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Paediatric Sepsis Guideline

Definitions:

Systemic Inflammatory Response (SIRS):[1]

The presence of at least two of the following criteria, one of which must be abnormal temperature or leukocyte count:

- Core temperature of > 38.5°C or < 36°C.
- 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 0.5-4hour period or for children < 1 years old; bradycardia; defined as a mean heart rate < 10th percentile for age in the absence of external vagal stimulus, β blockers, or congenital heart disease; or otherwise unexplained persistent depression over a 0.5 hour time period.
- 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.
- Leukocyte count elevated or depressed for age (not secondary to chemotherapy induced leukopenia) or > 10% immature neutrophils.

Infection:[1]

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 (i.e. white blood cells in a normally sterile body fluid, perforated viscus, chest radiograph consistent with pneumonia, petechial or purpuric rash or purpura fulminans).

Sepsis:[1]

SIRS in the presence of or as a result of suspected or proven infection.

Severe Sepsis:[1]

Sepsis plus one of the following: cardiovascular organ dysfunction or acute respiratory distress syndrome or two or more other organ dysfunction. (Table 1)

Septic Shock:[1,2]

Sepsis and cardiovascular organ dysfunction as defined in table 1. Septic shock in children is defined as tachycardia (which may be absent in the hypothermic

patient) with signs of decreased perfusion including decreased peripheral pulses compared with central pulses, flash capillary refill or capillary refill > 2 seconds, mottled or cool extremities, decreased urine output or altered alertness. Hypotension is a late sign in children and is not needed for the clinical diagnosis of septic shock, however if present in a child with proven or suspected infection, the diagnosis is confirmed.

Table 1: Organ dysfunction criteria:[1]

Cardiovascular dysfunction
Despite administration of isotonic intravenous fluid bolus ≥40 mL/kg in 1 hr
- Decrease in BP (hypotension) <5th percentile for age or systolic BP <2 SD below normal for age[a]

OR
- Need for vasoactive drug to maintain BP in normal range (dopamine >5 μg/kg/min or dobutamine, epinephrine, or norepinephrine at any dose)

OR
- Two of the following
  Unexplained metabolic acidosis: base deficit >5.0 mEq/L
  Increased arterial lactate >2 times upper limit of normal
  Oliguria: urine output <0.5 mL/kg/hr
  Prolonged capillary refill: >5 secs
  Core to peripheral temperature gap >3°C

Respiratory[b]
- Pao_2/Fio_2 <300 in absence of cyanotic heart disease or preexisting lung disease

OR
- $Paco_2$ >65 torr or 20 mm Hg over baseline $Paco_2$

OR
- Proven need[c] or >50% Fio_2 to maintain saturation ≥92%

OR
- Need for nonelective invasive or noninvasive mechanical ventilation[d]

Neurologic
- Glasgow Coma Score ≤11 (57)

OR
- Acute change in mental status with a decrease in Glasgow Coma Score ≥3 points from abnormal baseline

Hematologic
- Platelet count <80,000/mm^3 or a decline of 50% in platelet count from highest value recorded over the past 3 days (for chronic hematology/oncology patients)

OR
- International normalized ratio >2

Renal
- Serum creatinine ≥2 times upper limit of normal for age or 2-fold increase in baseline creatinine

Hepatic
- Total bilirubin ≥4 mg/dL (not applicable for newborn)

OR
- ALT 2 times upper limit of normal for age

Sepsis in children:

Paediatric septic shock is generally associated with severe hypovolaemia and children frequently respond to aggressive volume resuscitation. The majority of children show a low cardiac output (CO)/high systemic vascular resistance (SVR) state – cold shock and only a small proportion have a low CO/low SVR state – warm shock. Contrary to adults, low CO, not low SVR is associated with high mortality in paediatric sepsis. Also, a reduction in oxygen delivery rather than a defect in oxygen extraction can be the major determinant of oxygen deficit in children.

