Guideline

# Sepsis: Recognition and Early Management in Children

| | | | | | |
|---|---|---|---|---|---|
| **Document ID** | CHQ-GDL-07449 | **Version no.** | 1.0 | **Approval date** | 25/05/2017 |
| **Executive sponsor** | Executive Director Medical Services | | | **Effective date** | 25/05/2017 |
| **Author/custodian** | Paediatric Emergency Department | | | **Review date** | 25/05/2020 |
| **Supercedes** | New | | | | |
| **Applicable to** | CHQ HHS Clinical Staff | | | | |
| **Authorisation** | Executive Director Hospital Services | | | | |

## Purpose

To guide the identification and early management of children with sepsis.

## Scope

This guideline applies to all staff involved in the care and management of infants and children with suspected or proven sepsis in the emergency or ward setting and interfaces with the established guidelines for the Febrile Illness and Management of Paediatric Septic Shock.

## Related documents

**Policy and standard(s)**

- CHQ Guideline – Febrile Illness – Emergency Management in Children
- CHQ Guideline – Management of Paediatric Septic Shock
- CHQ – Antimicrobial Stewardship – Sepsis
- CHQ Paediatric Antibiocard: Empirical Antibiotic Guidelines
- CHQ Guideline – Fever in a Child with Central Venous Access Device

# Guideline

## Introduction

Despite advances in prevention and treatment of invasive bacterial infections, sepsis remains a leading cause of childhood morbidity and mortality in Australia.[1] Without treatment, septic shock carries a mortality rate more than 80% and, even with treatment, overall mortality for septic shock remains around 15-20% in children.[1-4] Delays in the initiation of appropriate antibiotic treatment and shock treatment leads to significantly increased mortality.[5-7] Therefore, sepsis is a medical emergency with the goal of early recognition and treatment. Sepsis must be considered in every paediatric patient with acute illness or new onset of organ dysfunction. The difficulty being that the initial presentation can be vague and non-specific, particularly in neonates. Once identified, management includes rapid fluid resuscitation, early consideration of inotropes and administration of appropriate antibiotics; ideally within the first 15 minutes of presentation.[8] Furthermore, early involvement of the Paediatric Intensive Care Unit (PICU) services onsite or via Retrieval Services Queensland (RSQ) is essential for optimising the outcome of these children, given that supportive treatment should be delivered according to internationally recognised, consensus based guidelines.[8-10]

**ALERT**

**Sepsis is a medical emergency: early recognition and treatment is imperative for survival**

## Definitions

Sepsis in adults was recently redefined as 'life-threatening organ dysfunction caused by a dysregulated host response to infection'.[11] However, the international consensus for paediatric sepsis remains defined as 'the systemic inflammatory response syndrome in the presence of, or as the result of, suspected or proven infection'.[10] It is a syndrome shaped by both pathogen and host factors.[12-13] The most common type of pathogens are bacteria (viruses and fungi can result in a similar presentation), which vary according to host factors, including age, comorbidity and geographic location.[14]

Septic shock is a subset of sepsis in which profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality.[11] It is identified by sepsis and cardiovascular organ dysfunction, acknowledging that hypotension is a late sign in paediatrics.[10]

## Early Recognition

Given the time critical nature of sepsis progressing to organ failure and death, early recognition and prompt treatment is imperative to survival.[14] Sepsis should be suspected in any acute illness, or in any high-risk group (Box 1), if there is any change from the patient's normal pattern of observations.[15] A diagnosis of sepsis is made using clinical judgement, supported by laboratory testing. Moreover, there is no clinical finding or test that is conclusive on its own. If suspected, it is best to initiate sepsis investigations and treatment and to continue until sepsis has been excluded. Early recognition of children presenting to hospital with sepsis enables appropriate triage for rapid assessment and treatment. Validated triage tools for paediatric sepsis are currently being developed but are generally based on the identification of risk factors, abnormal vital signs and/or suggestive clinical features.[15]

**Box 1: High Risk Groups**

- Neonates and premature infants
- Unimmunised or incomplete immunisation status
- Malignancy and/or chemotherapy
- Immune deficiency
- Asplenia (surgical or functional eg sickle cell disease)
- Long-term steroid use
- Immunosuppressant drug therapy
- Recent surgical procedure (within 6 weeks)
- Intravenous recreational drug use
- Indwelling lines or catheters (e.g. VP shunt or CVAD)

The presentation of sepsis varies according to the age of the child. Infants and neonates tend to present with non-specific symptoms and signs, such as feed intolerance and/or apnoea. Whereas older children may present with a focus of infection and/or a constellation of features including fever or hypothermia, vomiting, inappropriate tachycardia, altered mental state and reduced peripheral perfusion.[14-15] Deviations from pre-existing trends in vital signs (Table 1) can be a red flag. Refer to the Febrile Illness guideline for more detail. It is important to pay attention to concerns expressed by the caregiver, particularly changes in usual behaviour of the child.

