

Diagnosing and managing sepsis in children

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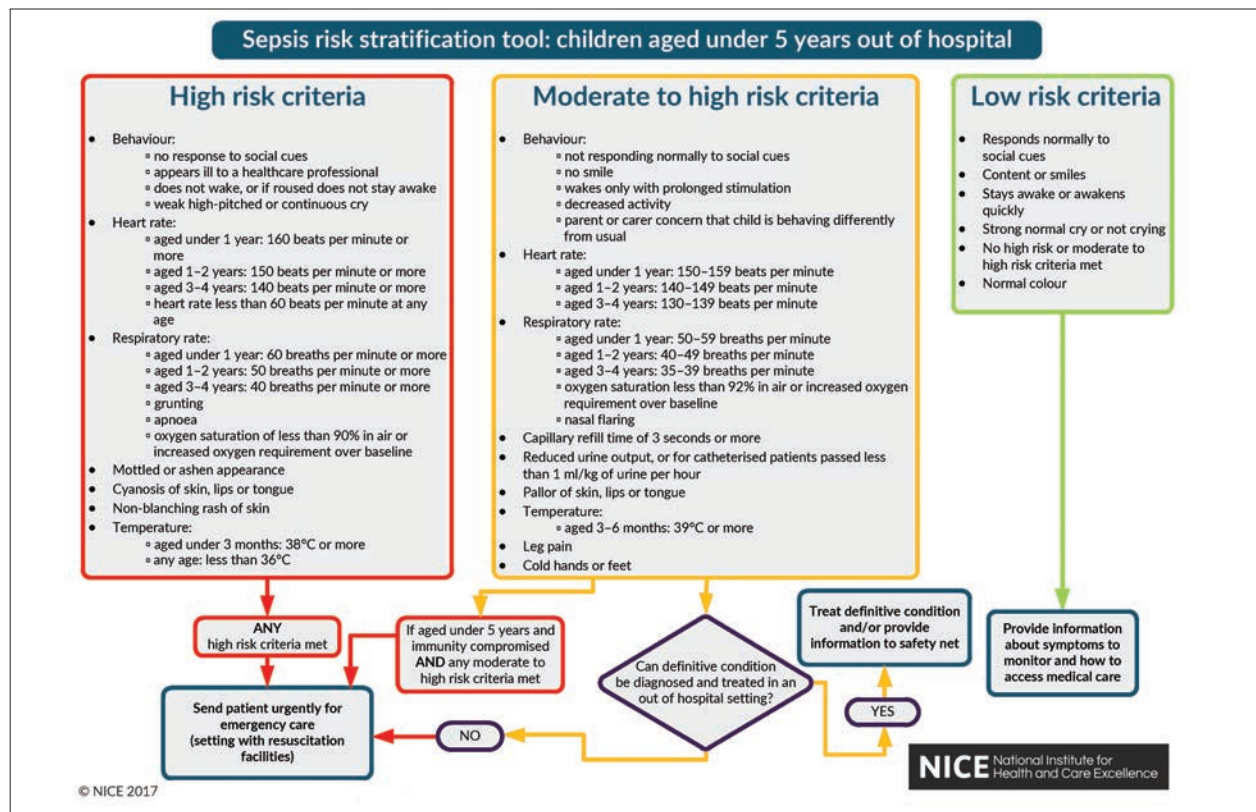
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Diagnosing and managing sepsis in children

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FIGURE
NICE algorithm
for managing
suspected sepsis
in children aged
under five years
outside an acute
hospital setting



Which children are at increased risk of sepsis?

How should illness severity be assessed?

Which children should be referred urgently?



EVERY CHILD WILL HAVE MULTIPLE EPISODES OF INFECTION DURING THE FIRST YEARS OF LIFE,

most commonly respiratory and gastrointestinal viral infection. Many such episodes may never present to a health professional, and are mild and self-limiting.

However, an increasing number present to primary care and to emergency departments. All clinicians who provide these services need to be able to distinguish the child who has, or is at risk of developing, sepsis from the vast majority who have self-limiting infection, requiring only symptomatic or simple treatment such as a course of oral antibiotics. This can be especially challenging when these children are

only rarely encountered. The NICE guideline on sepsis, published in 2016, aims to help healthcare professionals diagnose sepsis in children, as well as adults, and improve outcomes.¹

‘In children under 5 BP measurement is only necessary if there is an abnormal capillary refill time’

Sepsis is the clinical consequence of systemic inflammation triggered by an infective agent. The response of the host to an infective agent is to mount an immune response, initially involving

macrophages which produce inflammatory cytokines that recruit other components of the immune system. When the potential pathogen is controlled or eliminated, there are regulatory mechanisms which then turn off this process.

