 18 (54%) of those occurring 2 months to 11 years after diagnosis.

In a report of 33 deaths in 4919 children with type I diabetes in Sweden (Sartor, 1995), 7 (21%) were DKA-related.

In a UK report of 83 diabetes-related deaths in patients <20 years of age (Edge, 1999), DKA was implicated in 69 (83%).

A multicentre study of 6977 hospitalisations for DKA (Glaser, 2001) recorded 61 (0.8%) episodes of cerebral oedema. Of these 61 children, 13 (21%) died. Two more children died during the episode of DKA, but not from cerebral oedema, bringing the overall mortality rate from DKA to 0.21%. This was similar to the rate of 0.25% previously reported from US paediatric institutions (Levitsky, 1991).


Evidence Level: IV

Last amended March 2011
**DIARRHOEA & VOMITING (D&V) IN CHILDHOOD**

**Supporting information**

**D&V in infants may be a sign of sepsis?**
The online Merck Manual of Diagnosis and Therapy lists D&V as two of the possible symptoms of neonatal sepsis. Vomiting was one of 31 clinical signs used to predict 43 sepsis deaths amongst 3567 neonates in an Indian study (Bang, 2005).


Evidence Level: V

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:


Prolonged QTc is associated with sudden death?
An editorial on the subject of long QT interval (Sumitomo, 2010) states that:
“LQTS is characterized as prolonged ventricular repolarization with a high incidence of sudden cardiac death because of ventricular arrhythmias, such as torsades de pointes or ventricular fibrillation. Recent advances in genetic studies have revealed 12 genetic abnormalities on the locus of the chromosomes in chromosome 3, 4, 7, 11, 12, 17, 20 and 21. These genetic abnormalities result in decreased function of the potassium channels, increased or prolonged function of calcium channels, or increased function of the sodium channels, which are responsible for the prolongation of ventricular repolarization and consequently cause prolongation of the QT interval.”


Evidence Level: V

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:


Last amended November 2012
This guideline and supporting information has been prepared with reference to the following:


Last amended November 2012
**Steroids are not a useful treatment in facial palsy?**

Randomised trial evidence is lacking in children. A Cochrane review of 8 trials in a total of 1569 adults (Salinas, 2010) found that overall, 175/754 (23%) of the participants allocated to corticosteroids had incomplete recovery of facial motor function six months or more after randomisation, significantly less than 245/753 (33%) in the control group (RR 0.71, 95% CI 0.61 to 0.83). There was, also, a significant reduction in motor synkinesis during follow-up in those receiving corticosteroids (RR 0.6, 95% CI 0.44 to 0.81). The reduction in the proportion of patients with cosmetically disabling sequelae six months after randomisation, however, was not significant (RR 0.97, 95% CI 0.44 to 2.15). The trial not included in the primary outcome of this meta-analysis showed a non-significant difference in outcomes between the arms. The authors concluded that corticosteroids were of significant benefit in adults. It is not known whether these results can be extrapolated for use in children.

The rate of spontaneous recovery from facial palsy in children has been estimated at 97.6% (Jenke, 2011).

**References**


**Evidence Level:** I

---

**Last amended April 2012**
What are the risk factors for failure to thrive in infancy?
An analytical study (Olsen, 2010) using the Copenhagen Child Cohort (6090 children born during the year 2000 and followed prospectively from birth) found that, regardless of the age of onset, slow weight gain was strongly associated with feeding problems, although the risk factors involved differed according to age of onset. Onset within the first weeks of life clearly differed from faltering later on, the former being strongly associated with low birthweight and gestational age, with single parenthood and with mother having smoked during pregnancy. Onset between 2 weeks and 4 months was associated with congenital disorders and serious somatic illness, and with deviant mother-child relationship, whereas, onset between 4 and 8 months seemed to represent a group of children with feeding problems arising de novo in otherwise healthy children. The authors concluded that weight faltering in infancy was clearly associated with contemporary measured feeding problems, but the risk mechanisms involved differed in early vs. late onset.


Evidence Level: IV

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:


What is the evidence for the appropriate pre-dose trough for gentamicin in febrile neutropenia beyond the neonatal period?
Gentamicin administration carries the danger of ototoxicity or nephrotoxicity if the serum concentration of the drug is at any point too high. The BNF for Children recommends that the pre-dose trough concentration should be < 2 mg/L in multiple daily dose regimens, and < 1 mg/L for once-daily dosing.

A number of studies suggest that once-daily dosing achieves more stable trough levels than twice or three-times daily dosing. A review of 13 comparison studies (Miron, 2001) found that steady state trough concentrations > 2mg/L occurred in 5-55% of those on multiple doses, vs 0-24% of those on single doses.

A meta-analysis of 24 studies published between 1991 and 2003 (Contopoulos-Ionnidis, 2004) found that 22 of the 23 RCTs that had performed pharmacokinetic analyses showed that once-daily dosing achieved higher peak and lower trough levels, compared with multiple daily dosing.

Consensus opinion, based on clinical observation, appears to follow the advice given in BNF for Children.


Evidence Level: V (Consensus opinion)

Last amended March 2011
What is the value of laboratory tests in establishing the severity of infection?
A systematic review of 14 studies (Van den Bruel, 2011) found that the prevalence of serious infections ranged from 4.5% to 29.3%. Tests were carried out for C reactive protein (five studies), procalcitonin (three), erythrocyte sedimentation rate (one), interleukins (two), white blood cell count (seven), absolute neutrophil count (two), band count (three), and left shift (one). The tests providing most diagnostic value were C reactive protein and procalcitonin. Bivariate random effects meta-analysis (five studies, 1379 children) for C reactive protein yielded a pooled positive likelihood ratio of 3.15 (95% CI 2.67 to 3.71) and a pooled negative likelihood ratio of 0.33 (0.22 to 0.49). To rule in serious infection, cut-off levels of 2 ng/mL for procalcitonin (two studies, positive likelihood ratio 13.7, 7.4 to 25.3 and 3.6, 1.4 to 8.9) and 80 mg/L for C reactive protein (one study, positive likelihood ratio 8.4, 5.1 to 14.1) are recommended; lower cut-off values of 0.5 ng/mL for procalcitonin or 20 mg/L for C reactive protein are necessary to rule out serious infection. White blood cell indicators were less valuable than inflammatory markers for ruling in serious infection (positive likelihood ratio 0.87-2.43), and had no value for ruling out serious infection (negative likelihood ratio 0.61-1.14). The best performing clinical decision rule (recently validated in an independent dataset) combined testing for C reactive protein, procalcitonin, and urinalysis and had a positive likelihood ratio of 4.92 (3.26 to 7.43) and a negative likelihood ratio of 0.07 (0.02 to 0.27).


Evidence Level: I

Are paracetamol and ibuprofen equally effective for reducing fever?
An expert review (Sullivan, 2011) states that “Current evidence suggests that there is no substantial difference in the safety and effectiveness of acetaminophen and ibuprofen in the care of a generally healthy child with fever”.


Evidence Level: I

Last amended July 2012
The Glasgow Coma Scale (GCS) is appropriate for use in younger children?

The authors of a review on this subject (Simpson, 1991) state that:

“The normal verbal and motor responses embodied in the standard Glasgow Coma Scale (GCS) are not achievable during the first few years of life. The recent literature contains numerous reports of attempts to devise scales of responses quantitating the conscious level in infants and young children, both for research purposes and as clinical guides; some of these scales incorporate items, e.g. brainstem reflexes, that are not included in the GCS. We have reported on a simple paediatric version of the GCS, which uses the standard scale with minor modifications in the verbal component, and sets realistic age-related normal responses. This has been tested prospectively in a series of 60 head-injured infants and children (age range 0-72 months). Of 6 cases recorded as comatose 6 h after injury, 4 have confirmed or suspected residual disabilities. Of 35 cases considered to be fully conscious at 6 h, 31 have made good recoveries and only 1 has suspected residual disabilities. The study suggests that the scale accords with the realities of neurological immaturity, and confirms that it can be used in routine paediatric practice.


Evidence Level: IV

Last amended March 2011
What is the incidence of primary glomerulonephritis?

A systematic literature review of 40 studies (McGrogan, 2011) found an incidence in children of around 0.1/100,000/year with the exception of minimal change disease where incidence was reported to be 2.0/100,000/year in Caucasian children.


Evidence Level: III
This guideline and supporting information has been prepared with reference to the following:


Is any intervention other than supportive treatment indicated in HUS?

A systematic review and meta-analysis of seven RCTs in 476 young children with postdiarrheal HUS (Michael, 2009) found that none of the evaluated interventions (fresh frozen plasma transfusion, heparin with or without urokinase or dipyridamole, Shiga toxin-binding protein, and steroid) were superior to supportive therapy alone for any outcomes.


Evidence Level: I

Last amended November 2012
Desmopressin (DDAVP) is the treatment of choice for spontaneous bleeding, trauma and minor surgery?
A retrospective cohort study (Sanchez-Luceros, 2010) of 221 children (median age 11 years; 137 females) with low Von Willebrand Factor (VWF) performed the DDAVP infusion-test in 214 children, 93.4% of whom showed good response. Patients with type 1 were at higher risk of DDAVP-test failure: 9/26 (34.6%) vs. 18/188 (9.6%) with possible type 1 (RR 3.44, 1.75-6.79; p= 0.002, Fisher's exact test). In 68 children, the clinical response to DDAVP was evaluated 87 times: i) to stop bleeding: menorrhagia (13), mucocutaneous (12), haemarthrosis (1); and ii) to prevent surgical bleeding: adenotonsillectomy (17), major (15) and minor surgery (10); and dental procedures (19). No major adverse events or bleeding were observed. The treatment was effective with one single dose of DDAVP in almost all patients, without antifibrinolytic or local therapy., except in a girl with severe haemorrhage during menarche who required replacement therapy.


Evidence Level: III

Last amended March 2011
HEART FAILURE & WEAK PULSES
Supporting information

This guideline and supporting information has been prepared with reference to the following:


**Does carvedilol have a role in the treatment of paediatric heart failure?**

A multicentre, randomised, double-blind, placebo-controlled trial in 161 children and adolescents (Shaddy, 2007) found no statistically significant difference for either low dose (0.2 mg/kg if weight < 62.5 kg or 12.5 mg per dose if heavier) or high dose (0.4 mg/kg if weight < 62.5 kg or 25 mg per dose if heavier) carvedilol, compared to placebo. Among 54 patients assigned to placebo, 30 improved (56%), 16 worsened (30%) and 8 were unchanged (15%); among 103 patients assigned to carvedilol, 58 improved (56%), 25 worsened (24%) and 20 were unchanged (19%). In contrast, reductions in mortality of 30% have been seen in adults on carvedilol therapy (Bristow, 1996).

A Cochrane Systematic Review of 3 studies in 203 patients (Frobel, 2009) found insufficient evidence with which to reach a firm conclusion on this question.


**Evidence Level: I**

Last amended April 2009
Are corticosteroids of use in HSP?

In a small retrospective study in 12 patients with HSP nephritis (Flynn, 2001), treatment was given for 12 weeks with either iv pulse methylprednisolone (10 mg/kg/dose up to a maximum of 1 g/day) or oral prednisolone in high doses (2mg/kg/day up to a maximum of 80 mg/day) followed by oral cyclophosphamide (2 mg/kg/day). Daily or alternate-day oral prednisolone was also given. Proteinuria (a risk factor for the development of renal insufficiency in HSP) was reduced, in terms of serial protein-to-creatinine ratios, from 6.3 +/- 4.4 to 0.8 +/- 0.8 (p = 0.002).

Proteinuria was also reduced in 19 of 21 patients given prednisone in combination with azathioprine (Bergstein, 1998). 13 patients received oral prednisone and 8 were treated with iv methylprednisolone. Proteinuria decreased from 8.8 +/- 7.5 to 0.47 +/- 0.39 g/24 h (p < 0.01).

Methylprednisolone pulse therapy was also found to be effective in a prospective study in 38 patients (Niaudet, 1998). At follow up (1-16 years after treatment), 27 children had clinically recovered. Renal biopsy in 18 of these patients showed a significant decrease of the activity index from 5.1 +/- 1.1 to 0.4 +/- 0.8 with a decrease in (or in some cases, disappearance of) IgA deposits.