**Table 1: Normal range for age specific vital signs**

| Age | Heart Rate (bpm) | Minimum Systolic BP (mmHg) | Respiratory Rate (bpm) |
|---|---|---|---|
| Term | 100-180 | 60 | 40-60 |
| 6mth | 100-180 | 70 | 30-50 |
| 1yr | 100-170 | 70 | 20-40 |
| 2yr | 100-160 | 70 | 20-30 |
| 4yr | 80-130 | 75 | 20-30 |
| 8yr | 70-110 | 80 | 16-25 |
| 12yr | 60-110 | 90 | 16-25 |
| 16yr + | 60-100 | 90 | 10-16 |

## Septic Shock

Children with septic shock may have normal blood pressure. Hypotension is often a terminal sign given that children compensate with normal blood pressure, even in the late stages of shock. Once sepsis has progressed it will manifest in two main clinical pictures: cold and warm shock (Table 2). Although the implications of such a distinction is increasingly being disputed, it is important to be able to recognise these alternative presentations of septic shock.

**ALERT**

Hypotension is a late, and often terminal, sign in paediatric septic shock. Initiate treatment and contact PICU.

**Table 2: Shock subtypes[16]**

| | |
|---|---|
| Cold Shock | - A more common presentation in infants and young children<br>- Constricted peripheral systemic vasculature: cold peripheries and prolonged capillary refill time<br>- Tachycardia is usually present<br>- Blood pressure can be maintained until late<br>- Underlying problem is a low cardiac output state, secondary to impaired myocontractility |
| Warm Shock | - More common presentation in older children (and adults)<br>- Characterised by vasoplegia, in which the systemic vascular resistance is low: brisk capillary refill time ('flash' capillary refill) and pulses are usually felt to be full or bounding<br>- Tachycardia is usually present<br>- Pulse pressure is high, often due to a low diastolic blood pressure<br>- Hyperdynamic or high cardiac output state associated with shock due to enlargement of the circulation exceeding cardiac output<br>- Progression to low cardiac output can occur anytime |

Clinical findings consistent with insufficient end-organ perfusion:

- *Mental status*: progressive lethargy, drowsiness or obtundation. Alternatively, restlessness and/or agitation are often seen and can be mistaken for "a vigorous child" but reflects compromised cerebral perfusion due to shock. Infants tend to have irritability and/or apnoeas.
- *Skin*: temperature gradient from core to extremities (note that either hyperthermia or hypothermia can be present), mottled colour, prolonged capillary refill time (>2 seconds but note that brisk capillary refill time can be seen in warm shock), petechial or purpuric rash. Purpura fulminans is a widespread non-blanching purpuric rash classically seen in meningococcaemia but may also be associated with severe sepsis from *Pneumococcus*.
- *Cardiovascular*: Tachycardia is usually one of the earliest signs. Mean arterial pressure (MAP) can be maintained and the pulse pressure typically is narrow (vasoconstriction to maintain MAP), but may be high (vasodilation in "warm shock"). There may be evidence of cardiac failure (hepatomegaly, gallop rhythm and jugular venous distension) with myocardial depression. A classic pitfall in the recognition of shock is attributing difficulty in obtaining non-invasive blood pressure due to technical issues rather than recognising the presence of hypotension/hypoperfusion.
- *Respiratory*: rate is increased to compensate for metabolic acidosis including lactic acidosis (Kussmaul breathing). Acute respiratory distress syndrome (ARDS) may develop with progressive worsening of respiratory distress (tachypnoea, increased work of breathing) and focal chest signs (reduced breath sounds, inspiratory crepitations, and expiratory wheeze).
- *Renal*: Reduced urine output

### Toxic Shock Syndrome

This is a potentially life-threatening subset of paediatric sepsis, caused by superantigens from toxin-producing strains of *Staphylococcus aureus* or *Streptococcal pyogenes*.[17] Symptoms may include high fever, vomiting, diarrhoea, myalgia, confusion, collapse and a widespread erythematous rash. It can occur in any patient. It is important to distinguish this entity as treatment requires the addition of IV Lincomycin and IV Intragam 2g/kg for their antitoxin properties.