In sepsis this response is not brought under control so the inflammation escalates and itself causes tissue damage, which can progress to multiorgan failure. Whether or not this occurs depends on characteristics of the infecting organism, and of the host.

The clinical features of sepsis are:

- Fever
- Tachycardia, with no other explanation
- Tachypnoea, with no other explanation
- Leukocytosis or leucopenia

To meet the International Pediatric

SPECIAL REPORT

SEPSIS IN CHILDREN

Sepsis Consensus Conference definition,² a patient should have two of these features (with defined parameters), one of which should be fever or abnormal white cell count, in the presence of infection.

In severe sepsis, in addition to the above, there is cardiovascular organ dysfunction, acute respiratory distress syndrome or two or more other organ dysfunctions. Septic shock describes sepsis with cardiovascular organ dysfunction.

CAUSES

In previously healthy children presenting in the community, bacterial infection is by far the most common cause.³ In the neonatal period, group B streptococcus, coliforms, such as *E. coli*, and *Staphylococcus aureus* are the usual culprits. *Listeria monocytogenes* sepsis is rare, but important to consider when choosing empirical antibiotic regimens.

In older infants and preschool

children, the majority of cases of paediatric sepsis used to be caused by encapsulated organisms such as *Haemophilus influenzae type b*, meningococcus and pneumococcus. The introduction of effective immunisations against these organisms has virtually eliminated *Haemophilus influenzae type b* sepsis, and there has been a significant reduction in the incidence of meningococcal and pneumococcal sepsis in the past

Table 1

NICE (NG51) risk stratification tool for children aged under 5 years with suspected sepsis¹

Category	Age	High risk criteria	Moderate to high risk criteria	Low risk criteria
Behaviour	Any	No response to social cues Appears ill to a healthcare professional Does not wake, or if roused does not stay awake Weak high-pitched or continuous cry	Not responding normally to social cues No smile Wakes only with prolonged stimulation Decreased activity Parent or carer concern that child is behaving differently from usual	Responds normally to social cues Content or smiles Stays awake or awakens quickly Strong normal cry or not crying
Respiratory	Any	Grunting Apnoea Oxygen saturation of less than 90% in air or increased oxygen requirement over baseline	Oxygen saturation of less than 92% in air or increased oxygen requirement over baseline Nasal flaring	No high risk or moderate to high risk criteria met
	Under 1 year	Raised respiratory rate: 60 breaths per minute or more	Raised respiratory rate: 50–59 breaths per minute	
	1–2 years	Raised respiratory rate: 50 breaths per minute or more	Raised respiratory rate: 40–49 breaths per minute	
	3–4 years	Raised respiratory rate: 40 breaths per minute or more	Raised respiratory rate: 35–39 breaths per minute	
Circulation and hydration	Any	Bradycardia: heart rate less than 60 beats per minute	Capillary refill time of 3 seconds or more Reduced urine output For catheterised patients, passed less than 1 ml/kg of urine per hour	No high risk or moderate to high risk criteria met
	Under 1 year	Rapid heart rate: 160 beats per minute or more	Rapid heart rate: 150–159 beats per minute	
	1–2 years	Rapid heart rate: 150 beats per minute or more	Rapid heart rate: 140–149 beats per minute	
	3–4 years	Rapid heart rate: 140 beats per minute or more	Rapid heart rate: 130–139 beats per minute	
Skin	Any	Mottled or ashen appearance Cyanosis of skin, lips or tongue Non-blanching rash of skin	Pallor of skin, lips or tongue	Normal colour
Temperature	Any	Less than 36°C		
	Under 3 months	38°C or more		
	3–6 months		39°C or more	
Other	Any		Leg pain Cold hands or feet	No high risk or high to moderate risk criteria met

20 years. However, the vaccines in the current universal schedule do not protect against all strains of meningococcus, only the 13 most common strains of pneumococcus, so we will continue to see these infections, albeit less frequently, and need to remain aware of them.