In another retrospective analysis in 101 children with HSP (Reinehr, 2000), 57 with severe abdominal pain (n=34) or GI bleeding with abdominal pain (n=23) as features of their disease were treated with steroids. Treatment with prednisone (2 mg/kg, rising to 3-5 mg/kg if symptoms persisted for more than 24 hours) resulted in a 100% cure rate within 48 hours (77% within 24 hours). A further 43 children who were not given steroids had abdominal pain for a median of 5 days (range 1-28 days). The 26 patients who had received 1 week of prednisone treatment within the first 3 weeks of their disease had renal involvement in 2 (8%) of cases. This compared with 39 (52%) of the other 75 patients in the study.

In a report of 100 cases with a review of the literature (Saulsbury, 1999), 57 patients received corticosteroids. Patients were given oral or intravenous prednisone (mean dose 1.6 +/- 0.4 mg/kg per day) for 5 – 28 days (mean 8.9 +/- 3.7 days). Corticosteroids “seemed to be beneficial in hastening the resolution of abdominal pain and arthritis” but as neither randomisation nor a control group was used, the authors felt that no conclusions could be inferred from this observation. Corticosteroids in normal doses had no effect on rash, recurrence of symptoms, or acute or delayed nephritis.

A retrospective study of 69 children by the same author (Saulsbury, 1993) also found that steroids had no effect on preventing nephritis.

A randomised, controlled prospective study on this subject (Mollica, 1992) did find a “highly significant (P < 0.001) benefit for steroid therapy in preventing nephritis. Eighty four patients received oral delta-prednisone (1 mg/kg/d for 2 weeks) and 84 did not. None of the steroid group vs 10 (11.9%) of the controls developed nephropathy 2-6 weeks after the acute episode.

In contrast, another randomised trial, in 171 patients (84 given prednisone and 87 given placebo), found once again that renal symptoms were not prevented by prednisone, although it was effective in treating them (Ronkainen, 2006). Abdominal and joint pain were, however, both reduced in intensity (pain score 2.5 vs 4.8; p = .029 and 4.6 vs 7.3; p = .030 respectively).

A retrospective analysis of 17 HSP patients with nephritis (Foster, 2000), treated with prednisone (1-2 mg/kg/d) and azathioprine in a similar dose, compared outcomes with a control group of 59. 15 of 17 (88%) in the treatment group vs 32 of 59 (54%) controls had a favourable outcome. Relative risk of an unfavourable outcome in controls was 6.3.

A systematic review of 15 studies (Weiss, 2007) found that corticosteroid treatment did not reduce the median time to resolution of abdominal pain but did significantly reduce the mean resolution time and increased the odds of resolution within 24 hours. The odds of developing persistent renal disease were also significantly reduced.

It appears that corticosteroid treatment does not shorten the duration of HSP, but does decrease morbidity (Rosenblum, 1987), including that associated with cutaneous vasculitis and fibrinolysis (Prandota, 2001).
Evidence Level: I

What is the most appropriate analgesic/anti-inflammatory in HSP?
Non-steroidal anti-inflammatory drugs are commonly used to treat arthritic pain in HSP (Cron, 1999) although no particular NSAID is recommended. There are a number of anecdotal reports of dapsone being efficacious in HSP, including paediatric patients (Ramelli, 1997; Sarma, 1994; Hoffbrand, 1991; Ledermann, 1983).


No follow-up is required if urinalysis results are normal?
A systematic review of 12 studies in 1133 children with follow-up periods ranging from 6 weeks to 36 years (Narchi, 2005) showed that no cases of permanent renal impairment developed following a normal urinalysis result.

Narchy H. Risk of long term renal impairment and duration of follow up recommended for Henoch-Schonlein purpura with normal or minimal urinary findings: a systematic review. Arch Dis Child 2005;90:916-20

Evidence Level: I

Last amended January 2008
How frequently does Hepatitis C infection spontaneously resolve in children?
In a retrospective study in 157 children with Hepatitis C infection (Yeung, 2007), 28% resolved spontaneously (34 transfusional and 10 nontransfusional cases). The 123 transfusional cases were older at time of infection and at follow-up, compared with the 34 nontransfusional cases. Younger age at follow-up (p < 0.0001) and normal ALT levels (p < 0.0001) favoured clearance. Among cases of neonatal infection, 25% demonstrated spontaneous clearance by 7.3 years. The rate of spontaneous clearance of childhood HCV infection was comparable between transfusional and nontransfusional cases. The authors noted that, if clearance occurred, it tended to happen early in infection, at a younger age.


Evidence Level: IV

Last amended March 2011
HIV AND HEPATITIS B POST-EXPOSURE PROPHYLAXIS (PEP)
Supporting information

In high-risk patients, Kaletra (lopinavir/ritonavir) should be given in addition to Zidovudine and Lamivudine?
A review of Kaletra (Oldfield, 2006) states that, based on evidence from randomised trials, “Combination antiretroviral therapy with lopinavir/ritonavir effectively reduced viral load in ART-naive patients at both the 400mg/100mg twice-daily and 800mg/200mg once-daily dosages; viral load decreased to <50 copies/mL in at least 50% of ART-naive patients receiving either lopinavir/ritonavir dosage. Lopinavir/ritonavir 400mg/100mg twice daily was more likely than nefavir 750mg three times daily to produce sustained virological suppression. The antiviral efficacy of lopinavir/ritonavir-based therapy was maintained for up to 7 years. Thus, lopinavir/ritonavir is a convenient, effective option for use in the treatment of HIV infection in ART-naive and -experienced adults, adolescents and children.”


Evidence Level: II

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:
http://www.chiva.org.uk/files/guidelines/hiv-testing2.pdf

Last amended July 2012
This guideline and supporting information has been prepared with reference to:


**The definition of hypertension depends on knowledge of the normal range for the age or the height of the child?**

“There is no current standard UK definition of hypertension in children. However, the issue has been researched in some detail in America where a working group in 2004 defined the condition as an average systolic and/or diastolic blood pressure ≥ 95th percentile for gender, age, and height on 3 or more separate occasions. (Anon, 2004). The working group also introduced the concept of 'pre-hypertension' which it defines as a blood pressure level ≥ 90th percentile but <95th percentile.”

[http://www.patient.co.uk/showdoc/40000573/](http://www.patient.co.uk/showdoc/40000573/)


**Evidence Level: V**

Last amended January 2010
What is the appropriate dose of glucose with which to correct hypoglycaemia?
Textbooks and reviews alike recommend 2-4 ml/kg of 25% glucose at a rate of 1 ml/min
(Sperling, 2000; McCabe, 1994; Shah, 1992; Schwartz, 1991) without quoting a source of
reference. In a small study of 22 neonates (Lilien, 1977), hypoglycaemia was corrected within
10 minutes in 18 of them by a constant infusion of 8 mg/kg/min. A further 3 normalised within
30-50 minutes. The remaining patient had hyperinsulinaemia and responded only to
diazoxide. A later study of 23 hypoglycaemic infants by the same team (Lilien, 1980) used a
200 mg/kg bolus over 1 minute, followed by a constant infusion of 8 mg/kg/min. All patients
were normoglycaemic after 1 minute, with 1 patient developing transient hyperglycaemia.

Lilien LD, Grajwer LA, Pildes RS. Treatment of neonatal hypoglycemia with continuous


Schwartz R. Neonatal hypoglycemia: back to basics in diagnosis and treatment. Diabetes
1991;40(Suppl 2):71-3

Shah A, Stanhope R, Matthew D. Hazards of pharmacological tests of growth hormone

Sperling MA. Hypoglycemia. In: Behrman RE, Kliegman RM, Jenson HB (eds). Nelson

Evidence level: V

What is the basis for the definition of hyperinsulinism?
Considerable controversy surrounds the definition of hyperinsulinism (Aynsley-Green, 2000;
Cornblath, 1990; Koh, 1988), although European Network for Research into Hyperinsulinism
consensus favours the following criteria (Aynsley-Green, 2000):

Glucose requirements > 6-8 mg/kg/min to maintain blood glucose above 2.6 – 3 mmol/litre
Laboratory blood glucose < 2.6 mmol/litre
Detectable insulin at the point of hypoglycaemia with raised C peptide
Inappropriately low blood free fatty acid and ketone body concentrations at the time of
hypoglycaemia
Glycaemic response after the administration of glucagon when hypoglycaemic
Absence of ketonuria

Aynsley-Green A, Hussain K, Hall J, et al. Practical management of hyperinsulinism in


Koh TH, Eyre JA, Aynsley-Green A. Neonatal hypoglycaemia: the controversy regarding

Evidence level: V
Should blood glucose of 2.6 mmol/l be the cut-off point for investigating neonatal hypoglycaemia?
The definition of hypoglycaemia in the newborn has remained controversial because of lack of significant correlation between plasma glucose concentration, clinical symptoms, and long-term sequelae (Kalhan, 2000). The authors of this review consider that, in clinically symptomatic infants, the cut-off point for investigation should be 2.5 mmol/l or less. In those who are asymptomatic or who are considered to be at risk for hypoglycaemia (e.g. preterm), 2.0 mmol/L should be the threshold level.

A study on blood glucose concentration in 17 children (Koh, 1988) found abnormal evoked potentials in 10 of 11 children who recorded levels below 2.6 mmol/L. Thus a cut-off point of 2.6 mmol/L for investigation was suggested. Only 5 infants in this study, however, were less than 1 month old, and there was no indication of how many infants were studied in the first few days of life (Eidelman, 2001).

Pointing out that glucose requirements in the neonatal brain are at least equal to those in adults, and that healthy adults show adverse reactions to blood glucose concentrations of 2.8-3.3 mmol/L, another authority recommends a minimum level of 2.8 mmol/L for infants (Schwartz, 1997).

A questionnaire sent to 420 neonatal paediatricians in the UK and 88 in Australia in 1992 (Koh, 1996) revealed a wide range in their definition of hypoglycaemia (<1(-4) mmol/L). Compared with a similar survey conducted in 1986 (Koh, 1988), there was a significant increase in the number of paediatricians defining safe blood glucose concentrations as being at least 2 mmol/L (78% vs 34% for term babies, 87% vs 22% for preterm babies). The number preferring to maintain levels of >= 2.6 mmol/L trebled as compared to 1986. This change was also noted in textbooks over the same 6-year period.


Evidence Level: V

Are lower blood sugars acceptable in breastfed babies, due to their use of ketone bodies as a fuel source?
A cross-sectional study of 156 term and 62 preterm infants (Hawdon, 1992) found that blood glucose concentrations were significantly lower in breastfed as compared to formula fed babies (mean, 3.6 mmol/L; range, 1.5-5.3 mmol/L vs mean, 4.0 mmol/L; range, 2.5 – 6.2 mmol/L). Absolute concentrations also varied more for preterm than for term infants (1.5 – 12.2 mmol/L vs 1.5- 6.2 mmol/L). None of the breastfed infants were symptomatic, despite 12% having blood glucose concentrations < 2.6 mmol/L. Breastfed infants were shown to respond to low blood glucose concentrations by increased production of ketone bodies, although the preterm infants did not have this ability.

Glucose concentration in symptomatic infants should be maintained at > 2.6 mmol/L. Asymptomatic infants with documented hypoglycaemia should continue breastfeeding and have the blood glucose concentration rechecked within 2 hours, starting iv glucose treatment if the hypoglycaemia persists (Eidelman, 2001).

What are the minimum blood requirements for investigation of persistent hypoglycaemia?
In a series of 26 patients diagnosed between 1975 and 1995 (Cresto, 1998), diagnosis was obtained by blood testing following a fasting tolerance test discontinued when symptoms appeared or blood sugar concentration reached 2.2 mmol/L or below. Blood was tested to measure insulin, glucose, C-peptide, free fatty acid and 3-hydroxybutyrate. The insulin:glucose ratio was calculated as pmol/L insulin:mmol/L glucose. A ratio less than 40 was considered normal and > 100 diagnostic of hyperinsulinism. Values between 40 and 100 were considered suggestive of persistent hyperinsulinaemic hypoglycaemia of infancy. Hyperinsulinism also inhibits the normal response to hypoglycaemia, preventing the increase of free fatty acids (normal values 478 +/- 14.3) and 3-hydroxybutyrate (normal values 58-170); low values for these will therefore reinforce the diagnosis (Landau, 1982). Elevated serum C-peptide concentration is also a useful tool in diagnosing hyperinsulinism. Normal values are 150 – 350 pmol/L (Bommen, 1984).