### Meningitis

Meningitis should be considered in children with suspected sepsis as it can result in serious complications, such as raised intracranial pressure (ICP). More specific features may include photophobia, headache, nuchal rigidity, seizures, posturing and a bulging fontanelle (<3 month age). Possible signs of raised ICP include fluctuating consciousness despite resuscitation, hypertension, bradycardia, abnormal pupils, posturing, seizures or focal neurology. Do not perform a lumbar puncture if any of these features are present, due to the risk of cerebral herniation if there is raised ICP. It can be initially treated with IV administration of 3mL/kg of 3% Sodium chloride (hypertonic saline). Antibiotic coverage in all ages includes the addition of IV Cefotaxime 50mg/kg (Max 2g). If more than 3 months of age give IV Dexamethasone 0.15mg/kg prior to or within 1 hour of antibiotics.

### Investigations

No single laboratory test will confirm or refute the diagnosis of sepsis, but many can provide support or additional information. Although there is growing interest, there is currently no evidence to support the use of a specific biomarker for the diagnosis of sepsis.[14] Biomarkers may be of more use to decide if antibiotics can be stopped at 48 hours. Empirical antibiotic therapy should not be delayed to wait for results of any investigations if clinical suspicion is high. Furthermore, clinical findings and host factors should direct specific microbiological sampling. However, despite adequate microbiological sampling, in some children with sepsis the pathogen is not identified (culture-negative sepsis).[18]

**ALERT**

Do not delay antibiotic administration for investigations, which includes the collection of microbiological samples

*Blood gas*

- Venous blood is typically used in the emergency department setting.
- A large base deficit is a marker of sepsis and its severity (>5.0mEq/L)
- Hypercarbia and/or hypoxaemia are supportive of a diagnosis of respiratory dysfunction.
- Lactate
  - Increased lactate (>2-4 mmol/L) is indicative of inadequate oxygen delivery to tissue and, in the context of sepsis, is suggestive of septic shock.[10]
  - Although it is not a sensitive marker for sepsis, an increased lactate is a marker of severity and is strongly correlated with mortality.
  - Increased lactate should not be attributed to "difficult access" before the presence of sepsis is excluded.
- Glucose
  - Hypoglycaemia (blood glucose level <3 mmol/L) can result depletion of glycogen stores.
  - Hyperglycaemia is common as part of the stress response to sepsis.

*White blood cell count*
- High or low cell count can be a feature of early sepsis but is not sensitive or specific.

*Thrombocytopaenia*
- Platelet count <80,000uL, or a decrease by 50% from the highest value in the past 3 days, can been seen in sepsis but is indicative of disseminated intravascular coagulation (DIC) when associated with coagulopathy.

*C-reactive protein*
- Can be useful in the diagnosis and monitoring of sepsis.
- More readily available but less specific than procalcitonin.
- A low value does not exclude early sepsis and, alternatively, a high value does not confirm sepsis but may be supportive.

*Liver function tests*
- Increased bilirubin or alanine aminotransferase can be seen in sepsis related liver dysfunction.

*Electrolytes*
- Often deranged in sepsis and an increased creatinine level can be indicative of sepsis related renal failure

*Coagulation studies*
- Derangement in the context of sepsis and thrombocytopaenia is indicative of DIC
- Abnormalities may include an international normalised ratio >2, prolonged activated partial thromboplastin time, decreased fibrinogen level or increased D dimer levels

*Blood culture*
- Many infants and young children with sepsis can have a primary bacteraemia.
- This should ideally be taken as soon as possible, prior to administration of antibiotic therapy but should not delay antibiotic administration.
- Culture sensitivity is proportional to the volume of blood taken
- When using a neonatal aerobic culture bottle in neonates (Figure 1), a minimum of 1mL of blood from venepuncture or freshly inserted vascular catheter (arterial or venous) is likely to be adequate to diagnose bacteraemia.[19]
- When standard aerobic culture bottles are used (Figure 1), a minimum of 4mL of blood is required for a valid negative culture at 48 hours.
- If the child has a CVAD, blood cultures should be taken from each lumen as per protocol.

**Figure 1**: Neonatal aerobic culture bottle (yellow) and standard aerobic culture bottle (green)

*Urine sample*
- Collection may not be possible until after fluid resuscitation but antibiotic treatment should not be withheld if there is significant delay in obtaining a sample

*Lumbar puncture*
- Only performed in a child who is alert and has no features of potentially raised ICP or coagulopathy
- It is usually contraindicated in established sepsis until the patient is stabilised and antibiotic treatment should not be withheld if there is significant delay in obtaining a sample
- Delayed collection of cerebrospinal fluid can still be sent for white cell count and polymerase chain reaction (PCR) testing to support a diagnosis of meningitis.