The importance of early recognition and treatment:

Sepsis is still a major cause of mortality and morbidity within paediatrics. The WHO reported that in the UK sepsis accounts for more than 10% of deaths in

children < 4 years of age. [3] Up to 20% of children admitted to PICUs with severe sepsis die.[4] The American College of Critical Care Medicine/Paediatric Advanced Life Support published guidelines in 2002 [2] and subsequently updated them in 2007. [5] They emphasize the importance of early recognition, adequate fluid resuscitation, appropriate use of inotropes/vasopressors and early administration of antibiotics. **Delayed adequate resuscitation has shown to double the mortality rates with each hour of persistent shock.** [6]

Recognition:[5]

Suspected infection manifested by:

- Hypothermia or hyperthermia
- Altered mental status (irritability, inappropriate crying, drowsiness etc)
- Tachypnoea
- Tachycardia or bradycardia
- Decreased urine output (<1ml/kg/min)
- Signs of either cold or warm shock

Cold Shock	Warm Shock
Capillary refill > 3 seconds	Flash capillary refill
Reduced peripheral pulses	Bounding peripheral pulses
Cool mottled extremities	Warm extremities
Narrow pulse pressure	Wide pulse pressure

It is a clinical diagnosis and treatment should not be delayed waiting for biochemical tests.

A normal BP can be falsely reassuring as can a normal neurological status. Hypotension is a late sign in children and is not needed for the clinical diagnosis of septic shock, however if present in a child with proven or suspected infection, the diagnosis is confirmed.

Normal physiological ranges for age [7]

Age (years)	Respiratory Rate (bpm)	Heart Rate (bpm)	Systolic BP (mmHg)
<1	30-40	110-160	80-90
1-2	25-35	100-150	85-95
2-5	25-30	95-140	85-100
5-12	20-25	80-120	90-110
>12	15-20	60-100	100-120

The first hour of resuscitation:

On arrival in the Emergency department the child should be assessed following an ABCDE approach and resuscitation should be started immediately. **Delayed adequate resuscitation has shown to double the mortality rates with each**

hour of persistent shock. [6] The child needs to be reassessed on a regular basis.

Goals of 1st hour:[5]

- Normal mental status
- Normal physiological parameters for age: HR, BP, RR (see above)
- Normal perfusion:
  - Capillary refill ≤ 2 seconds
  - Normal pulses with no differential between the quality of peripheral and central pulses
  - Warm extremities
  - Urine output > 1ml/kg/hr
- Normal glucose concentration and ionized calcium
- Serum lactate < 2

Indicators of disease severity despite 'how good they look':

- Low neutrophils
- Low platelets
- Rapid onset (< 6 hours)
- Rapidly spreading rash
- High (≥ 60 mls/kg) fluid volume requirements

Management within the 1st hour:[5]

- Recognise decreased mental status and perfusion
- Maintain or restore a patent airway.
- Give high flow O_2 - maintaining O_2 saturations > 95%.
- Establish monitoring: Pulse oximeter, ECG, BP, Temperature, Urine output.
- Obtain IV access x 2 – **Do not waste time** - IO access if reliable venous access cannot be established within minutes.
- Bloods: FBC, U&Es, LFTS, CRP, Coagulation, lactate, glucose, magnesium, calcium, phosphate, blood gas (if possible) and blood cultures.
- If signs of shock – give 20ml/Kg of 0.9% saline over 5 minutes and then reassess.
- Begin high dose broad spectrum antibiotics (see local guidelines)
- Correct hypoglycaemia – 5 ml/kg 10% dextrose IV
- Correct hypocalcaemia – 10% Calcium Gluconate 1-2ml/kg IV

Shock not reversed

- If no improvement in physiological parameters and no signs of fluid overload (increased work of breathing, crepitations, gallop rhythm or hepatomegaly) give a further 20ml/kg of 0.9% saline.
- Continue this cycle up to and over 60ml/kg until perfusion improves or signs of fluid overload.
- Children commonly require 40-60ml/kg in the first hour but much larger volumes may be necessary.