Evidence Level: V

N.B. No protocols or policies from other units have been identified

Last amended December 2007
What is the predictive value of 
a) Clinical features 
b) Laboratory investigation in petechial/purpuric rashes in children?

Children presenting with petechial/purpuric rashes need prompt treatment if they have a meningococcal infection, but 90% or more of them do not and may suffer more from receiving unnecessary antibiotics (Nielson, 2001). A prospective study involving 264 infants and children hospitalised with fever and skin haemorrhage (Nielsen, 2001) identified five clinical variables that distinguished between meningococcal disease and other conditions on admission:

1. Skin haemorrhages of characteristic appearance
2. Universal distribution of skin haemorrhages
3. Maximum diameter of one or more skin haemorrhages greater than 2 mm
4. Poor general condition (based on a scoring system by McCarthy et al, 1982)
5. Nuchal rigidity

If any two or more of these were present, the probability of identifying a patient with meningococcal disease was 97%, with a false positive rate of 12%. The only laboratory tests found useful in this study were absolute band count (p=0.002, adjusted OR 38.3, 95% CI 3.8 to 385.1) and C reactive protein (p=0.0001, adjusted OR 12.4, 95% CI 4.7 to 32.7).

Another prospective study, involving 233 infants and children (Wells, 2001) also found the C reactive protein test helpful in that no child with a normal result (< 6mg/l) had meningococcal infection. Again, however, clinical features were found to be of most use; children with meningococcal infection were found to be:

1. More likely to be ill (OR 16.7, 95% CI 5.8 to 47.6)
2. To have an axillary temperature >38.5°C (OR 8.0, 95% CI 2.7 to 23.8)
3. To have extensive purpura (OR 37.2, 95% CI 11.7 to 118.3)
4. To have a capillary refill time of > 2 secs (OR 29.4, 95% CI 9.4 to 92.6)

No child with a rash confined to the distribution of the superior vena cava (head, neck, and chest above the nipple line) had meningococcal infection. This study was the only one identified that looked at the significance of rash alone, without accompanying fever.

The authors of a prospective and retrospective audit of 55 children presenting with fever and a petechial rash (Brogan, 2000) propose using the “ILL criteria” (Irritability, Lethargy, Low capillary refill). These criteria were combined with total peripheral white blood cell count outside the range 5-15 x 10^9/l, and a C reactive protein > 5mg/l to provide a screening test for significant bacterial sepsis. This had a sensitivity (in those patients who had blood cultures performed (n=33)) of 100% (95% CI 48 to 100); specificity 57% (95% CI 37 to 76); positive predictive value 29% (95% CI 14 to 45); negative predictive value 100% (95% CI 79 to 100); pretest number needed to treat (NNT) 6.7; post-positive test NNT 3.3.

The findings of these three papers substantially confirm those of three earlier studies (in 411 (Mandl, 1997), 190 (Baker, 1989) and 129 (Van Nguyen, 1984) patients respectively), i.e. that the general appearance of the child and the extent of the rash were better indications of meningococcal infection than were the findings of laboratory tests.


Evidence Level: IV

No treatment is necessary unless condition is life-threatening?
ITP is, for the majority of children, “a benign self-limiting disorder” (Blanchette, 2008). A study of Nordic centres managing children with ITP divided them according to whether they had treated more than 2/3, from 1/3 to 2/3, or less than 1/3 of children within 14 days of diagnosis (Treutiger, 2007). At one month, there was no difference between the groups in recovery rates or in the numbers of children who developed chronic disease.


Evidence Level: IV

Last amended July 2008
The incidence of primary immunodeficiency disease (PID) is between 1 in 10,000 and 1 in 100,000.

The reported incidence of PID varies widely, according to the source consulted. For example, a review on the subject (Turvey, 2009) states that: “While individual PIDs are rare, as a group, it is estimated that between 1:2000 and 1:10,000 live births are affected by a PID”. At the other extreme, a national probability sample of 10,000 households in the US (Boyle, 2007) suggested an incidence of 1 in 1,200.


Evidence Level: V

Last amended March 2011
What is the best access site for intraosseous infusion of the tibia?

Most authorities recommend insertion 1-3 cm distal to the tibial tuberosity (Cilley, 1992; Ryder, 1991). A study comparing insertion sites in 28 tibias from 14 infant cadavers (Boon, 2003) advised that a site at least 10 mm distal to the tibial tuberosity combined ease of insertion with maximum protection for the epiphyseal growth plate. Complication rates from this procedure are low, however, and a prospective, blinded, observational study in 10 children (Fiser, 1997) found no significant difference in tibial length one year following intraosseous infusion using the usual insertion site.


Evidence Level: IV

Last amended December 2007
Toxicity is likely at levels of iron $\geq 20$ mg/kg?

A review on this subject (McGuigan, 1996) suggests that “Although a single value for the toxic dose has not been established, significant gastrointestinal manifestations occur following the ingestion of 20 mg of elemental iron per kilogram of body weight while systemic toxicity may occur following the ingestion of at least 60 mg of elemental iron per kilogram of body weight.”

A second, more recent review (Madiwale, 2006) states that: “Evidence-based consensus guidelines have determined that the threshold for referral to a healthcare facility is 40 mg/kg of elemental iron in the form of adult iron formulations.”


Evidence Level: V

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:


Are isotonic fluids less likely than hypotonic fluids to cause hyponatraemia?
A randomised controlled trial in 258 children aged 6 months to 16 years of age (Choong, 2011) compared postoperative fluid maintenance with isotonic (0.9% saline) with hypotonic (0.45% saline) regimens. The hypotonic group (n=130) had significantly increased risk of hyponatraemia (40.8% vs 22.7%; RR 1.82 [95% CI: 1.21-2.74]; P = .004) compared to the isotonic group (n=128). Administering isotonic fluids did not increase the risk of hypernatraemia (RR 1.30 [95% CI 0.30-5.59]; P = .722).


Evidence Level: II

Last amended July 2012
JAUNDICE
Supporting Information

This guideline and supporting information has been prepared with reference to the following:


What is the incidence of prolonged neonatal jaundice in term and preterm newborns?
Jaundice persisting beyond 14 days of age (prolonged jaundice) can (rarely) be a sign of serious underlying liver disease (Hussein, 1991). Jaundice persists beyond 14 days in 15-40% of breastfed infants, depending on the series studied (Hannam, 2000). A prospective study of all 7139 term infants born at King’s College Hospital (London) between January 1997 and June 1998 (Hannam, 2000) found 154 with prolonged jaundice, one of which had conjugated hyperbilirubinaemia (0.14 per 1000 live births).

Another study of 3661 babies in Sheffield (Crofts, 1999) found 127 who were jaundiced at 28 days, of which 125 were breastfed (9.2%).

Although preterm infants, whose livers are more immature, have prolonged jaundice more commonly than term infants (Fenton, 1998) there appear to be no studies of incidence in this group (Lucas, 1986).

The first large, prospective study of severe hyperbilirubinaemia in UK infants in the first month of life (Manning, 2007) found an incidence of 0.7 per 1,000 live births (95% CI 0.5 – 0.8).

Evidence level: IV

When does serum bilirubin level of a neonate fall to adult level?
High serum bilirubin levels in the first days of life “decline during the next several weeks to the values commonly found in adults” (Dennery, 2001). This time period is inexact, although 14 days is commonly accepted as a cut-off point for investigation of sustained jaundice (Fenton, 1998).

Evidence level: V
What is the incidence of glucose-6PD deficiency in British white children?
Glucose-6PD deficiency is most common amongst Greek, Sardinian, Chinese, Jamaican and South East Asian populations (Beutler, 1994; Valaes, 1994; Singh, 1986; Doxiadis, 1961). There appear to be no epidemiological studies in British white children. The prevalence amongst white northern European populations has been estimated as less than 1 in 1,000 (Beutler, 1995).


Singh H. Glucose-6-phosphate dehydrogenase deficiency: a preventable cause of mental retardation. BMJ 1986;292:397-8


Evidence level: V

What is the incidence of hereditary spherocytosis presenting with prolonged neonatal jaundice only?
The incidence of hereditary spherocytosis in Northern Europeans has been estimated at 1:5,000 (Morton, 1962), although milder forms may be asymptomatic and therefore the true incidence may be higher. A recent review (Delhommeau, 2000) has taken this into consideration and suggested an incidence of 1:2,000. This condition has received little attention in the neonatal period (Delhommeau, 2000) and consequently no information can be identified concerning prolonged jaundice as the sole presenting symptom.


Evidence level: V

What is the incidence of sickle cell anaemia in the British white population?
The first evidence-based rates for sickle-cell in the UK (Hickman, 1999) give a zero incidence in the white population. The evidence level for this is “D” which equates to “Expert advice based on unpublished data”.


Evidence level: V

What percentage of congenital hypothyroidism is missed in the Guthrie test?
The first screening programme (Dussault, 1975) used a T4 assay alone, which had the potential for missing some babies with ectopic glands in whom T4 concentrations could be in the low-to-normal range. Later programs used TSH assay, which, although unable to detect secondary (pituitary or hypothalmic) hypothyroidism, proved extremely effective in identifying even mild cases of primary hypothyroidism (Hulse, 1980).

A report of the first 3 years of the UK national screening programme (Grant, 1988) recorded 493 cases in a total of 1,941,146 live births (incidence 1:3937). 4 cases were missed (0.8%).
which was similar to the North American experience (Holtzman, 1986) of 2 missed cases for every 1 million infants screened.


Evidence level: V

What percentage of urinary tract infection in newborns presents with jaundice only?

The association of urinary tract infection with neonatal jaundice has been well-recognised (Anon, 1971; Arthur, 1967), but no percentages can be identified for newborns presenting with jaundice alone. Most infants in published series have anaemia and/or sepsicaemia in addition to their jaundice (Hannam, 2000). Jaundice as the main presenting symptom of UTI appears to predominate in male infants at a ratio of 3:1 (Seeler, 1969), unlike the female preponderance generally found in paediatric UTI.

A study in 102 infants with asymptomatic, unexplained indirect hyperbilirubinaemia in the first two weeks of life (Bilgen, 2006) found UTI in 8 cases (8%). The authors concluded that urine culture should be considered in the bilirubin work-up of infants older than three days of age with an unknown etiology.

Anon. Urinary tract infection presenting as jaundice. BMJ 1971;iii:546-7


Evidence level: V

At what level of total serum bilirubin (TSB) does kernicterus occur in a) the term baby b) the preterm baby of 32 weeks? At what level should phototherapy be started in the term baby?

The American Academy of Pediatrics (Anon, 2004) states that “It is not known at what bilirubin concentration…significant risk of brain damage occurs or when the risk of damage exceeds the risk of treatment”. Cases of kernicterus have occurred at TSB levels below 200 micromol/l (Gustafson, 1995). This level of uncertainty persists (Wennberg, 2006): “There are insufficient published data to precisely define sensitivity and specificity (of TSB) in determining risk for acute bilirubin neurotoxicity or chronic sequelae (kernicterus).”

One authority (Ives, 1999) suggests that the threshold lies “somewhere between 400 and 650 micromol/l”. The AAP (Anon, 1994) recommends exchange transfusion and intensive phototherapy when serum bilirubin is >/= 430 mmol/l if age 25-48 hours or >/= 510 mol/l if >48 hours. Standard phototherapy should begin at 257 micromol/l or 308 micromol/l for the same age bands, in the term or near term infant.
Data from the Pilot Kernicterus Registry (Johnson, 2002) showed that the median total serum bilirubin (TSB) concentration of infants on readmission to hospital with kernicterus was 600 micromol/l (350 mg/l).

The most recent information on this subject (Bhutani, 2004) indicates that TSB concentrations of >342 micromol/l (>200 mg/l) should be a cause for concern and that values >/= 513 micromol/l (>=/= 300 mg/l) should be considered “dangerous”. TSB concentrations are, however, poor predictors of bilirubin toxicity in the sick or preterm infant (Bhutani, 2004). Although “free” or unbound bilirubin may provide a more accurate measure, no tests for this have been validated to date (Bhutani, 2004).