*Radiography*
- A chest x-ray can be considered for respiratory distress or clinical features of a pneumonic process.
- Other imaging modalities are directed by the focus of infection e.g. septic joint.

**Early Management**

Review of sepsis related mortality in children suggests that failure to recognise sepsis and the delay in appropriate treatment are common themes.[20] Early aggressive treatment should ensue once sepsis is suspected, with the aim of decreasing tachycardia, improving peripheral perfusion and restoring a normal level of consciousness. (Refer to the Appendix 1 flow diagram.)

*Interventions within the first 15 minutes*:
- Involve experienced clinicians, including PICU (onsite or via **RSQ 1300 799 127**), particularly if there is insufficient response to fluids or needing inotropes/intubation (Box 2)
- Delivery of supplemental oxygen and respiratory support with an appropriate device
- Intravenous or intraosseous access should be immediately obtained and bloods sent
- Umbilical line access can be considered in newborns up to 2 weeks of life
- Initial bloods should include blood cultures, venous blood gas and glucose
- Further bloods can be obtained if possible, including full blood count, C-reactive protein, biochemistry and coagulation profile
- Urgent doses of broad spectrum antibiotics should be given via the IV or IO route

**ALERT**

Refer to the CHQ Paediatric Antibiocard: Empirical Antibiotic Guidelines for more detail, including ongoing frequency of administration and dosing for neonates i.e. <1 month age

- If there is no IV or IO access within 15 minutes, intramuscular Ceftriaxone 50mg/kg (maximum 2 grams BD) should be administered and assistance sought.
- Once IV access is obtained, the full IV antibiotic doses should be provided, including cefotaxime if they are above 2 months of age or for any age if meningitis is suspected.
- Immediate fluid resuscitation starting with 20mL/kg of Sodium chloride 0.9% (normal saline) to be pushed in <5 minutes using 50mL syringe with a staff member dedicated to pushing fluids, with the goal to restore normal circulating volume and physiological parameters.
- Titrate to response: decrease in heart rate and the improvement of end-organ perfusion. This should be repeated as necessary, evaluating for signs of fluid overload.
- Inotropes should be commenced if normal physiological parameters are not restored after giving >40mL/kg of fluids or anytime if hypotension is present
- Echocardiography can guide fluid administration and commencement of inotropes

**Box 2: Triggers for PICU involvement**

- Tachycardia not improving after 40mL/kg fluid boluses
- Significantly altered GCS
- Hypotension
- Septic shock
- Toxic shock
- Coagulopathy/DIC
- Lactate >4 mmol/L
- Inotropes

*Airway and Breathing*

- Give high concentration supplemental oxygen
- Delivery can initially be via a Hudson mask non-rebreather with escalation as required
- The patient's airway should be maintained with positioning and airway adjuncts
- High-Flow nasal cannulae may be considered as an alternative transitory support in awake and responsive patients
- Children that are grunting, obtunded, or hypoxic despite supplemental oxygen, should be given PEEP through a T-piece (anaesthetic) bag while preparing for intubation.
- Consider inserting a nasogastric tube for gastric distension, which can otherwise impede ventilation
- Intubation may be required for additional respiratory support or airway protection in a child with reduced conscious state, and children in shock (to facilitate the insertion of lines, and support of cardiac function) (Refer to the Management of Paediatric Septic Shock guideline).
- PICU (onsite or via RSQ) should be consulted and ideally be in attendance prior to intubation. Other experienced clinicians, such as an anaesthetist, can be utilised.
- However, extreme caution needs to be exerted and clinicians need to be prepared that the child may arrest from cardiovascular collapse on induction (drugs with negative inotropy should be avoided, such as midazolam or propofol). Have the arrest dose of IV adrenaline ready (0.1mL/kg of 1:10,000).
- The child should be adequately pre-oxygenated and have haemodynamics optimised with concomitant fluid resuscitation and inotrope infusion prior to intubation.
- The induction drug dose is reduced when a child has significant cardiovascular compromise (i.e. 50% of weight based dose).
- Ketamine (0.5 – 1mg/kg) and/or Fentanyl (1-2mcg/kg) for induction, which are less cardiodepressant, and Rocuronium (1.2mg/kg) for muscle relaxation, are generally a suitable combination for rapid sequence induction in sepsis.