There is currently no vaccine against group A streptococcus. Children with invasive group A streptococcal disease may present with septicaemia, or with streptococcal toxic shock. Clinical features which may point to this diagnosis include the classical scarlatiniform rash, which can sometimes have petechial elements, strawberry tongue, tonsillitis and cervical lymphadenopathy, but these signs are not always present.

Staphylococcal sepsis is uncommon in the absence of focal disease, such as skin abscesses, cellulitis, osteomyelitis, or necrotising pneumonia, so it is important to look for focal symptoms and signs, as these may influence antibiotic choices.

Gram-negative sepsis may be associated with urinary tract infection, particularly in infants, or patients with abnormal renal tracts. It is a particular risk in immunocompromised children. Groups of children who are at increased risk of sepsis are listed in box 1, below.

ASSESSING ILLNESS SEVERITY

Every time a child who has symptoms or signs suggestive of infection is assessed, it is important to consider whether this could be sepsis. This may seem obvious in a child presenting with

fever, but not all children with sepsis present with high fever or focal signs. As is so often the case, obtaining a good history from the child and the parent or carer is vital. This can be challenging in people whose first language is not English, or who have communication problems, so extra care is needed. It is imperative to ask about:

- Recent fevers or rigors
- Recent surgery or injury
- Symptoms that may identify the focus of infection
- Any other risk factors for sepsis, see box 1, below.

‘Not all children with sepsis present with high fever or focal signs’

It is also important to check if the child has had any medications which may affect your assessment, such as antipyretics or beta-blockers. It is particularly important to ascertain whether there has been a change in the child's behaviour, such as irritability, lethargy, difficulty in waking or confusion, and whether their colour has changed, particularly if the child is pale, mottled, or has cold hands and feet despite having a fever. Also note when the child last passed urine. If this assessment is being made over the phone the answers to these questions will help you decide whether you need to see the child, and if so, how urgently.

When you see the patient, take note

of the general appearance, and how active and alert the child is. Many children are easily upset when they feel ill, and may cry and be combative, though they are usually consolable if a parent is present and reassuring. The more worrying case is the child who lies very quietly and is indifferent to the examination. The skin should be examined for signs of mottling, and ashen appearance, for rash (especially non-blanching rash), and any cuts, burns or skin infections, and the lips and tongue for pallor or cyanosis.

Temperature, heart rate, respiratory rate, and in children under 12 years capillary refill time, should be measured. Blood pressure should always be taken in children over 12. In younger children, blood pressure should be measured if the right size cuff is available (beware of using too small a cuff if you have a choice of paediatric ones). In children under five years, blood pressure measurement is only necessary if there is an abnormal capillary refill time. The rest of the assessment and ongoing management should not be delayed if this equipment is not immediately available. If the child is not obviously alert and interactive, the level of consciousness should be documented formally.

RISK STRATIFICATION

Tables 1 (p22), 2 and 3 (p24), outline the clinical criteria on which the NICE risk stratification for sepsis is based.¹ It is important to remember that the child's temperature is only one of the factors to consider, and that sepsis can occur in children with a normal temperature. This is particularly true of children with severe sepsis. Conversely, a raised temperature is not always a sign of infection, and may occur, for example after surgery or trauma.

‘Hypotension is a preterminal event in children with sepsis’

Heart rate may be misleadingly low if the child is on beta-blockers or has a pacemaker (though these situations are rare). Hypotension is a preterminal event in children with sepsis, so do not be reassured if the blood pressure is still normal. Listen to the parents if they express concerns about their child's behaviour, or feel that the child is uncharacteristically irritable as cognitive changes can be subtle. If an oxygen saturation monitor is used, it is »

Box 1

Risk factors for sepsis in children

- Infants under 12 months of age, and particularly those under 3 months, are more likely to have bacterial infection when they present with fever, and if they develop bacterial infection are more likely to progress to sepsis.
- Children with an impaired immune system
 - Primary immune deficiency
 - Other diseases that affect immune function e.g. congenital asplenia (or children who have undergone splenectomy), sickle cell disease. NB these children are particularly at risk of pneumococcal sepsis and should receive penicillin prophylaxis
 - Cancer patients treated with chemotherapy
 - Those on long-term oral steroids
 - Children treated with other immunosuppressive drugs for conditions such as juvenile arthritis and inflammatory bowel disease
- Those who have had surgery or other invasive procedures within the past six weeks
- Any breach of skin integrity e.g. cuts, burns, blisters, skin infections, particularly those resulting from chickenpox
- Indwelling lines or catheters