A sliding scale has been suggested, based on infant weight, to indicate when intensive phototherapy should be started, but exchange transfusion is recommended when TSB >190 mL/kg (Bhutani, 2004).

NICE guidelines (2010) found that “There is a lack of good-quality evidence on the association between hyperbilirubinaemia and kernicterus or other adverse sequelae.”


Evidence Level: V

Can gamma-glutamyl transpeptidase (GGTP) be useful in distinguishing neonatal hepatitis (NH) from extrahepatic biliary atresia (EHBA)?

A study in 132 patients (Arora, 1992) found that serum GGTP at a cut-off level maintaining 100% sensitivity for EHBA (< 150 IU L(-1)), used in conjunction with non-excreting 99mTc-mebrofenin IDA scans, reduced the false positivity of individual tests. In this series, operative cholangiograms would have been avoided in 21 patients having both tests, vs 9 when only IDA scan was performed.

A study in 47 infants with EHBA, 10 with NH and 130 age-matched healthy controls (Yamagiwa, 1996), noted significant differences in GGTP levels between the EHBA and NH infants at 6 weeks of age (314 +/- 232 IU/L vs 69 +/- 58 IU/L).

A much earlier study in 17 infants aged 5-16 weeks (Wright, 1960) found that the mean maximal GGTP level in NH patients (183 +/- 54 IU/L) was significantly lower than that found in EHBA patients (760 +/- 492 IU/L).


Evidence Level: IV

What is the optimal dose and duration of treatment in total parenteral nutrition (TPN) related cholestasis?

“To date, there is no universally accepted treatment for intractable TPN-associated cholestasis” (Al-Hathlol, 2006).

BNF for Children advises ursodeoxycholic acid (UDCA), 10 mg/kg 3 times a day.

Most studies have included very small numbers of patients. A pilot study in 7 children (Spagnuolo, 1996) found that UDCA took 4-8 weeks to normalise biochemical markers of cholestasis. Another, in 13 infants (Al-Hathlol, 2006) used a dose of 15-20 mg/kg/day and found that although patients responded from the second week of therapy, about four months of treatment were needed before normalisation occurred.

An alternative treatment is cholecystokinin, which needs to be administered intravenously for 3-5 days in a dose of 2-4 IDU/kg (Teitelbaum, 1997; Teitelbaum, 1995; Rintala, 1995).


Evidence Level: IV

What is the threshold for home phototherapy in patients with criggler najar?

No firm evidence has been identified with which to answer this question, but case reports mention a threshold serum bilirubin concentration of 15 mg/dL (0.833 mmol/L) (O’Reilly, 1988; Shevell, 1987). Home phototherapy is a relatively recent service in the UK, the first such service being reported in 2004 (Walls, 2004).


Evidence Level: V

What are the most appropriate tests to be ordered for prolonged jaundice?

A prospective study in 144 infants (Hannam, 2000) concluded that “the number of investigations may safely be reduced to: a total and conjugated bilirubin, packed cell volume, glucose-6-phosphate dehydrogenase level (where appropriate), a urine for culture and inspection of a recent stool sample for bile pigmentation”.
How frequently are the classic diagnostic criteria seen?
The cause of Kawasaki disease is still unknown and thus no diagnostic tests exist (Rowley, 1999). Diagnosis is therefore by clinical criteria (Dajani, 1993). This is defined as fever of at least 5 days’ duration, plus the presence of four of the following:
changes in extremities
polymorphous exanthem
bilateral conjunctival injection
changes in the lips and oral cavity
cervical lymphadenopathy
and no evidence of another disease with similar clinical features.
Prompt diagnosis is vital in reducing the risk of cardiac complications (Rowley, 1999). The incidence of these complications can be reduced from 20-25% to <5% by early treatment with intravenous immune globulin and this, coupled with the increased appearance of atypical cases, has meant that more children are being treated for the condition without meeting diagnostic criteria.
In a retrospective review of 127 patients diagnosed with Kawasaki disease (Witt, 1999), 81 (64%) met the diagnostic criteria and 46 (36%) did not. Of the 15 patients who were found to have coronary artery abnormalities, 9 were from the 46 not meeting the criteria and 6 were from the 81 who did. The authors concluded that the criteria were an insensitive predictor of coronary artery abnormalities and that the treatment of patients not fully meeting the criteria had been justified.
In another retrospective review of 132 Kawasaki patients (Hsieh, 2002), 20 (15%) did not meet the diagnostic criteria, but 5 of these (25%) had coronary artery lesions. Similar conclusions were reached by another retrospective review of 44 cases (Joffe, 1995) in which 9 (20%) were atypical, 5 of which (56%) were in infants, one in 56 patients in which 8 (14%) were atypical (Stapp, 2000) and a small case series of 4 patients (Rowley, 1987).

Witt MT, Minich L, Bohnsack JF, et al. Kawasaki disease: more patients are being diagnosed who do not meet American Heart Association criteria. Pediatrics 1999;104:e10-14

Evidence level: IV

Is echocardiography of value in Kawasaki disease?
American Heart Association guidelines (Newburger, 2004) state that patients with fever and fewer than four principal clinical features can be diagnosed as having Kawasaki disease when coronary artery disease is detected by two-dimensional echocardiography (or coronary angiography). Echocardiography also detects pericardial effusion in approximately 30% of patients with Kawasaki disease (Dajani, 1993). AHA guidelines for long-term management (Dajani, 1994) recommend echocardiography at presentation and at 6-8 weeks and 6-12 months following the onset of symptoms.

The necessity of performing the second follow-up (at 6-12 months) has been questioned by retrospective reviews of 50 patients (Scott, 1999) and 536 patients in a multi-centre study (Tuohy, 2001). Both of these found that no patient having a normal echocardiogram result at 2 weeks – 2 months after onset of symptoms had shown coronary abnormalities at the later follow-up.


Evidence level: IV

What is the optimum dose and timing for intravenous immune globulin? Is a second dose required if fever persists?
The optimal dose of IVIG remains controversial (Sato, 1999). American Heart Association guidelines (Dajani, 1993) recommend a dose of 2 g/kg as a single infusion over 12 hours. This advice has been reinforced in a meta-analysis of 7 RCTs comparing different doses of IVIG (Terai, 1997). Of 1629 patients, those given IVIG at 2 g/kg had a prevalence of coronary abnormalities (at day 30 of the illness) of 5.3%. This compared with 18.1% at doses of < 1 g/kg, and 17.3% at doses of 1.0 - 1.2 g/kg.

A study of 8,751 Japanese patients (Muta, 2004) found no evidence that IVIG treatment on day 4 or earlier (n=4731) was better at preventing cardiac sequelae than later treatment on days 5-9 (n=4020).

A Cochrane review (Oates, 2004) of 16 trials concluded that optimum treatment and timing was 2g/kg within 10 days of onset of symptoms.

Fever persisted for more than 3 days after treatment in 20%-30% of children in a randomised controlled trial in 549 patients comparing single to multiple infusions of IVIG (Newburger, 1991).

In a retrospective report on 13 patients (Sundel, 1993) whose fever did not respond to initial treatment with IVIG, 10 responded to a second dose within 36 hours. In the remaining 3, one responded to a further dose; the other 2 had eventually to be given iv methylprednisolone at 30 mg/kg before resolution of fever was achieved.

A retrospective, multicentre study of 378 patients (Burns, 1998) found that persistent fever was associated with an increased risk of treatment failure (P=0.002) and called for randomised trials to establish the efficacy of re-treatment.
Children with a C-reactive protein level >10 mg/dL, LDH level >590 IU/L and/or haemoglobin value <10 g/dL can be considered non-responsive to IVIG and should be considered for additional treatment at an early stage (Fukunishi, 2000).


Terai M, Shulman ST. Prevalence of coronary artery abnormalities in Kawasaki disease is highly dependent on gamma globulin dose but independent of salicylate dose. J Pediatr 1997;131:888-93

**Evidence Level: I (for initial treatment at 2 g/kg) IV (for re-treatment)**

**Is aspirin efficacious in the treatment of Kawasaki disease?**

Aspirin is administered to patients with Kawasaki disease for its anti-inflammatory and anti-thrombotic effects (Rowley, 1999). In a multicentre, randomised controlled trial involving 549 children (Newburger, 1991) aspirin 80-100 mg/kg/d, with IVIG 2 g/kg reduced the prevalence of coronary abnormalities from 20%-25% to 2%-4%. An American Heart Association consensus statement (Newburger, 2004) recommends the same regime. After fever resolves, aspirin is continued at a lower dose (3-5 mg/kg/d) to decrease platelet adhesiveness (Chung, 1998; Dajani, 1993).

A retrospective case review of 70 patients (Saulsbury, 2002), treated with either high-dose (80-100 mg/kg/d, n=24) or low-dose (3-5 mg/kg/d, n=46) aspirin as an adjunct to IVIG, found no benefit in the high-dose group. None of the 60 patients without coronary abnormalities at the start of treatment had developed them by the end. Mean duration of fever after initiation of therapy was 47 +/- 8 hours in the high-dose group vs 34 +/- 5 hours in the low-dose group.

When the groups were differentiated by IVIG dose, the figures were 44 +/- 6 hours in patients given IVIG 400 mg/kg/dose on 4 consecutive days and 35 +/- 5 hours in patients given 2 g/kg as a single infusion. These findings accord with those of a meta-analysis of 7 RCTs (Terai, 1997) and indicate that IVIG, rather than aspirin, determines the duration of fever.

A UK evidence-based guideline (Brogan, 2002) suggests medium dose (30-50 mg/kg/day in 4 divided doses) aspirin as a compromise.
A Cochrane Review (Baumer, 2006) has concluded that, pending the availability of results from good quality RCTs, there is “insufficient evidence to indicate whether children with Kawasaki disease should continue to receive salicylate as part of their treatment regimen”.


Chung CJ, Stein L. Kawasaki disease: a review. Radiology 1998;208:25-33


Terai M, Shulman ST. Prevalence of coronary artery abnormalities in Kawasaki disease is highly dependent on gamma globulin dose but independent of salicylate dose. J Pediatr 1997;131:888-93

Evidence level: II

Should physical activity be restricted in post-acute patients?
An American Heart Association consensus statement (Newburger, 2004) links permitted physical activity with risk levels I-V as follows:

I (no coronary artery changes at any stage of illness): No restrictions beyond initial 6-8 weeks
II (transient coronary artery ectasia that disappears during acute illness): No restrictions beyond initial 6–8 weeks
III (small to medium solitary coronary artery aneurysm): Patients in 1st decade of life – no restriction beyond initial 6-8 weeks; Patients in 2nd decade – Physical activity guided by stress testing every other year. Competitive contact athletics with endurance training discouraged IV (one or more giant coronary artery aneurysms, or multiple small to medium aneurysms, without obstruction): Patients in 1st decade of life – no restriction beyond initial 6-8 weeks; Patients in 2nd decade – Annual stress testing guides recommendations. Strenuous athletics strongly discouraged. If stress test rules out ischaemia, non-contact recreational sports allowed V (coronary artery obstruction): Contact sports, isometrics, and weight training should be avoided. Other physical activity recommendations guided by outcome of stress testing or myocardial perfusion scan

These risk levels are based on clinical experience and further evidence with which to update the recommendations has not yet been forthcoming (Rowley, 1999).


Evidence Level: V
What follow-up investigations are indicated in Kawasaki disease?
These are again guided by initial risk level, related to the degree of coronary arterial involvement (Dajani, 1994), as follows:

I: None beyond the first year unless cardiac disease suspected
II: None beyond the first year unless cardiac disease suspected; Physician may choose to see patient at 3- to 5-year intervals
III: Annual follow-up with echocardiogram +/- electrocardiogram in first decade of life
IV: Annual follow-up with echocardiogram +/- electrocardiogram +/- chest x-ray +/- additional electrocardiogram at 6-month intervals. For patients in the first decade of life, pharmacologic stress testing should be considered
V: Echocardiogram and electrocardiogram at 6-month intervals and annual Holter and stress testing

In a survey of 308 US paediatric cardiologists on their management of Kawasaki disease patients (Kahwaji, 2002), replies were received from 97 (32%). Despite 1994 guidelines (Dajani, 1994), 61% of respondents provided follow-up for Risk Level I patients and a similar number would prefer to do so for Level II patients.