Shock not reversed

- **Fluid refractory Shock**:
- Commence peripheral inotrope/vasopressor. Cold shock titrate dopamine, if resistant add in adrenaline and warm shock titrate noradrenaline – see appendix 1
- Watch for tissue integrity
- Intubate – see appendix 2
- Obtain central and arterial line access

Shock not reversed

- **Catecholamine resistant shock**:
- Give Hydrocortisone 2.5-5mg/kg/day in divided doses 6 hourly
- Transfer to PICU

Beyond the 1st hour:

- Monitor in PICU: Pulse oximeter, EtCO2, ECG, intra-arterial BP, CVP, CO, Urine output and core temperature

Shock not reversed

• **Cold shock with normal BP**: • Titrate fluid and adrenaline, ScVO2 > 70%, Hb > 100g/L • If ScVO2 still < 70% add in a vasodilator with volume loading(i.e. milrinone)	• **Cold shock with low BP**: • Titrate fluid and adrenaline, ScVO2 > 70%, Hb > 100g/L • If still hypotensive consider noradrenaline • If ScVO2 still < 70% consider dobutamine or milrinone	• **Warm shock with low BP**: • Titrate fluid and noradrenaline, ScVO2 > 70%, Hb > 100g/L • It still hypotensive consider vasopressin • If ScVO2 still < 70% consider low dose adrenaline

Shock not reversed

- **Persistent catecholamine resistant shock**:
- Rule out and correct pericardial effusion, pneumothorax and intra-abdominal pressure > 12mmHg
- Consider cardiac monitoring to guide fluid, inotrope, vasopressor, vasodilator and hormonal therapies
- Goal: Cardiac Index > 3.3 and < 6.0L/min/m2

Shock not reversed

- **Refractory Shock**: Consider continuous Renal Replacement Therapy (RRT) or ECMO

Beyond the 1st hour (PICU):

Monitoring:

- Pulse oximetry
- $EtCO_2$
- Continuous ECG
- Intra-arterial blood pressure and pulse pressure
- Cardiac output if available
- Continuous central venous pressure (CVP)
- Mixed venous saturations ($ScVO_2$) (see appendix 3)
- Urine output
- Core temperature
- Peripheral temperature

Management:

Respiratory:

- Pulmonary oedema is common in sepsis induced MODS due to capillary leak and myocardial failure.
- Use lung protective ventilation strategies: tidal volumes 4-7ml/kg and avoid PIP > $30cmH_2O$
- Often the use of high PEEP and prolonged inspiratory times (1.0-1.5s) can help to maintain lung volumes
- Consider tolerating a permissive hypercapnia – aiming for arterial pH > 7.25
- Maintain SaO_2 > 90%
- Consider prone positioning in children with sepsis induced ARDS with a PaO_2/FiO_2 Ratio ≤ 13.3kPa
- Consider high frequency oscillatory ventilation if PIP > $30cmH_2O$ and FiO_2 > 0.6. Children may require extra cardiovascular support because ventilation can induce decrease preload and RV dysfunction
- Neuromuscular blocking agents (NMBAs) should be avoided if possible in the septic patient but may be necessary to improve compliance with ventilation

Cardiovascular:

Optimal fluid resuscitation:

In sepsis diffuse capillary leak leading to persistent hypovolaemia is commonly seen and can last for days. Ongoing fluid resuscitation should be goal directed using clinical end points including:

- Perfusion (warm extremities, normal pulses – no difference in peripheral and central pulses, capillary refill ≤ 2 seconds)
- Aim for a central venous pressure (CVP) 8-12mmHg (remember the CVP will be affected by the PEEP)
- Cardiac index > 3. 3 and < $6.0L/min/m^2$
- $ScVO_2$ >70% (see appendix 3)

Albumin 4.5% is the fluid of choice in patients with a Hb > 100g/L and should be given in boluses of 20ml/kg as required. Crystalloid may be used if faster available. Red blood cell transfusion can be given to children with a Hb < 100g/L.

Adrenaline resistant shock with low CI, normal BP and high SVR i.e. cold shock:

Aim to reduce afterload and thus increase stroke volume and therefore reduce end diastolic volume. 1st Line choice in this situation is Milrinone (see appendix 1)

Adrenaline resistant shock with low CI, low BP and Low SVR i.e. cold shock:

Aim to increase preload by increasing SVR by titrating in noradrenaline. Once an adequate BP is achieved Dobutamine or Milrinone can be added in order to increase cardiac contractility (see appendix 1).

Noradrenaline resistant shock with high CI and low SVR i.e. warm shock:

Aim to increase SVR. Low dose vasopressin can be used to restore BP (see appendix 1). It should be used with caution as it is a potent vasoconstrictor and can reduce CO.