*Circulation*

- Profound fluid loss from the intravascular space occurs due to capillary leak from the systemic inflammatory response
- Fluid resuscitation is aimed at restoring normal physiological parameters, particularly heart rate and blood pressure[21]
- Only isotonic fluids should be rapidly infused and in the emergency environment the preference is Sodium chloride 0.9% (normal saline), given that it is readily available. Alternative options include Hartmanns solution or 4% human albumin. Hypotonic fluids should never be used as bolus therapy.
- Although there could be a theoretical advantage in using colloids (e.g. 4% human albumin) in the setting of paediatric sepsis, there is currently insufficient evidence to support or refute their routine use[22]
- Administer fluids as a rapid bolus (20mL/kg) and repeat as necessary being mindful of the development of fluid overload (inspiratory crepitations, hepatomegaly, and/or gallop rhythm)
- Inotropes should be considered in fluid-refractory shock, to be started as early as within 15 minutes of presentation, which has been shown to improve outcomes[22-23]

- First-line choice is adrenaline starting at 0.05-0.1mcg/kg/min (maximum 1mcg/kg/min), which can be administered temporarily via a peripheral IV or IO line before central access is gained in a suitable environment. (Alternative: dopamine starting dose 5-10mcg/kg/min)
- Aliquots of IV adrenaline can be given as 1mcg/kg (i.e. 0.1mL/kg of a 1:100,000 adrenaline solution) if an infusion is still being prepared and the patient remains in shock. A 1:100,000 adrenaline solution can be prepared by diluting 1mL of 1:10,000 adrenaline solution (i.e. 100 micrograms of adrenaline) with 9mL of Sodium chloride 0.9% (normal saline)
- For further advice on inotropes, please contact PICU as per your site

**ALERT**

First-line inotropes can be commenced peripherally. Lack of central access should not delay the commencement of inotropes when indicated.

*Antibiotic therapy*

- Refer to the CHQ Paediatric Antibiocard: Empirical Antibiotic Guidelines
- Early appropriate administration can save lives.
- Several studies have demonstrated that early antibiotic administration resulted in shorter time to reversal of shock and lower rate of mortality.[5,24]
- The initial choice of antibiotic therapy is complex and is based on the clinical syndrome, focus of infection, underlying disease, drug intolerances and local pathogen susceptibility.
- Initial treatment will have broad spectrum coverage suited for the prevalent organisms for each age group and geographical area, which can be narrowed once a causative pathogen is identified.
- Please consult a paediatric infectious disease specialist for further advice for unusual circumstances
- Any high risk child (Box 1) presenting with fever should be discussed with their treating paediatrician or subspecialist, as there is generally a lower threshold for the initiation of antibiotic treatment

*Other considerations*

- IV hydrocortisone (1mg/kg) is administered in patients with suspected or proven adrenal insufficiency[8,25] It can be considered in fluid and inotrope resistant shock but data for its efficacy in this setting is limited in the paediatric population.
- Alternative diagnoses need to be considered in all patients, especially neonates who may have a metabolic or cardiogenic (congenital duct dependent lesions or acquired cardiac failure eg. myocarditis) cause of their shock
- Electrolyte disturbance (e.g. hypocalcaemia) is common in critically ill children with sepsis and can contribute to poor cardiac function. Replacement should be in accordance with local guidelines.
- Source control is an important consideration, for instance abdominal related sepsis or necrotising fasciitis, and should have early involvement of surgical services

## Supporting documents

**Procedures, Guidelines and Protocols**

- CHQ Guideline – Febrile Illness – Emergency Management in Children http://qheps.health.qld.gov.au/childrenshealth/resources/proc/docs/proc_00707.pdf
- CHQ Guideline – Management of Paediatric Septic Shock http://qheps.health.qld.gov.au/childrenshealth/resources/clinguide/docs/guide-mgt-paed-septic-shock.pdf
- CHQ Paediatric Antibiocard: Empirical Antibiotic Guidelines http://qheps.health.qld.gov.au/childrenshealth/docs/lcch/ams/Antibiocard.pdf
- CHQ Empiric Antibiotic Guidelines for Paediatric Intensive Care Unit (PICU)

https://www.childrens.health.qld.gov.au/wp-content/uploads/PDF/ams/DUG_Empiric.pdf
- Management of Fever in the Neutropenic Paediatric Oncology Patient http://qheps.health.qld.gov.au/childrenshealth/resources/clinguide/docs/CPG_Cancer_Neut.pdf
- Management of the Paediatric Non-Neutropenic Oncology Patient with Fever http://qheps.health.qld.gov.au/childrenshealth/resources/clinguide/docs/CPG_Cancer_Non.pdf
- CHQ Guideline – Fever in a Child with Central Venous Access Device https://www.childrens.health.qld.gov.au/wp-content/uploads/PDF/ams/guide-fever-cvad.pdf
- CHQ Procedure: Medication Administration – Consideration by various routes in children http://qheps.health.qld.gov.au/childrenshealth/resources/proc/docs/proc_01043.pdf