Evidence Level: V
Blood ketone levels give more accurate readings than urinary ketone levels?
A study in 14 children with DKA or diabetic ketosis (Turan, 2008) found no correlation between urinary ketone and blood pH (P = 0.06) and HCO3 (P = 0.79), but a significant negative correlation between capillary betaOHB and blood pH (r = -0.41, P < 0.05) and HCO3 (r = -0.35, P < 0.05). Capillary betaOHB and urinary ketone levels did not correlate at the beginning and 3.3 +/- 1.4 h after treatment, but did correlate in the third samples taken 7.8 +/- 2.0 h after treatment (r = 0.8, P < 0.05). Capillary betaOHB levels showed good correlation with the degree of acidosis (pH and HCO3). The authors concluded that capillary betaOHB measurement was more sensitive than urinary ketone measurement in reflecting the patient's metabolic status and improvement during treatment.


Evidence Level: IV

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:


What evidence supports a physiological parameter based approach to diagnosis and severity assessment?
A retrospective review of 350 patients up to the age of 12 who received hip x-rays over a 2 year period at a hospital in Auckland (Reed, 2009) looked for signs predictive of osteomyelitis and septic arthritis. Fever, non-weight bearing, raised white cell count, raised erythrocyte sedimentation rate and raised CRP were all associated with increased risk. The optimum inflammatory marker cut-off was a CRP of 12 with a sensitivity of 87% and specificity of 91%. X-ray investigation was found to be “of little value” in patients below the age of 9.

A review of the literature (Taekema, 2009) concluded that no single investigation or blood test was capable of distinguishing between septic arthritis (SA) and transient synovitis (TS). No clinical prediction rule had been validated by multi-centre prospective studies involving large numbers of patients. The combined presence of fever, non-weight bearing, CRP >20 or ERP >40, and a WBC >12 was indicative of septic arthritis.

Sonography of the hip joint by the emergency physician (SHEP) may provide additional information to aid the distinction between SA and TS and help to minimize unnecessary blood tests and diagnostic imaging (Shavit, 2006). It has not yet, however, been validated in large scale studies.

A case review of 286 limping children (Delaney, 2007) used multivariate analysis to demonstrate that when all of three variables (duration of symptoms >1, <5 days; temperature >37.0 degrees C; ESR >35 mm/h) were present, predicted probability of infection was 0.66, falling to 0.01 when none were present.

CRP is a better negative predictor than a positive predictor; if CRP is <1.0 mg/dl, the probability that the patient does not have septic arthritis is 87% (Levine, 2003).


Taekema HC, Landham PR, Maconochie I. Towards evidence based medicine for paediatricians. Distinguishing between transient synovitis and septic arthritis in the limping child: how useful are clinical prediction tools? Arch Dis Child 2009;94:167-8

Evidence Level: IV
**Erythrocyte sedimentation rate (ESR) >20 mm/1st hr is indicative of septic arthritis?**

In a retrospective review of 58 children with septic arthritis (Wang, 2003), ESR was elevated (>20 mm/h) in 89% of cases.

A review of 299 children who had ESR measured for an undiagnosed condition (Huttenlocher, 1997) found that serious underlying disease was about 7 times more likely in patients with ESR >50 mm/hr (57/102) than in patients with ESR<20 mm/hr (7/89). ESR >50 mm/hr was “most informative” in patients presenting with limp (likelihood ratio [LR] =8.2) and ESR<20 mm/hr was “reassuring” in the same group of patients (LR=0.3).

A case report (Perry, 1996) demonstrated that a normal ESR (as well as a normal CRP and WCC) cannot be used to confidently exclude suppurative osteomyelitis.


Perry M. Erythrocyte sedimentation rate and C reactive protein in the assessment of suspected bone infection—are they reliable indices? J Roy Coll Surg Edin 1996;41:116-8


**Evidence Level: IV**

**Patients with suspected septic arthritis should be referred for diagnostic aspiration/washout before starting antimicrobials?**

A comprehensive systematic literature review (Kang, 2009) concluded that “Early administration of antibiotics is widely supported in the literature, and although microbiological evidence of infection is preferred, antimicrobials should not be withheld once diagnostic procedures have been performed.”


**Evidence Level: III**

**Polymerase Chain Reaction (PCR) testing is superior to conventional methods of identifying the organisms responsible in cases of septic arthritis?**

“Broad-range PCR followed by sequencing offers several advantages when used to complement culture results for the diagnosis of fastidious bacteria and for patients taking antibiotics” (Fenollar, 2008).

Probe-based real-time PCR assay was found to be extremely accurate in a study of 121 synovial fluid samples from patients with suspected SA (Yang, 2008). The sensitivity and specificity of the assay were 95% and 97%, respectively, versus synovial fluid culture results.

Real-time techniques are easier to interpret and may detect more cases of SA than conventional PCR (Rosey, 2007).

A study in 89 children with suspected SA (Ilharreborde, 2009) found that thirty-six (40%) of the 89 cases had positive culture. Staphylococcus aureus was the main isolate (n = 19/36, 53%), followed by K. kingae (n = 7/36, 19%). Specific real-time PCR identified K. kingae in 24 of the 53 culture-negative cases. Thus, K. kingae was present in 31 (52%) of the 60 documented cases, making it the leading pathogen.

Fenollar F, Levy PY, Raoult D. Usefulness of broad-range PCR for the diagnosis of osteoarticular infections. Curr Opin Rheumatol 2008;20:463-70


Evidence Level: IV

Last amended March 2011
What is the incidence of deep vein thrombosis (DVT) related to long line insertion in children?
A prospective study in a total of 214 patients (101 girls, 113 boys) (Dubois, 2007) found that partial or complete DVT occurred in 20 patients (an incidence of 93.5 per 1000 patients and 3.85 per 1000 catheter-days). Only 1 of the cases was symptomatic. In the univariable analyses, the only variable significantly associated with deep vein thrombosis was the presence of factor II mutation G20210A (OR 7.08, 95% CI 1.11-45.15, p = 0.04), a genetic mutation that increases the risk of a blood clot and that was present in 5 (2.3%) of the 214 patients. This reported incidence is lower than that related to centrally inserted venous catheters described in the paediatric literature (11%-50%).


Evidence Level: IV

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:


Artemisinin combination therapies are of use in the treatment of children with malaria? A systematic review and meta-analysis of seven studies involving 2515 children (Kurth, 2010) found similar efficacy and safety in pooled analyses of paediatric and conventional formulations. 23 (2.0%) of 1154 patients in the paediatric formulation groups and 19 (1.7%) of 1137 in the tablet formulation groups were not cured (RR 1.27, 95% CI 0.66-2.44). Despite similar overall tolerability, the tolerability of drug administration was improved for paediatric formulations as shown by significantly fewer patients with drug-induced vomiting (93 of 1018 and 114 of 837 patients; RR 0.78, 95% CI 0.61-0.99), and drug-related gastrointestinal disorders (8 of 545 and 15 of 358 patients; RR 0.36, 95% CI 0.15-0.85).


Evidence Level: I

Last amended March 2011
This guideline and supporting information has been prepared with reference to:


http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1237797269168


http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1194947389261

It is not possible to differentiate viral from bacterial meningitis clinically?

Secondary analysis of a retrospective multicentre hospital-based cohort study in 198 children with a mean age of 4.8 years (Dubos, 2010) compared the sensitivity and specificity of the BMS (start antibiotics in case of seizure, positive cerebrospinal fluid (CSF) Gram staining, blood neutrophil count >=10 x10(9)/l, CSF protein level >=80 mg/dl or CSF neutrophil count >=1000 x10(6)/l) and the Meningitest (start antibiotics in case of seizure, purpura, toxic appearance, PCT level >=0.5 ng/ml, positive CSF Gram staining or CSF protein level >=50 mg/dl) using a McNemar test.

The BMS and Meningitest both showed 100% sensitivity (95% CI 96% to 100%). The BMS had a significantly higher specificity (52%, 95% CI 42% to 62% vs 36%, 95% CI 27% to 46%; p<10(-8)). The authors concluded that both tests could be usefully used with caution, but that the BMS test would avoid more unnecessary treatment with antibiotics.


Evidence Level: IV

Corticosteroids are of benefit in any case of suspected meningitis without a purpuric rash?

A Cochrane systematic review of 18 studies in 2750 children and adults (van de Beek, 2007) found that dexamethasone in doses ranging from 0.4 to 0.9 mg/kg given for 2- 4 days reduced severe hearing loss (RR 0.61, 95% CI 0.44 to 0.88) in children. There was also reduced mortality amongst the study population as a whole (RR 0.83, 95% CI 0.71 to 0.99).


Evidence Level: I
Excessive fluid boluses should be avoided?
It is generally believed (Maconochie, 2008; Brown, 1994) that brain oedema may be caused
or aggravated by the administration of large amounts of fluid, although this has not been
demonstrated in experimental studies (Tauber, 1993). SIGN guidelines (2008, see above)
state that fluid resuscitation > 60/ml/kg may be “often required” but that fluids should be
carefully administered according to clinical need.

1994;23:93-8

Maconochie I, Baumer H, Stewart MER. Fluid therapy for acute bacterial meningitis.
Cochrane Database of Systematic Reviews 2008, Issue 1. Art. No.: CD004786

Tauber MG, Sande E, Fournier MA, et al. Fluid administration, brain edema, and
cerebrospinal fluid lactate and glucose concentrations in experimental Escherichia coli

Evidence Level: V

What is the risk of cerebral herniation (coning) associated with lumbar puncture to
diagnose bacterial meningitis? Is the age of the patient a factor?
Herniation or coning of the brain, the result of markedly raised intracranial pressure, is a
common post-mortem finding in acute bacterial meningitis and may be the direct cause of
death in up to 30% of child cases (Addy, 1987). Symptoms and signs of herniation occur in
about 5% of cases of bacterial meningitis (Joffe, 2007; Horwitz, 1980).
No consensus exists on the subject of whether lumbar puncture should or should not be
routine in all cases of suspected bacterial meningitis (Flidel-Rimon, 2011). Coning can
happen with or without lumbar puncture and also may occur in patients with a normal CT scan
(Shetty, 1999; Stephenson, 1998; Rennick, 1993).
A retrospective review of 445 children over 30 days old (Rennick, 1993) identified herniation
in 14 (45%) of the 31 children who died. 19 episodes of herniation occurred in the 17 children
who had a lumbar puncture; 12 episodes occurred in the first 12 hours following lumbar
puncture. CT results were normal in 5 (36%) of the 14 episodes in which scanning was
performed around the time of the herniation.
A retrospective review of 252 cases in west Gloucestershire (Wylie, 1997) recorded 17 deaths
(6.7%), of which 4 were “directly or indirectly associated with lumbar puncture”.
In a study of 123 children between 6 weeks and 15 years old seen consecutively at a
university teaching hospital in Nigeria (Akpede, 2000), 18 (15%) showed evidence of
herniation. Patients were divided into low or high risk groups according to a scoring system
recording the presence or otherwise of convulsions, fever >3 days, age <= 12 months, shock,
coma and temperature <36.6°C. RR of herniation in high vs low risk groups was 66.6 (95% CI
9.3 – 477.1) and of death or neurological sequelae, 2.6 (95% CI 1.8 – 3.7). The authors
concluded that lumbar puncture should not be performed in patients categorised as high risk.
Lumbar puncture is still performed in up to a third of patients with contraindications in some
units (Winrow, 1998).
A Dutch team (Oostenbrink, 2001) have designed a clinical prediction rule that successfully
identified 99 of 286 patients (aged 1 month to 15 years) with suspected bacterial meningitis
that did not in fact have the disease. No cases were missed, and the authors suggest that the
rule could be used to identify those patients not needing lumbar puncture.
A similar study from an Israeli team (Brik, 1997) proposed that lumbar puncture need not be
routine in infants under 3 months of age not meeting the proposed criteria for being at high
risk.
Other investigators (Wiswell, 1995) have claimed that the diagnosis of neonatal bacterial
meningitis “occasionally will be delayed or missed completely” if lumbar puncture is omitted.
It is unclear whether older children are at higher risk of coning. The 19 children who suffered
21 episodes of coning in the Rennick series (1993) ranged in age from 4 months to 15 years,
with an average age of 41 months.