Table 2**NICE (NG51) risk stratification tool for children aged 5-11 years with suspected sepsis¹**

Category	Age	High risk criteria	Moderate to high risk criteria	Low risk criteria
Behaviour	Any	Objective evidence of altered behaviour or mental state Appears ill to a healthcare professional Does not wake or if roused does not stay awake	Not behaving normally Decreased activity Parent or carer concern that the child is behaving differently from usual	Behaving normally
Respiratory	Any	Oxygen saturation of less than 90% in air or increased oxygen requirement over baseline	Oxygen saturation of less than 92% in air or increased oxygen requirement over baseline	No high risk or moderate to high risk criteria met
	Aged 5 years	Raised respiratory rate: 29 breaths per minute or more	Raised respiratory rate: 24–28 breaths per minute	
	Aged 6–7 years	Raised respiratory rate: 27 breaths per minute or more	Raised respiratory rate: 24–26 breaths per minute	
	Aged 8–11 years	Raised respiratory rate: 25 breaths per minute or more	Raised respiratory rate: 22–24 breaths per minute	
Circulation and hydration	Any	Heart rate less than 60 beats per minute	Capillary refill time of 3 seconds or more Reduced urine output For catheterised patients, passed less than 1 ml/kg of urine per hour	No high risk or moderate to high risk criteria met
	Aged 5 years	Raised heart rate: 130 beats per minute or more	Raised heart rate: 120–129 beats per minute	
	Aged 6–7 years	Raised heart rate: 120 beats per minute or more	Raised heart rate: 110–119 beats per minute	
	Aged 8–11 years	Raised heart rate: 115 beats per minute or more	Raised heart rate: 105–114 beats per minute	
Temperature	Any		Tympanic temperature less than 36°C	
Skin	Any	Mottled or ashen appearance Cyanosis of skin, lips or tongue Non-blanching rash of skin		
Other	Any		Leg pain Cold hands or feet	No high or moderate to high risk criteria met

Table 3**NICE (NG51) risk stratification tool for adults, children and young people aged 12 years and over with suspected sepsis¹**

Category	High risk criteria	Moderate to high risk criteria	Low risk criteria
History	Objective evidence of new altered mental state	History from patient, friend or relative of new onset of altered behaviour or mental state History of acute deterioration of functional ability Impaired immune system (illness or drugs including oral steroids) Trauma, surgery or invasive procedures in the last 6 weeks	Normal behaviour
Respiratory	Raised respiratory rate: 25 breaths per minute or more New need for oxygen (40% FiO ₂ or more) to maintain saturation more than 92% (or more than 88% in known chronic obstructive pulmonary disease)	Raised respiratory rate: 21–24 breaths per minute	No high risk or moderate to high risk criteria met
Blood pressure	Systolic blood pressure 90 mmHg or less or systolic blood pressure more than 40 mmHg below normal	Systolic blood pressure 91–100 mmHg	No high risk or moderate to high risk criteria met
Circulation and hydration	Raised heart rate: more than 130 beats per minute Not passed urine in previous 18 hours. For catheterised patients, passed less than 0.5 ml/kg of urine per hour	Raised heart rate: 91–130 beats per minute (for pregnant women 100–130 beats per minute) or new onset arrhythmia Not passed urine in the past 12–18 hours For catheterised patients, passed 0.5–1 ml/kg of urine per hour	No high risk or moderate to high risk criteria met
Temperature		Tympanic temperature less than 36°C	
Skin	Mottled or ashen appearance Cyanosis of skin, lips or tongue Non-blanching rash of skin	Signs of potential infection, including redness, swelling or discharge at surgical site or breakdown of wound	No non-blanching rash

key points

SELECTED BY

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Sepsis is the clinical consequence of systemic inflammation

triggered by an infective agent. In sepsis the immune response is not brought under control so the inflammation escalates and causes tissue damage, which can progress to multiorgan failure. The clinical features of sepsis are: fever; tachycardia, with no other explanation; tachypnoea, with no other explanation; leukocytosis or leucopenia. To meet the International Pediatric Sepsis Consensus Conference definition, a patient should have two of these features, one of which should be fever or abnormal white cell count, in the presence of infection.