Refractory shock:

Rule out the presence of the following:

- Pneumothorax
- Pericardial effusion
- Hypoadrenalism
- Hypothyroidism
- Ongoing blood loss
- Increased intra-abdominal pressure (e.g. ascites). Might need abdominocentesis and drain (rare)
- Necrotic tissue
- Inappropriate source control of infection
- Excessive immunosuppression
- Toxic shock (consider change in antibiotics and iv immunoglobulin (see appendix 5)

Sodium Bicarbonate:

Sodium bicarbonate is not recommended for the purpose of improving haemodynamics or reducing vasopressor requirements in patients with hypoperfusion-induced lactic acidaemia with pH ≥ 7.15.[15]

Replacement steroids:

Please see below under endocrine.

Continuous Renal Replacement Therapy (CRRT):

Should be considered in patients with refractory shock. The use of high flux CRRT (>35ml/kg/hr) has been shown to reduce inotropic/vasopressor requirements in children with refractory septic shock.[10,11]

Indications in sepsis:

- Oliguria (urine output < 1ml/kg/hr in infants and < 0.5ml/kg/hr in children)
- Anuria
- Potassium (> 6.5mmol/L or rapidly rising)
- Fluid overload (better outcomes when < 10% fluid overloaded then >10% fluid overloaded)
- Persistent uncompensated metabolic acidosis (pH < 7.1)
- Persistent temperature > 40^0C
- Uraemic complications (encephalopathy, bleeding, pericarditis)
- In practice: just about every child with septic shock on inotropes

Extracorporeal membrane oxygenation (ECMO):

ECMO should be considered in patients with refractory shock. If cardiovascular instability remains despite increasing cardiovascular support the patient should be discussed early with the ECMO team before cardiovascular collapse. The expected survival with ECMO is no greater than 50%.[9]

Renal:

- Pre-renal failure is common in septic shock but its incidence can be reduced with early, adequate resuscitation.
- Diuretics/renal replacement therapy should be considered early (within first few hours) in children who show signs of fluid overload and who are unable to maintain their fluid balance with native urine output/extra-renal losses.
- Ventilated children receiving intravenous fluid only should be restricted to 70% of their maintenance requirements, unless receiving CVVH. (see appendix 4).

Metabolic:

- Electrolyte abnormalities are common in sepsis and can affect myocardial and skeletal muscle function and can precipitate arrhythmias.
- Hypokalaemia:
    - Assess need for urgent correction of deficit – is the child symptomatic (cardiac arrhythmias, severe muscle weakness, ileus), are they at risk (congenital heart disease, myopathy, severe illness)
    - Urgent replacement – 0.5mmol/kg over 1 hour via a central line and then recheck K^+.
    - Non-urgent replacement – K^+ additives in maintenance fluid (max concentration 40mmol/L) or enteral supplements
- Hypocalcaemia:
    - Use ionized Calcium as a guide to treatment.
    - Calcium supplementation should be commenced if ionized calcium is < 1.0 mmol/l unless symptomatic
    - Calcium is corrosive and should therefore be given through a large vein.
    - Give 10% calcium gluconate at 1-2ml/kg as a slow IV injection
- Hypomagnesaemia:
    - Can cause arrhythmias

  - Replace with 0.2mmol/kg – can cause hypotension therefore administer over 30 minutes.
- Hypophosphataemia:
  - Can lead to muscle weakness
  - Replace with 0.5mmol/kg over 10 hours

Coagulopathy/thrombocytopenia:

- Coagulopathy is commonly seen in severe sepsis due to consumption (Disseminate intravascular coagulopathy (DIC)) and dilution (fluid resuscitation).
- FFP is recommended for children with a coagulopathy. If required 10-20ml/kg should be given as an infusion over 30 minutes, not a bolus.
- Low fibrinogen (< 1) is suggestive of DIC; give 5-10ml/kg of cryoprecipitate
- In patients with severe sepsis, administer platelets prophylactically when counts are < 10×10^9/L in the absence of apparent bleeding. Prophylactic platelet transfusion when counts are < 20×10^9/L if the patient has a significant risk of bleeding. Higher platelet counts ≥ 50×10^9/L are advised for active bleeding, surgery, or invasive procedures [15].