## Consultation

Key stakeholders who reviewed this version:

- Dr Peter Snelling, Paediatric Emergency Physician (CHQ)
- A/Prof Luregn Schlapbach, Paediatric Intensive Care Physician (CHQ)
- A/Prof Julia Clark, Director Infection Management and Prevention (CHQ)
- Nicolette Graham, Antimicrobial Stewardship Pharmacist (CHQ)

Children's Health Queensland would like to acknowledge the contribution made by the Greater Brisbane Metropolitan Area Clinical Procedures Working Group who developed the original guideline.

### List of Abbreviations

| | |
|---|---|
| ARDS | Acute respiratory distress syndrome |
| CHQ | Children's Health Queensland |
| CVAD | Central venous access device |
| DIC | Disseminated intravascular coagulation |
| GCS | Glasgow Coma Scale |
| ICP | Intracranial pressure |
| IO | Intraosseous |
| IM | Intramuscular |
| IV | Intravenous |
| MAP | Mean arterial pressure |
| nmMRSA | Non multi-resistant Methicillin resistant Staphylococcus aureus |
| PCR | Polymerase chain reaction |
| PEEP | Positive end expiratory pressure |
| PICU | Paediatric Intensive Care Unit |
| RSI | Rapid sequence induction |
| RSQ | Retrieval Services Queensland |
| SCHHS | Sunshine Coast Hospital and Health Service |
| VP | Ventriculoperitoneal |

## Definition of terms

| Term | Definition | Source |
|---|---|---|
| SIRS | Systemic inflammatory response syndrome. The presence of at least two of the following four criteria, one of which must be abnormal temperature or leukocyte count:<br>• Core temperature of >38.5$^{o}$C or <36$^{o}$C<br>• Tachycardia, defined as a mean heart rate ≥2 SD above normal for age in the absence of external stimulus, chronic drugs, or painful stimuli; or otherwise unexplained persistent elevation over a 0.5-4 hour time period OR for children <1 yr old: bradycardia, defined as a mean heart rate <10$^{th}$ percentile for age in the absence of external vagal stimulus, β blocker drugs, or congenital heart disease; or otherwise unexplained persistent depression over a 0.5hr time period<br>• Mean respiratory rate >2 SD above normal for age or mechanical ventilation for an acute process not related to underlying neuromuscular disease or the receipt of general anaesthesia<br>• Leukocyte count elevated or depressed for age (not secondary to chemotherapy-induced leukopaenia) or >10% immature neutrophils. | Goldstein 2005 |
| Infection | A suspected or proven (by positive culture, tissue stain, or polymerase chain reaction test) infection caused by any pathogen OR a clinical syndrome associated with a high probability of infection. Evidence of infection includes positive findings on clinical exam, imaging, or laboratory tests (e.g. white blood cells in a normally sterile body fluid, perforated viscus, chest radiograph consistent with pneumonia, petechial or purpuric rash, or purpura fulminans) | |
| Sepsis | SIRS in the presence of or as a result of suspected or proven infection. | |
| Severe sepsis | Sepsis plus one of the following: cardiovascular organ dysfunction OR acute respiratory distress syndrome OR two or more other organ dysfunctions | |
| Septic shock | Sepsis and cardiovascular organ dysfunction:<br>Despite administration of isotonic intravenous fluid bolus of 40mL/kg in 1 hr<br>• Decrease in BP (hypotension) <5$^{th}$ percentile for age or systolic BP <2 SD below normal for age OR<br>• Need for vasoactive drug to maintain BP in normal range<br>• Two of the following:<br>o Unexplained metabolic acidosis: base deficit >5.0 mEq/L<br>o Increased arterial lactate >2 times upper limit of normal<br>o Oliguria: urine output <0.5mL/kg/hr<br>o Prolonged capillary refill: >5 secs<br>o Core to peripheral temperature gap >3$^{o}$C | |