In previously healthy children presenting in the community,

bacterial infection is by far the most common cause. In the neonatal period, group B streptococcus, coliforms, such as *E. coli*, and *Staphylococcus aureus* are the usual culprits. In older infants and preschool children, the introduction of effective immunisation has virtually eliminated *Haemophilus influenzae type b* sepsis. However, the vaccines in the current universal schedule do not protect against all strains of meningococcus, and only protect against the 13 most common strains of pneumococcus, so we will continue to see these infections, albeit less often.

There is currently no vaccine against group A streptococcus.

Children with invasive group A streptococcal disease may present with septicaemia, or with streptococcal toxic shock. Staphylococcal sepsis is uncommon in the absence of focal disease, such as skin abscesses, cellulitis, osteomyelitis, or necrotising pneumonia. Gram-negative sepsis may be associated with urinary tract infection, particularly in infants, or patients with abnormal renal tracts.

Every time a child who has symptoms or signs suggestive

of infection is assessed, it is important to consider whether this could be sepsis. This may seem obvious in a child presenting with fever, but not all children with sepsis present with high fever or focal signs. It is imperative to ask about recent fevers or rigors, recent surgery or injury, symptoms which may identify the focus of infection, and any other risk factors for sepsis. It is particularly important to ascertain whether there has been a change in the child's behaviour, such as irritability, lethargy, difficulty in waking or confusion, and whether their colour has changed, particularly if the child is pale, mottled, or has cold hands and feet despite having a fever.

Temperature, heart rate, respiratory rate, and in children

under 12 years capillary refill time, should be measured. Blood pressure should always be taken in children over 12. Hypotension is a preterminal event in children with sepsis, so do not be reassured if the blood pressure is still normal. All children who meet any of the high-risk criteria, as defined by NICE, need to be referred urgently, usually by 999 ambulance. Children with impaired immunity who meet any of the moderate- to high-risk criteria should also be referred urgently. Whatever the measurements, the gut feeling that a child is unwell should never be ignored.

important to remember that it may not give a true reading if the peripheral perfusion is poor.

REFERRAL

All children who meet any of the high-risk criteria listed in tables 1-3 need to be referred urgently, usually by 999 ambulance. The hospital should be informed that the child is on the way. Children with impaired immunity who meet any of the moderate- to high-risk criteria should also be referred urgently. If a child has any moderate- to high-risk criteria, but you are clear about the underlying diagnosis, then the child can be treated in primary care. However, if you are unsure about the diagnosis, or feel that the child cannot safely be treated outside hospital, then you should refer the patient urgently.

In the case of children not meeting these criteria, it is important to make sure that the parents or carers know what symptoms and signs to look for which may indicate that the child has deteriorated, and ensure that they know how to obtain medical care if they are worried.

MANAGEMENT

Children with suspected meningococcal disease should receive IM benzylpenicillin or, if available, IM or IV ceftriaxone as soon as the diagnosis is suspected.⁴ In other high-risk cases, antibiotics should be given if transfer to hospital will take more than an hour. If the source of infection is known, it should be treated according to local guidelines. When the source is unclear, ceftriaxone is the drug of choice, with the addition of amoxycillin to cover *Listeria* in babies younger than three months.

If the child has previously been infected or colonised with ceftriaxone-resistant organisms, then local guidelines will need to be consulted or advice obtained from the on-call microbiologist. If there are signs of shock or the child has an oxygen saturation less than 91% in air, then oxygen should be administered. If no oxygen saturation monitor is available or there are concerns about the accuracy of the reading in these circumstances, oxygen is unlikely to be harmful, so if in doubt, oxygen should be given.

In children who do not need hospital referral, a clean catch urine sample should be obtained for analysis and culture, and a chest X-ray considered. Whenever possible, specimens such as urine for culture or swabs for

microbiology should be taken before giving antibiotics. Local antimicrobial prescribing guidelines can be used to determine choice of antibiotic if the diagnosis is clear. It is crucial to chase up the results, so that the treatment can be adjusted if needed.

‘Whatever the measurements, the gut feeling that a child is unwell should never be ignored’

Recognition of the sick child is an essential skill for any doctor whose practice involves children. Gaining sufficient experience to do this is challenging when such children are rarely encountered. The dangers of missing the diagnosis of sepsis need to be balanced against the consequences of unnecessary referral and investigation of children who do not need to be seen in secondary care. Whatever the measurements, the gut feeling that a child is unwell should never be ignored.

Competing interests: None

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Useful information

UK Sepsis Trust

Information for healthcare professionals and patients
<https://sepsistrust.org>

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