Endocrine

- Risk factors for inadequate cortisol/aldosterone production include:
  - Purpura fulminans
  - Waterhouse Friderichsen syndrome
  - Recent steroid therapy for chronic illness
  - Pituitary or adrenal abnormalities

  The role of steroids in the treatment of septic shock is still unclear. The American college of critical care medicine recommends a stress dose of Hydrocortisone rather than the shock dose, which is 25 times greater. [5] Hydrocortisone therapy – 1mg/kg QDS for 7 days (max 50mg/kg QDS) recommended for children with:
  - Catecholamine resistant shock
  - Absolute adrenal insufficiency (peak cortisol concentration attained after corticotrophin stimulation < 18µg/dL)
  - Adrenal pituitary axis failure
- Hypothyroidism is common in children with trisomy 21 and children with central nervous system pathology (i.e. pituitary abnormalities). Thyroid replacement with triiodothyronine is warranted in thyroid insufficiency.
- Monitor BMs. If hypoglycaemic give 5ml/kg of IV 10% dextrose slowly. Consider increasing glucose concentration of maintenance fluids. If sustained hyperglycaemic BMs > 10mmol/L consider titrating an insulin infusion but monitor closely to avoid hypoglycaemia.

Nutrition:

- Enteral nutrition should be given to children who can be fed enterally and parenteral feeding in those who cannot.
- If unable to establish full enteral feeds stress ulcer prophylaxis (ranitidine or omeprazole, aiming for gastric pH ≥ 4) should be administered, especially when steroids are administered.

Antibiotics:

- Re-evaluate antibiotic therapy with microbiology cultures
- Consider the possibility of nosocomial superinfections including fungal
- Note that Ceftriazone is NOT to be given if Calcium supplementation is required (precipitation).
- Give Ciprofloxacin throat eradication after full course of Cefotaxime in meningococcal septic shock (see intranet guideline meningococcal septic shock)

Other:

- Consider surgical or radiological interventions

Goals:

- Normal mental status (if not intubated)
- Capillary refill ≤ 2seconds
- Threshold HRs for age
- Normal pulses with no differential between the quality of the peripheral and central pulses
- Warm extremities
- Normal perfusion pressures (MAP-CVP) for age
- Mean arterial pressure (MAP) within normal range for age
- CVP 8-12mmHg
- Urine output > 1ml/kg/hr in infants/younger children, 0.5ml/kg/hr in older children.
- $ScVO_2$ > 70% (see appendix 3)
- Normal INR, PT and APTT
- Normal Lactate
- Normal anion gap

Appendix 1: Newcastle PICU standard infusions:

Drug	To make standard solution	Concentration	Dose range [2]
Respiratory			
Aminophylline	1 mg/ml solution in 5% dextrose	1 ml/kg/hr = 1 mg/kg/hr	0.5 -1 mg/kg/hr
Salbutamol	1 mg/ml solution in 5% dextrose	0.06 ml/kg/hr = 1 microg/kg/min	1 - 8 microg/kg/min
Salbutamol (peripheral inf)	*200 microg/ml in 5% dextrose*	*0.012 ml/kg/hr = 1 microg/kg/min*	*Start 1-2 microg/kg/min*
Cardiovascular			
Adrenaline	0.3 mg/kg in 50ml 5% dextrose	1 ml/hr = 0.1 microg/kg/min	0.1 - 4 microg/kg/min
Amiodarone	15 mg/kg in 50ml 5% dextrose	1 ml/hr = 5 microg/kg/min	5 -15 microg/kg/min
Dobutamine [1]	15 mg/kg in 50ml 5% dextrose	1 ml/hr = 5 microg/kg/min	5 - 20 microg/kg/min
Dopamine [1]	15 mg/kg in 50ml 5% dextrose	1 ml/hr = 5 microg/kg/min	5 - 20 microg/kg/min
Dopamine (peripheral inf)	*3 mg/kg in 50 ml 5% dextrose*	*1 ml/hr = 1 microg/kg/min*	*5 – 10 microg/kg/min*
Esmolol	30 mg/kg in 50ml 5% dextrose	1 ml/hr = 10microg/kg/min	20 -200 microg/kg/min
Furosemide	25 mg/kg in 50 ml 0.9% NaCl	1 ml/hr = 0.5 mg/kg/hr	0.1 -1 mg/kg/hr (max 4mg/min)
GTN Glyceryl trinitrate	3 mg/kg in 50ml 5% dextrose	1 ml/hr = 1 microg/kg/min	1 - 8 microg/kg/min (max 200 microg/min)
Milrinone	1.5 mg/kg in 50ml 5% dextrose	1 ml/hr = 0.5 microg/kg/min	0.3 - 0.75 microg/kg/min
Noradrenaline	0.3 mg/kg in 50ml 5% dextrose	1 ml/hr = 0.1microg/kg/min	0.1 - 4 microg/kg/min
Phentolamine	30 mg/kg in 50ml 5% dextrose	1 ml/hr = 10 microg/kg/min	5 - 50 microg/kg/min
Prostaglandin E2	30 microg/kg in 50ml 5% dextrose	1 ml/hr = 10 nanograms/kg/min	5 - 20 nanograms/kg/min
SNP Sodium Nitroprusside	3 mg/kg in 50ml 5% dextrose	1 ml/hr = 1 microg/kg/min	1 - 8 microg/kg/min
Vasopressin	0.3 Units/kg in 50ml 5% dextrose (max 50 Units/50ml)	1 ml/hr = 0.0001 U/kg/min	0.0001 - 0.0008 Units/kg/min
Neurological			
Atracurium	NEAT	10 mg/ml	300 - 900 mcg/kg/hr
Fentanyl	0.1 mg/kg in 50ml 5% dextrose	1 ml/hr = 2 microg/kg/hr	1 - 5 microg/kg/hr