Akpede GO, Ambe JP. Cerebral herniation in pyogenic meningitis: prevalence and related dilemmas in emergency room populations in developing countries. Dev Med Child Neurol 2000;42:462-9


Stephenson T. Coning may occur without lumbar puncture being done. BMJ 1998;316:1015

Winrow AP. Lumbar puncture is still performed in patients with contraindications. BMJ 1998;316:1015


Evidence Level: IV (but no consensus)
NEPHROTIC SYNDROME
Supporting information

This guideline and supporting information has been prepared with reference to the following:

Anon. Consensus statement on management and audit potential for steroid responsive nephrotic syndrome. Report of a Workshop by the British Association for Paediatric Nephrology and Research Unit, Royal College of Physicians. Arch Dis Child 1994;70:151-7


http://pediatrics.aappublications.org/content/124/2/747.full.pdf+html

Is antibiotic prophylaxis to prevent peritonitis caused by *S Pneumoniae* indicated in children with nephrotic syndrome?

An American Academy of Pediatrics report (Overturf, 2000) on children at increased risk of pneumococcal infection states: “Reduction of infection risk, compliance with prophylaxis, and effects on nasopharyngeal colonization with pneumococci have not been studied in nephrotic syndrome.”

A review on the subject (McIntyre, 1998) concludes that although “penicillin prophylaxis…is not of proven benefit for nephrotic syndrome”, the following subgroups of patients are most likely to benefit: Children under 2 years of age, with unresponsive or frequently relapsing disease, or who have had a previous episode of pneumococcal infection. Serious infections may occur with the increase in penicillin-resistant pneumococci. A case report of two infants with penicillin resistant pneumococcal peritonitis whilst receiving penicillin prophylaxis (Milner, 1987) recommends pneumococcal vaccination at 2 years of age and no prophylaxis for under 2 years. Similar cases have been reported more recently (Ilyas, 1996).


Evidence Level: V

Is influenza vaccination safe and effective in children with nephrotic syndrome?

A case-control study in 19 children with nephrotic syndrome and 10 healthy controls (Poyrazoglu, 2004) found that influenza vaccine (0.25 ml for under 6 yrs of age and 0.5 ml for over 6 yrs of age) raised the percentage of children with protective antibody titres in the NS group from 10.5% before vaccination to 78.9% at 1 month and 87.5% at 6 months following vaccination. The mean concentration of specific IgG antibodies to influenza An increased 6-fold at 1 month and approximately 14-fold at 6 months. No adverse effects were recorded.
Similar results have been obtained in other studies (Brydak, 1998; Sheth, 1979; Sheth, 1978). Adverse effects have been uncommon and limited to transient rises in protein levels or mild cold-like illnesses, other than one child who had exacerbation of nephrotic syndrome (Sheth 1979).

Meningococcal C conjugate vaccine is also safe in this group of patients (Taylor, 2007).


Evidence Level: IV

**Femoral blood sampling is contraindicated due to the risk of thrombosis?**

The association between nephrotic syndrome and femoral arterial thrombosis is well recognised in a number of case reports in both children and adults (Holt, 2000; Nitatori, 1987; Sullivan, 1983; Patel, 1978; Harrison, 1972; Cameron 1971; Goldbloom, 1967).


Evidence Level: V

**For how long should corticosteroid therapy be continued?**

A Cochrane systematic review of 24 trials in 1726 children (Hodson, 2007), 1292 of whom were in their first episode of nephrotic syndrome, concluded that “first episodes” should be treated for at least 3 months, with an increase in benefit being seen for up to 7 months of treatment. The baseline risk of relapse after 2 months of therapy following a first episode was 60%, reducing by 33% with 4 weeks of daily prednisolone followed by alternate-day therapy for 6 months.
Children receiving long-term prednisolone alternate day treatment may be at risk of hypothalamic-pituitary-adrenal axis suppression and should therefore be monitored for this (Abeyagunawardena, 2007).

A randomised prospective study in 80 children (Mishra, 2012) compared standard (3 month) prednisolone treatment with a prolonged (5 month) regime. The mean relapse rate (0.63 vs. 1.54; p=0.011) and cumulative risk of relapse per patient per month (0.05 vs. 0.131) were significantly lower in the prolonged than the standard treatment. Total relapses in patients followed up for 12 months were significantly lower in the prolonged-therapy as compared with the standard-therapy group (21.6% vs. 70.2%; p=0.001). Cumulative percentage of patients with sustained remission at 12 months was significantly higher in the prolonged-therapy than the standard-therapy group (76% vs. 29%). Mean cumulative dose of prednisolone with prolonged therapy was significantly lower than with standard treatment (p=0.033). Steroid side effects such as cushingoid appearance, hirsutism, striae and hypertension were comparable in both treatment groups.

Evidence Level: I

What treatment is appropriate for the steroid-resistant patient?
A meta-analysis of 11 trials and 2 systematic reviews (Colquitt, 2007) found no convincing evidence of benefit from any of the interventions studied, although there was suggestive evidence of a beneficial effect of ciclosporin on remission rates and of cyclophosphamide on time to remission. The authors called for a well-designed, adequately powered RCT comparing ciclosporin with other treatments.

A Cochrane systematic review of 26 studies in 1173 children (Hodson, 2008) concluded that eight week courses of cyclophosphamide or chlorambucil and prolonged courses of ciclosporin and levamisole reduce the risk of relapse compared with corticosteroids alone. A small controlled multicentre randomised open label trial in 32 children (Plank, 2008) compared a group given ciclosporin (n = 15) with another group (n = 17) given cyclophosphamide. Partial remission was achieved by 7 (46%) of the ciclosporin group vs 2 (11%) of the cyclophosphamide group after 24 weeks. Numbers reaching complete remission were 2 (13%) and 1 (5%) respectively.

Evidence Level: I

Last amended November 2012
NOTIFIABLE INFECTIOUS DISEASES AND FOOD POISONING
Supporting information

This guideline and supporting information has been prepared with reference to the following:

Health Protection Agency list of notifiable diseases:

http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/NotificationsOfInfectiousDiseases/ListOfNotifiableDiseases/

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:


http://journals.lww.com/jpgn/toc/2005/11002

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:

Intravenous antibiotics are preferred to oral antibiotics?
No papers were identified that directly addressed this question. This lack of evidence was confirmed by a “BETS” report that also failed to find any relevant studies (Al-Nammari, 2007).
Al-Nammari S. Should a child with preseptal periorbital cellulitis be treated with intravenous or oral antibiotics? Emerg Med J 2007;24:128-9

Evidence Level: V

Last amended July 2012
What is the most appropriate antibiotic regimen in osteomyelitis?

A systematic review of the subject (Howard-Jones, 2010) found no randomised controlled trials comparing different antibiotic regimens or comparing duration of antibiotic treatment for chronic or sub-acute osteomyelitis in children. A total of 14 observational case series published between 1973 and 2008 were identified. Most children with chronic osteomyelitis received 4-6 weeks of parenteral antibiotics followed by oral antibiotics to a total duration of 3-6 months. Small observational studies suggest that a shorter duration of parenteral and oral antibiotics may be equally effective.


Evidence Level: I

Last amended May 2011
This guideline and supporting information has been prepared with reference to the following:


The Wong and Baker Pain Assessment Scale is an appropriate tool to use with children age ≥ 4 years of age?

A study in 75 children aged 3-15 years (Shavit, 2008) compared an observational tool (Alder Hey Triage Pain Score) with the Wong & Baker. The AHTPS scores were significantly lower than those measured by the Wong & Baker (p<0.001) and the authors concluded that observational tools underestimated children’s pain and should not be used in children younger than 3 years of age.  

A blinded study in 86 patients aged 3-15 years (Rajasagaram, 2009) compared pain assessment by the child, parent and triage nurse using the Wong & Baker scale. The median (inter-quartile range) pain scores recorded were 6.5 (5.0-8.0), 6.0 (5.0-7.5) and 4.0 (3.0-6.0), respectively. There were significant differences between the pain scores of the three groups (P < 0.001, Kruskal-Wallis test). The nurses’ score was significantly lower than both the parents’ and the children's scores (P < 0.001, Mann-Whitney U test). There was no significant difference between the parents and children's scores (P = 0.11, Mann-Whitney U test). The nurses scored consistently lowest regardless of the cause of the pain or the child's age or gender. The authors noted that pain relief should ideally be based on the assessment of the child or parent, rather than that of the nurse.


Evidence Level: IV

Last amended May 2011
PARACETAMOL POISONING IN CHILDHOOD
Supporting information

This guideline and supporting information has been prepared with reference to the following:

Ferner RE, Dear JW, Bateman DN. Management of paracetamol poisoning. BMJ 2011;342:d2218

**Gastric lavage/emesis is not indicated?**
Both of these treatments are now considered potentially hazardous and have largely given way to the use of activated charcoal or supportive treatment only. A retrospective review carried out at Christchurch Hospital in New Zealand (Dillon, 2002) found that in 1994, 36% of children were treated with syrup of ipecac. By 1996, only 9% were given ipecac, whilst 49% were treated with activated charcoal. By 1999, 12% were treated with activated charcoal and 88% received no decontamination treatment at all.


**Evidence Level: V**

Last amended June 2012
How likely is a rash of this sort to be indicative of a serious infection in a child?

A systematic review of 30 studies (Van den Bruel, 2010) found a positive likelihood ratio range of 6.18 – 83.70 for petechial rash as a marker of serious infection in children in developed countries.


Evidence Level: I
This guideline and supporting information has been prepared with reference to the following:


It is not necessary to send a pleural fluid culture routinely before chest drain insertion if the cause is likely to be infective?

BTS guidelines (Balfour-Lynn, 2005) state that cytological analysis of pleural fluid is only necessary “If there is any indication the effusion is not secondary to infection”.


Evidence Level: V (Expert consensus guideline)
This guideline and supporting information has been prepared with reference to:


The oral route is preferable to the IV route for the administration of antibiotics?
A Cochrane review of two RCTs in 1836 children (Rojas, 2006) concluded that “Oral antibiotics appear to be as effective as parenteral antibiotics in the treatment of severe pneumonia in children”. Patient acceptance and compliance is significantly better with oral administration, which is thus to be preferred wherever possible. This echoes the advice given in BTS guidelines (Anon, 2002).
A randomised controlled equivalence trial in 246 children (Atkinson, 2007) found that the median time for temperature to settle was 1.3 days in both the oral and intravenous groups.


Evidence Level: I

Clarithromycin is indicated if mycoplasma is suspected?
A Cochrane review of 7 studies in a total of 1912 children (Mulholland, 2010) found “insufficient evidence to draw any specific conclusions about the efficacy of antibiotics for this condition in children (although one trial suggests macrolides may be efficacious in some children with LRTI secondary to Mycoplasma).” The continuing need for high-quality RCTs in this area was stressed.


Evidence Level: I

Physiotherapy is of benefit, once cough is productive?
A review of the literature (Gilchrist, 2008) found no evidence to support the use of physiotherapy in these patients. Only 3 poorly-constructed studies were identified, and better quality research is needed.
A randomised controlled trial in 98 children (Paludo, 2008) also found that physiotherapy did not hasten clinical resolution and that the intervention group (n=51) had a longer duration of coughing (5.0 vs 4.0 days, p=0.04) and of rhonchi on lung auscultation (2.0 vs 0.5 days, p=0.03) than the control group (n=47).

Gilchrist FJ. Is the use of chest physiotherapy beneficial in children with community acquired pneumonia? Arch Dis Child 2008;93:176-8


Evidence Level: II

Last amended December 2011
What evidence supports management decisions in paediatric pneumothorax?
A review of this subject (Robinson, 2009) states that: “There is a lack of paediatric evidence to guide management decisions, and extrapolation of predominantly adult data to younger age groups should not be encouraged. Given the relatively low apparent incidence, a multicentre approach to future research is required in order to generate the evidence required for informed management of PSP in children.”