## References and suggested reading


1. Shlapbach L, Straney L, Alexander J, MacLaren G, Festa M, Schibler A, Slater A. Mortality related to invasive infections, sepsis, and septic shock in critically ill children in Australia and New Zealand, 2002-13: a multicentre retrospective cohort study. *Lancet Infective Disease*. 2015; 15:46-54.
2. Weiss SL, Fitzgerald JC, Pappachan J, et al. Global epidemiology of pediatric severe sepsis: the sepsis prevalence, outcomes, and therapies study. *American Journal of Respiratory and Critical Care Medicine*. 2015; 191(10):1147-1157.
3. Friedman G, Silva E, Vincent JL. Has the mortality of septic shock changed with time? *Critical Care Medicine*. 1998; 26:2078-86.
4. Angus DC, Linde-Zwirble WT, Lidlicker J, et al. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Critical Care Medicine*. 2001; 29:1303-10.
5. Weiss SL, Fitzgerald JC, Balamuth F, et al. Delayed antimicrobial therapy increases mortality and organ dysfunction duration in pediatric sepsis. *Critical Care Medicine*. 2014; 42:2409-17.
6. Kumar A, Roberts D, Wood K, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Critical Care Medicine*. 2006; 34(6):1589-96
7. Launay E, Gras-Le Guen C, Martinot A et al. Why children with severe bacterial infection die: a population-based study of determinants and consequences of suboptimal care with a special emphasis on methodological issues. *PLoS ONE* 9(9): e107286
8. Dellinger RP, Levy MM, Rhodes A, et al; Surviving Sepsis Campaign Guidelines Committee. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Critical Care Medicine*. 2013; 41:580-637.
9. Rivers et al. Early goal directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*. 2001; 345:1368-77.
10. Goldstein B, Giroir B, Randolph A. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in paediatrics. *Pediatric Critical Care Medicine*. 2005; 6:2-8.
11. Singer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016; 315(8):801-810.
12. Bone RC. The sepsis syndrome. Definition and general approach to management. *Clin Chest Med*. 1996; 17:175-81.
13. Hotchkiss RS, Karl IE. The pathophysiology and treatment of sepsis. *N Engl J Med*. 2003; 348:138-150.
14. Plunket A, Tong T. Sepsis in Children. BMJ. 2015; 350:h3017(1-12)
15. https://pathways.nice.org.uk/pathways/sepsis
16. Brierley J, Peters MJ. Distinct hemodynamic patterns of septic shock at presentation to pediatric intensive care. *Pediatrics* 2008; 122:752-9.
17. Adalat S, Dawson T, Hackett SJ, Clark JE, et al. Toxic shock syndrome surveillance in UK children. *Arch Dis Child*. 2014; 0:1-5.
18. Kayange N, Kamugisha E, Mwizamholya DL, et al. Predictors of positive blood culture and deaths among neonates with suspected neonatal sepsis in a tertiary hospital, Mwanza-Tanzania. *BMC Pediatr*. 2010; 10:39
19. Polin RA; Committee on Fetus and Newborn. Management of neonates with suspected or proven early-onset bacterial sepsis. *Pediatrics* 2012; 129:1006-15.
20. Pearson GA, ed. Why children die: a pilot study 2006; England (South West, North East and West Midlands), Wales and Northern Ireland. *CEMACH*; 2008.
21. Brierley J, Carcillo JA, Choong
22. K, et al. Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. *Critical Care Medicine*. 2009;37:666-88.
23. Carcillo JA. Intravenous fluid choices in critically ill children. *Curr Opin Crit Care*. 2014;20:396-401.
24. Ninis N, Phillips C, Bailey L, et al. The role of healthcare delivery in the outcome of meningococcal disease in children: case-control study of fatal and non-fatal cases. *BMJ* 2005; 330:1475.
25. Wang XD, Huo XM, XU MX, et al. Clinical research of timing of application of antibiotics in septic shock of pediatric patients. *Zhonghua Wei Zhong ing Ji Jiu Yi Xue*. 2013; 25:207-10.

26. Aneja R, Carcillo JA. What is the rationale for hydrocortisone treatment in children with infected-related adrenal insufficiency and septic shock? *Arch Dis Child* 2007; 92:165-9.