		OR Neat (50 microg/ml) if over 25kg		
Ketamine		2.5 mg/kg (max 125 mg) in 50 ml 0.9% saline	1 ml/hr = 50microg/kg/hr	< 50 weeks corrected: 0.5 - 1 ml/hr ≥ 50 weeks corrected: 1 - 2 ml/hr
Midazolam [1]		3 mg/kg in 50ml 5% dextrose	1 ml/hr = 1 microg/kg/min	1 - 4 microg/kg/min
Morphine [1]		1 mg/kg in 50ml 5% dextrose	1 ml/hr = 20 microg/kg/hr	10 - 40 microg/kg/hr
Propofol		NEAT	10 mg/ml (1%)	2 - 4 mg/kg/hr
Thiopental [3]		125mg (NOT mg/kg) in 50ml with 0.9% saline (0.25% solution)	1 ml/hr = 2.5 mg/hr 0.4ml/hr = 1 mg/hr	1 - 8 mg/kg/hr (max 48 hours continuous infusion)
Vecuronium [1]		3 mg/kg in 50ml 5% dextrose	1 ml/hr = 1 microg/kg/min	1 - 4 microg/kg/min

The basis of many of these infusions is the rule of 3s, i.e. 3 x Wt (kg) of drug (mg) in 50ml will produce a solution of strength such that 1ml/hr = 1microg/kg/min.

1 To be doubled for infants less than 10kg

2 Dose may changed on PICU Consultants' instructions

3 Thiopental infusion: Note this is a standard infusion (0.25%). Consider use of adult concentration (2.5%) in older children where large volumes required

Appendix 2 - Indications for intubation:[5]

- Impaired mental status
- Reduced level of consciousness – Glasgow Coma Scale ≤ 8 or AVPU ≤ P
- Increased work of breathing, worsening tachypnoea or oxygen requirements
- Impending cardiovascular collapse
- Fluid refractory shock (≥ 60ml/kg fluid resuscitation in the 1st hour without reversal of shock)

Up to 40% of CO may be required to support the work of breathing and this can be unloaded by ventilation, diverting blood to vital organs.

Increased intrathoracic pressure reduces left ventricular afterload which may be beneficial in patients with low CI and high SVR.