Evidence Level: V

Last amended March 2011
Most childhood poisoning incidents are accidental?
An analysis of deaths certified as due to poisoning in England & Wales, 1968-2000, in children aged <10 years (Flanagan, 2005) found that accidental deaths declined from 151 in 1968 to 23 in 2000, but homicides and open verdicts varied from 5 to 20 per year, with no clear trend. Homicide or open verdict was recorded in half of the 47 fatal opiate poisonings. Opioids have superseded antidepressants as the commonest agents encountered in fatal poisoning with drugs in children.


Evidence Level: IV

Last amended March 2011
Intraoperative caffeine can help prevent postoperative apnoea?
A Cochrane review of 3 studies in 88 infants (Henderson-Smart, 2001) found that a single intravenous dose of caffeine 5-10 mg/kg during general anaesthesia reduced the risk of postoperative apnoea (RR 0.09, NNT < 2).

Henderson-Smart DJ, Steer P. Prophylactic caffeine to prevent postoperative apnea following general anesthesia in preterm infants. Cochrane Database of Systematic Reviews 2001, Issue 4. Art. No.: CD000048

Evidence Level: I

Last amended December 2007
This guideline and supporting information has been prepared with reference to the following:

Anon. Perioperative fasting in adults and children: an RCN guideline for the multidisciplinary team. London: Royal College of Nursing, 2005

**Solid food up to 6 hrs and clear fluids up to 2 hrs pre-operatively may be taken without adverse effects?**

A Cochrane systematic review of 47 randomised controlled comparisons from 25 trials involving 2,543 children (Brady, 2009) found that those following this regime did not experience higher gastric volumes or lower gastric pH values than those who fasted.


**Evidence Level: I**

Last amended April 2010
Initial investigations should include both renal ultrasound scan and plain abdominal film?
A retrospective study in 28 children with proven renal calculi (Smith, 2000) demonstrated that, while 100% of the calculi visible on plain films were also visible on ultrasound scan, the scan provided other clinically significant findings that were not apparent on plain films. Ultrasound gave a better indication of the size and distribution of calculi, as well as showing areas of unqualified matrix that were not otherwise visible.


Evidence Level: IV

Last amended November 2012
What is the incidence of acute renal failure in children?
A review of this topic (Andreoli, 2009) states that: “No epidemiology studies using an established definition of AKI have been conducted in pediatric patients”.


Evidence Level: V

Last amended March 2011
Serum creatinine is a good diagnostic indicator of renal injury?
A retrospective study of all 3396 admissions to a 20-bed PICU between July 2003 and March 2007 (Schneider, 2010) calculated a RIFLE score for each patient based on percent change of serum creatinine from baseline (risk = serum creatinine x1.5; injury = serum creatinine x2; failure = serum creatinine x3). Primary outcome measures were mortality and PICU length of stay. Logistic and linear regressions were performed to control for potential confounders and determine the association between RIFLE score and mortality and length of stay, respectively. One hundred and ninety-four (5.7%) patients had some degree of acute kidney injury at the time of admission, and 339 (10%) patients had acute kidney injury develop during the PICU course. Almost half of all patients with acute kidney injury had their maximum RIFLE score within 24 hrs of PICU admission, and approximately 75% achieved their maximum RIFLE score by the seventh day. After regression analysis, any acute kidney injury on admission and any development of or worsening of acute kidney injury during the PICU stay were independently associated with increased mortality, with the odds of mortality increasing with each grade increase in RIFLE score (p < .01). Patients with acute kidney injury at the time of admission had a length of stay twice that of those with normal renal function, and those who had any acute kidney injury develop during the PICU course had a four-fold increase in length of stay. Also, other than being admitted with RIFLE risk score, an independent relationship between any acute kidney injury at the time of admission, any acute kidney injury present during the PICU course, or any worsening RIFLE scores during the course and increased length of stay were identified after controlling for the same high-risk covariates (p < .01).


Evidence Level: IV

Last amended March 2011
Children < 10 years of age have an increased risk of salicylate toxicity and may require haemodialysis at an earlier stage?

An “evidence based flowchart” (Dargan, 2002) states that “Children (< 12 y) and the elderly (> 65 yr) are more susceptible to the effects of salicylate poisoning and tend to get more severe clinical effects at lower blood concentrations”. No reference for this is given.

A letter to the Lancet (Mendelson, 1975) remarks that “Although the sensitivity of children to aspirin is often noted, no direct studies, to our knowledge, have been carried out to test the influence of age on salicylate toxicity”.


Mendelson J, Grisolia S. Age-dependent sensitivity to salicylate. Lancet 1975;II:974

Evidence Level: V

Last amended May 2006
This guideline and supporting information has been prepared with reference to the following:


Last amended January 2011
SEPTICAEMIA (INCLUDING MENINGOCOCCAL)
Supporting information

This guideline and supporting information has been prepared with reference to the following:

http://www.meningitis.org/assets/x/50150

If there is evidence/suspicion of bacterial infection prompt effective antibiotic treatment should be initiated within one hour of diagnosis (or as soon as possible) in patients with life threatening infections?
This is in accordance with advice from the Department of Health publication “Antimicrobial stewardship: start smart, then focus. London: DoH, 2011


Last amended November 2012
STATUS EPILEPTICUS
Supporting information

This guideline and supporting information has been prepared with reference to the following:


**Intravenous lorazepam is the treatment of first choice if vascular access is possible?**

Evidence Level: II

A randomised controlled trial in 178 children (Sreenath, 2010) compared a group given intravenous lorazepam 0.1 mg/kg (n=90) with another given a combination of diazepam 0.2 mg/kg and phenytoin 18 mg/kg (N=88) to treat convulsive status epilepticus. There was no statistically significant difference in the two groups (lorazepam versus diazepam-phenytoin combination) in the median time taken to stop the seizure [20s in both groups], the number of subjects requiring more than one dose of the study drug to stop the presenting seizure [lorazepam 6(6.7%) versus diazepam-phenytoin combination: 14 (15.9%); adjusted RR (95% CI)=0.377 (0.377, 1.046); P=0.061] and the number (%) of patients having respiratory depression [lorazepam 4(4.4%) versus diazepam-phenytoin combination 5 (5.6%)]. The authors concluded that lorazepam was as efficacious and safe as the diazepam-phenytoin combination, and recommended the use of lorazepam as a single drug to replace the two drug combination of diazepam-phenytoin.


**Buccal midazolam or diazepam PR is appropriate treatment when vascular access is denied?**

Evidence Level: I

A systematic review (Sofou, 2009) found that buccal midazolam was significantly more effective than rectal diazepam, reaching a seizure-control rate of 70% and recurrence rate of 8%.


Last amended June 2010
Should the dose of hydrocortisone be doubled in the event of stress caused by surgery or illness?
The administration of stress doses of glucocorticoids is an inexact science and is not based on solid evidence (Miller, 2001). Most advice is to err on the side of overdosage, and doses of from 3 times replacement for febrile illness or minor surgery up to 10 times replacement for major accident or surgery have been recommended (Hoffman, 2002). More moderately, specific advice for surgery has been intramuscular administration of twice the day’s physiological requirement at 18 hours before surgery, repeated at 8 hours before (Miller, 2001).


Evidence level: V

Last amended December 2007
Supraventricular tachycardia (SVT) carries a small risk of mortality?
The mortality rate for SVT in childhood is estimated at 1% in congenital heart disease and 0.25% in normal anatomy (Wiest, 2006).

The author of a review (Gillette, 1985) has only encountered sudden death in SVT with two mechanisms: junctional automatic focus tachycardia and Wolff-Parkinson-White syndrome,


Evidence Level: V

Is the starting dose of adenosine given in the flowchart for supraventricular tachycardia appropriate?
Recommended starting doses range from 50 – 100 mcg/kg. A study which included 12 children with 21 episodes of supraventricular tachycardia (Dixon, 2005) found that a starting dose of 50 mcg/kg was effective in < 10% of cases, and that 100 mcg/kg was still only effective in < 50 %. The authors concluded that 100 mcg/kg should be adopted as the minimum starting dose, and expressed a preference for 150 mcg/kg (effective in around 80%).


Evidence Level: IV

Last amended December 2007
Flumazenil is contraindicated in mixed tricyclic and benzodiazepine overdose? Flumazenil has been known to induce convulsions and ventricular arrhythmias in the presence of both types of drugs (Weinbroum, 1997; Havkeros, 1994; Burr, 1989).


Evidence Level: V

Last amended May 2006
TUBERCULOSIS
Supporting information

This guideline and supporting information has been prepared with reference to the following:

NICE. Tuberculosis: Clinical diagnosis and management of tuberculosis and measures for its prevention and control. London, NICE, 2011


Treatment with isoniazid for 6 months helps to prevent recurrence of active disease?
A Cochrane review of 11 trials in 73,375 patients (Smieja, 1999) found that 6 or 12 months of treatment with isoniazid resulted in a reduced risk of developing active TB (RR 0.40; (95% CI 0.31 - 0.52)), over two years or longer. There was no significant difference between 6 and 12 month courses (RR 0.44; 95% CI 0.27 - 0.73 for six months, and 0.38; 95% CI 0.28 - 0.50 for 12 months).


Evidence Level: I

Last amended March 2011
This guideline and supporting information has been prepared with reference to the following:


What is the evidence for the optimal strategy for the use of antibiotics as immediate treatment?
A Cochrane systematic review of 16 RCTs in a total of 1,116 children (Fitzgerald, 2012) found that conventional 10-day antibiotic treatment significantly increased the number of children free of persistent bacteriuria compared to single-dose therapy (6 studies, 228 children: RR 2.01, 95%CI 1.06 to 3.80). Persistent bacteriuria at the end of treatment was reported in 24% of children receiving single-dose therapy compared to 10% of children who were randomised to 10-day therapy. The authors concluded that, although antibiotic treatment was undoubtedly effective, “there are insufficient data to answer the question of which type of antibiotic or which duration is most effective to treat symptomatic lower UTI.”


Evidence Level: I

Prophylactic antibiotics prevent urinary tract infection and/or subsequent scarring?
A systematic review of antimicrobial prophylaxis (Le Saux, 2000) found that most studies identified by a literature search were case series or cohort studies and that the six RCTs found were of low quality. Concern over bacterial resistance and antimicrobial side effects led the authors to conclude that more and better-designed trials were necessary in order to optimise the use of this therapy.
A Cochrane systematic review of 12 studies in 1557 children (Williams, 2011) came to the same conclusion. Although some antibiotics did prevent some infections, adverse effects outweighed benefits overall and more trials were needed.
A literature review on the subject (Mangiarotti, 2000), whilst acknowledging the risks and the lack of knowledge regarding the precise mechanism of action of low-dose antibiotics, concludes that “proper use may be of great value in clinical practice, by reducing the frequency and clinical expression of UTIs and, in some cases such as VUR, significantly helping to resolve the underlying pathology.”
A cohort study involving 74,974 children (Conway, 2007) found that antimicrobial prophylaxis was not associated with decreased risk of UTI (HR 1.01; 95% CI 0.95 – 2.02), but was associated with increased risk (HR 7.50; 95% CI 1.60 – 35.17) of resistant infections.
A systematic review of 8 trials in a total of 677 children ( Mori, 2009) found no evidence of difference between the intervention and control groups in recurrence of symptomatic UTI [four trials, RR 0.96 (95% CI: 0.69-1.32)] and incidence of new or progressive renal scarring [four trials, overall RR 1.15 (95% CI:0.75-1.78)]. The authors concluded that antibiotic prophylaxis was not recommended.
NICE guidelines (NCCWCH, 2007) do not recommend routine antibiotic prophylaxis.
A systematic review and meta-analysis of 11 trials in 2046 patients (Dai, 2010) concluded that “Evidence is lacking that prophylactic antibiotics reduce the incidence of recurrent childhood UTI. Since the reviewed studies had limitations in methodological design, large scale, high quality, placebo-controlled, double-blind trials are required.”


Evidence Level: I

The following tests should be recommended?

a) All children with proven UTI should have a renal ultrasound scan
b) Young children <1 year old should have a micturating cystourethrogram
c) Children <3 yrs should have a DMSA scan even if the ultrasound scan is negative

American Academy of Pediatrics consensus guidelines (AAP, 1999) recommend imaging of the urinary tract in every febrile infant or young child with a first UTI in order to identify those with abnormalities that predispose to renal damage. Imaging should consist of renal ultrasound to detect dilatation secondary to obstruction and a study to detect VUR. Repeat ultrasound scans are also considered unnecessary (Lowe, 2004).