## Guideline revision and approval history

| Version No. | Modified by | Amendments authorised by | Approved by |
|---|---|---|---|
| 1.0 | Dr Jason Acworth, Director Paediatric Emergency Department | Divisional Director, Critical Care | Executive Director Medical Services |

| | |
|---|---|
| **Keywords** | Sepsis, shock, critical ill, bacterial, emergency, SIRS, deteriorating child, toxic shock syndrome, meningitis, CVAD, community-acquired, nosocomial, antimicrobial stewardship, 07449 |
| **Accreditation references** | NSQHS Standards: 3, 4<br>EQuIPNational Standards: 7, 9, 12 |

# Appendix 1 EARLY MANAGEMENT OF PAEDIATRIC SEPSIS

**0 min**

**Recognition**

- High Risk **(Box 1)**
- Fever (>38.5°C) or hypothermia (<36°C)
- Abnormal
  - Appearance (unwell/colour)
  - Vital Signs **(Box 2)** / pulse
  - Conscious State/Irritability
  - Skin perfusion/purpura/petechiae

**<5 min**

**Immediate Actions**

- Call for help (experienced clinicians)
- Attach cardiorespiratory monitoring
- Assess airway and administer oxygen
- Initial assessment

**<15 min**

**Establish Vascular Access**

- Insert IO if 2 attempts at IV fail
- Consider UVC in a neonate <2wks of life
- Take bloods:
  - BC, VBG with lactate and glucose (priority)
  - FBC, CRP, CHEM20 +/- Coags, +/- Grp & hold
- **Administer IV antibiotics* (Box 3)**
  - IM ceftriaxone 50mg/kg (max 2g) if delayed
  - Give full dose(s) of IV antibiotic(s) once IV access established

**<30 min**

**Intravenous Fluid Administration**

- 20mL/kg Sodium chloride 0.9% over ~5min
- Repeat 20mL/kg Sodium chloride 0.9% bolus
- Each time assess response:
- Aim: HR, improved mentation/perfusion
- Overload: hepatomegaly, crepitations; Echo
- Prepare adrenaline 1:100,000 + infusion

**<60 min**

**Inotropes & Further Considerations**

- No improvement after 40ml/kg IV fluid or decreased BP
- Adrenaline infusion 0.05-0.5mcg/kg/min
  - Can be initially low dose via peripheral IV
  - Or IV bolus 0.1ml/kg of 1:100,000 adrenaline (i.e. 1mcg/kg)
- PICU involvement **(Box 4)**
  - **RSQ Contact: 1300 799 127**
  - Consider further IV fluid boluses
  - Consider early intubation **(Box 5)**
- Correct hypoglycaemia/hypocalcaemia
- Consider IV hydrocortisone (1mg/kg)

**Box 1: Risk Factors for Sepsis**

- <2 months/prematurity
- Unimmunised/incomplete status
- Immune deficiency
- Asplenia (surgical/functional)
- Immunosuppressant therapy
- Recent surgical procedure
- Indwelling lines/catheters
- Malignancy/chemotherapy *(refer to Febrile neutropenia/non-neutropenia Guidelines)*

**Box 2: Normal Values**

| Threshold values | HR (bpm) | Min Sys BP (mmHg) | RR (bpm) |
|---|---|---|---|
| Term | 100-180 | 60 | 40-60 |
| 6mth | 100-180 | 70 | 30-50 |
| 1yr | 100-170 | 70 | 20-40 |
| 2yr | 100-160 | 70 | 20-30 |
| 4yr | 80-130 | 75 | 20-30 |
| 8yr | 70-110 | 80 | 16-25 |
| 12yr | 60-110 | 90 | 16-25 |
| 16yr+ | 60-100 | 90 | 10-16 |

**Box 3: CHQ IV Antibiotic quick guide**

**<2 mths**
Ampicillin 50mg/kg plus
Gentamicin 7.5mg/kg (<1mth 4mg/kg)
+/- Cefotaxime 50mg/kg (meningitis)

**>2mths**
Cefotaxime 50mg/kg (max 2g)
*For penicillin allergy:*
Lincomycin 15mg/kg (max 1.2g)

**Septic Shock (inotropes)**
+ Gentamicin 7.5mg/kg (max 320mg <10yr / max 640mg >10y) then
+ Vancomycin 15mg/kg (max 750mg)

**Toxic Shock/nmMRSA**
+ Lincomycin 15mg/kg (max 1.2g)

**Nosocomial (refer to AMS*)**

**Box 4: Triggers for PICU Involvement**

- No improvement after 40ml/kg fluid administration
- Inotropes
- Reduced level of consciousness
- Hypotension
- Septic/toxic shock
- Coagulopathy/DIC
- Lactate >4mmol/L

**Box 5: RSI/Intubation**

Anticipate child could arrest
- Ketamine 0.5-1mg/kg
- +/- Fentanyl 1-2mcg/kg
- Rocuronium 1.2mg/kg

* March 2017. Refer to http://qheps.health.qld.gov.au/childrenshealth/docs/lcch/ams/Antibiocard.pdf for latest protocol