Whilst acknowledging the sensitivity of renal cortical scintigraphy with 99 m Tc-DMSA, the AAP guidelines consider its role is “unclear and requires additional study”.

A recent systematic review and meta-analysis (Gordon, 2003) has demonstrated that VCUG is a weak predictor of renal damage in paediatric patients hospitalised with UTI. A positive test result increased the risk of renal damage by 20%, but a negative result increased the chance of no renal involvement by only 8%.

A survey of 30 Belgian experts in the field (Piepsz, 1999) reveals wide consensus for the use of DMSA for detection of renal sequelae.

A retrospective review of 164 patients aged 0-12 years (Deshpande, 2001), on the other hand, concludes that the routine use of DMSA scans in children over 1 year with a straightforward simple infection “is unhelpful and unnecessary”. The authors argue that, on the basis of £120 per DMSA scan, the cost of detecting one scar in their series of patients was £1,100. This, coupled with the lack of evidence of impact on management (Hoberman, 2003), plus the psychological risks to the patient, supports the authors’ contention that guidelines in 1991 were not prepared with the same attention to risks/benefits that now pertains.

A systematic review of 73 studies (Westwood, 2005) concluded that “There is no evidence to support the clinical effectiveness of routine investigation of children with confirmed UTI”. This view is echoed in a more recent review (Blumenthal, 2006).


Deshpande PV, Jones KV. An audit of RCP guidelines on DMSA scanning after urinary tract infection. Arch Dis Child 2001;84:324-7


Kass EJ, Kernen KM, Carey JM. Paediatric urinary tract infection and the necessity of complete urological imaging. BJU Int 2000;86:94-6


Evidence level: II

Is surgery ever required for reflux?
In the United States, enthusiasm for surgical correction of VUR remains high (Marotte, 2001; Schiepers, 2001; Elder, 2000) and this may also be the case in Australia (Webster, 2000). Endoscopic correction is also supported (Caldamone, 2001; Ogan, 2001; Elder, 2000). In the UK and the rest of Europe, however, several well-designed studies have found no long-term difference in renal function or progression of scarring between medical and surgical treatment (Venhola, 2006; Smellie, 2001; Olbing, 2000; Jodal, 1999). A Cochrane review of 11 studies in 1148 children (Hodson, 2007) concludes: “It is uncertain whether the treatment of children with VUR confers clinically important benefit. The additional benefit of surgery over antibiotics alone is small at best”.

Most renal damage occurs at a very early stage and thus severely damaged or dysplastic kidneys either remain stable or progress to end-stage renal failure despite all efforts to cure the reflux (Nijman, 2001).


Marotte JB, Smith DP. Extravesical ureteral reimplantations for the correction of primary reflux can be done as outpatient procedures. J Urol 2001;165:2228-31

Nijman RJ. Vesicoureteric reflux: to operate or not? Lancet 2001;357:1309-10


Evidence level: I

Is testing fresh urine for nitrites and leukocytes an effective method for detecting urinary tract infection?

A study of 689 fresh paediatric urine samples from patients with symptoms of UTI (Lohr, 1993) found 102 (14.8%) with positive culture results. These were compared with dipstick analysis of leukocyte esterase and nitrite. The combination of dipstick analysis and microscopic examination had a sensitivity of 100% and a negative predictive value (NPV) of 100%. The nitrite test had a specificity of 100% and a positive predictive value (PPV) of 100%. All patients with a positive culture result had positive results on the dipstick test or bacteriuria test or both (i.e. no false-negatives). Negative results on both of these tests in combination predicted a sterile culture with 100% accuracy. Similar results (PPV of 100% if both nitrites and leukocytes detected, NPV of 100% if neither found) were obtained in another study of 133 paediatric samples (Woodward, 1993). Other studies have produced seemingly opposite results. In a study of 146 urine cultures from 56 women at risk for recurrent pyelonephritis (Lenke, 1981) the nitrite test failed to detect 14 of 18 positive cultures (a sensitivity of 22%). In another study, 420 samples from patients of both sexes and all ages (Zaman, 1998) were tested for both nitrites and leukocytes, with a PPV of 51% and NPV of 82%. Sensitivity was 23%, leading the authors to conclude that dipstick tests were not suitable for screening for UTI.

A more recent study involving 225 samples from patients of both sexes and all ages (van Nostrand, 2000) found the following:

- Leukocyte esterase test: sensitivity 75%, specificity 72%, PPV 42.9%, NPV 91.1%
Nitrite test: sensitivity 19.2%, specificity 94.9%, PPV 50.0, NPV 81.7%
The authors argue that increasing resistance among common urinary tract pathogens makes culturing necessary if patients are to receive appropriate antibiotic treatment. They also point out that one third to one half of the patients treated in their study would have received unnecessary antibiotics due to the low PPV of both tests.
A practice guideline from the American Academy of Pediatrics (AAP 1999) states that, whilst urinalysis cannot substitute for urine culture to confirm the presence of UTI, it can be valuable in selecting individuals for prompt initiation of treatment while waiting for the results of the urine culture. A positive leukocyte esterase or nitrite test is “suggestive (although not diagnostic) of UTI”. Recommendation 5 in the guideline is “Diagnosis of UTI requires a culture of the urine (strength of evidence: strong).”
A systematic literature review and meta-analysis (Gorelick, 1999) found that urine dipstick tests had a sensitivity of 0.88 for the presence of either leukocyte esterase or nitrite and a specificity of 0.04 for the presence of both.
A recent retrospective review of 11,089 patients (Bachur, 2001) gave a sensitivity of 82% for the standard urinalysis test, which did not vary according to the clinical situation in patients with fever who were younger than 2 years of age.

van Nostrand JD, Junkins AD, Bartholdi RK. Poor predictive ability of urinalysis and microscopic examination to detect urinary tract infection. Am J Clin Pathol 2000;113:709-13
Woodward MN, Griffiths DM. Use of dipsticks for routine analysis of urine from children with acute abdominal pain. BMJ 1993;306:1512

Evidence level: IV

Does perineal/genital cleaning reduce the risk of false-positive urine tests?
A randomised trial in 350 children (Vaillancourt, 2007) compared a group cleansed with soap before urine testing (n = 179) with a second group (n = 171) that were not cleansed. The rate of contamination in the cleansing group was 14 (7.8%), vs 41 (23.9%) in the non-cleansing group. Children in the cleansing group were less likely to have a positive urinalysis (37 of 179 (20.6%) than those in the non-cleansing group (63 of 171 (36.8%)). The authors concluded that cleansing may reduce the risk of having to return for repeat testing and for receiving unnecessary antibiotics or other interventions.


Evidence Level: II
It is beneficial to screen the urine of children attending outpatients or children admitted as emergencies to children’s wards?
The prevalence of UTI in febrile young children in the emergency department has been estimated at 3%-5% (Shaw, 1998). This study of 3873 infants under 2 years of age concluded that the most cost-effective strategy was to send urine for culture in all suspect cases and “begin presumptive treatment only on those with a significantly positive dipstick result”. Another emergency department study involving 236 children (Craver, 1997) found detection rates for UTI to be identical for dipstick testing only and for complete urinalysis. The authors recommended routine testing by dipstick only with microscopic analysis requested for positive results.
A retrospective review of 1019 symptomatic paediatric outpatients (Weinberg, 1991) recommends the dipstick for initial patient assessment, on the basis of its high NPV of 99.6%. American Academy of Pediatrics guidelines (AAP, 1999) recommend that, between the ages of 2 months and 2 years, unexplained fever should prompt investigation for UTI. No evidence suggests that there is benefit from screening completely asymptomatic children in either the emergency or outpatient departments.


Craver RD, Abermanis JG. Dipstick only urinalysis screen for the pediatric emergency room. Pediatr Nephrol 1997;11:331-3


Evidence level: V

Can renal scarring be prevented by early diagnosis and management of vesico-ureteric reflux?
A retrospective UK study of 52 children aged 1-12 years with bilateral renal scarring and severe vesico-ureteric reflux (VUR) (Smellie, 1994) found that there had been delay in diagnosis or effective treatment of urinary infection in 50 of the 52 children. The severity of scarring was significantly related to delay in diagnosis. Although the authors concluded that early diagnosis and treatment might have prevented some or all of the scarring that occurred, the retrospective design of the study could not confirm this.
A retrospective review in 306 children (Pirker, 2006) found that children diagnosed before the age of 3 years showed significantly less scarring than patients diagnosed later (23% vs 41%, p < 0.002).
Most studies on this subject comprise small numbers or are retrospective; no large-scale study has evaluated the results of surgical or medical treatment of VUR during childhood for the long-term risk of renal failure in the ones with established renal scarring (Jacobson, 1999).
Early diagnosis may be problematic; DMSA scintigraphy appears to be the best single means for identifying children at risk of renal scarring, but if performed at the time of the acute infection, results will be no better than C-reactive protein, since so many acute defects are transient (Jakobsson, 1999). However, the predictability will improve if the investigation is delayed for more than 2 months after the acute infection.
The evidence is equally unclear concerning early treatment. It is known that prophylaxis with long-term, low-dose antibacterial agents has the same long-term outcome as anti-reflux surgery (Bollgren, 1999). Again, however, the lack of suitable studies makes it difficult to evaluate the benefits of treatment. The authors consider an aggressive attitude to management of reflux reasonable in view of the high rates of renal impairment and hypertension in adults with a history of childhood reflux and scar formation.
The "Goteberg Study", a prospective epidemiologic study of 600 children, found that 41 girls who suffered therapeutic delay had four times the level of renal damage seen in 440 girls whose treatment began promptly (Winberg, 1982).
The Birmingham Reflux Study (Birmingham Reflux Study Group, 1987) first confirmed the equivalency of medical and surgical treatment, but concluded that neither was capable of completely protecting the kidneys from progression of scarring, or even, on occasion, the formation of a new scar. New scars were detected by urography in 6% of the patients in the Birmingham study, and in the International Reflux Study in Children (the only other randomised trial) the figures were 13% in the European branch and 26% in the US branch (Olbing, 1992).

The most recent guidelines on the subject (Jodal, 1999), based on the available evidence, recommend ultrasonography within 2-4 weeks and voiding cystourethrography (VCU) within 1-2 months for children below 2 years of age who have reflux and UTI. For children 2 years of age and older, ultrasonography within 1-2 months and DMSA scintigraphy after 6-12 months (or VCU if unavailable, or if there are uptake defects or a side distribution with one kidney having below 45% of total function).

At least 1 year of antibacterial prophylaxis is recommended for patients with reflux grade III-IV at first examination.

A retrospective study of 506 children (Silva 2006) concluded that “Few factors are amenable to intervention to modify the natural history of VUR. According to our findings, there are only two possible interventions: avoiding renal scars and managing voiding dysfunction.”

A prospective randomised study in 225 children (Roussey, 2008) found that, although antibiotic prophylaxis did not reduce the incidence of UTI overall (compared with no treatment), there was a significant reduction in a subgroup, boys with grade III reflux (p = 0.013).

A Cochrane review of 20 studies in a total of 2324 children (Nagler, 2011) concluded that “Compared with no treatment, use of long-term, low-dose antibiotics did not significantly reduce the number of repeat symptomatic and febrile UTIs in children with VUR.”


Pirker ME, Colhoun E, Puri P. Renal scarring in familial vesicoureteral reflux: is prevention possible? J Urol 2006;176:1842-6


All children with actual or suspected UTI need a renal ultrasound scan?

A prospective study was carried out in 209 children under 5 years of age, hospitalised for a first simple UTI and for whom results of late-pregnancy and post-UTI renal ultrasound scans were available (Miron, 2007). Complete concordance between the two scans was demonstrated in 201 children (96%). The authors concluded that, as findings from scans following UTI rarely influence patient management, these could be safely omitted in those children whose prenatal scans were normal.

NICE guidelines (NCCWCH, 2007) recommend that a scan should be carried out 4-6 months after infection in children < 3 years of age with atypical or recurrent infection.


Evidence Level: IV
This guideline and supporting information has been prepared with reference to the following:

Pearce SH, Cheetham TD. Diagnosis and management of vitamin D deficiency. BMJ 2010;340:b5664


Last amended November 2012