Suggested induction technique:

- Optimal volume loading + peripheral or central inotropic/vasoactive drug support is recommended before and during intubation
- Experienced personnel carrying out the procedure and an experienced assistant (i.e. ODP/ anaesthetic nurse/ PICU nurse)
- IV/IO access x 2
- Full monitoring: $ETCO_2$, Pulse oximetry, ECG and noninvasive BP
- IV fluids connected and running
- Pre-oxygenate with 100% oxygen
- Recommended induction agents due to their relative cardiovascular stability:[5*]
    - Ketamine 1-2mg/kg
    - Fentanyl 2-5µg/kg
    - Suxamethonium 1-2mg/kg (contraindicated in children with (suspected) muscle disease, burns and cerebral palsy) or Rocuronium 0.6mg/kg, Atracurium 1 mg/kg
    - +/- Atropine
- Have emergency drugs drawn up pre-induction
- Rapid sequence induction
- Correct size ET tube – have a size above and below available (consider a cuffed ET tube even in infants in the presence of pulmonary oedema in order to obtain adequate ventilation)
- Confirm ET tube position with CXR (Tip at T2-T3)
- Ventilate using lung protective measures – tidal volumes 4-7ml/kg
- Keep sedated with Morphine and Midazolam infusions (see appendix 1)

*Thiopentone, propofol, benzodiazepines and inhalation agents can cause significant myocardial depression and should therefore be used with caution in septic shock. NEVER use Etomidate because of adrenal insufficiency (even after 1 bolus dose)

Appendix 3: Central venous O_2 saturations ($ScVO_2$):

Central venous O_2 saturations can be obtained by the insertion of a central line into the superior vena cava via the internal jugular vein. They give you an indication to whether oxygen delivery and extraction is meeting tissue oxygen demand in critically ill patients.

Normal value of $ScVO_2$ > 70%

Low $ScVO_2$:

Classification:

- > 50% and < 70%: compensatory extraction due to increased O_2 demand or decreased O_2 supply.
- > 30% and < 50%: exhaustion of extraction. Lactic acidosis develops. O_2 supply < O_2 demand.
- > 25% and < 30%: severe lactic acidosis develops
- < 25% cellular death

Causes:

Increased O_2 consumption:

- Stress
- Pain
- Hyperthermia
- Shivering

Decreased O_2 delivery:

- Decreased CaO_2 (anaemia, hypoxia)
- Decreased cardiac output

Management of a low $ScVO_2$:

- Increase O_2 delivery:
  - Aim for a CVP > 12mmHg
  - Aim for a Hb > 100g/L
  - Aim for a CO > 3.3L/min/m^2 using adequate volume loading and inotrope/vasodilator support
- Decrease O_2 consumption by use of:
  - Mechanical ventilation
  - Analgesia
  - Sedation
  - Antipyretic measures

High $ScVO_2$ > 80%

- Impaired O_2 extraction at a cellular level
- O_2 supply > O_2 demand

Using goal directed therapy aiming for a $ScVO_2$ > 70% has shown a reduction in mortality related to septic shock.[8]

Appendix 4

Recommended maintenance fluids in GNCH PICU:

Patient	Fluid	100% Maintenance fluids
Neonate day 1	10% dextrose/0.18% saline	60ml/kg/day
Neonate day 2	10% dextrose/0.18% saline +/- KCl	90ml/kg/day
Neonate day 3	10% dextrose/0.18% saline +/- KCl	120ml/kg/day
Neonate day 4	10% dextrose/0.18% saline +/- KCl	150ml/kg/day
Infant 1-3 months	5% dextrose/0.9% saline +/- KCl	150ml/kg/day
Infant 3-12 months	5% dextrose/0.9% saline +/- KCl	120ml/kg/day
Children over 12 months	5% dextrose/0.9% saline +/- KCl	100ml/kg/day for 1st 10kg 50ml/kg/day for 2nd 10kg 20ml/kg/day for every kg over 20kg

In sepsis may need higher glucose concentrations to prevent hypoglycaemia.

Appendix 5: Staphylococcal/Streptococcal toxic shock syndrome (TSS):[16]

TSS is a rare life threatening systemic bacterial intoxication. It is caused by a number of Staphylococcal or streptococcal exotoxins that are released during bacterial growth.

Symptoms + Signs:

- Fever: Temperature ≥ 38.9^{0}C
- Diffuse macular erythroderma
- Hypotension
- Multi-system dysfunction:
    - GI: Diarrhoea and vomiting
    - Muscular: severe myalgia
    - Mucous membranes: vaginal, oropharyngeal or conjunctival hyperemia
    - Renal: creatinine > twice the upper limit of normal or pyuria
    - Hepatic: total serum bilirubin or transaminase level > twice the upper limit of normal
    - Haematology: platelets ≤ 100,000 per L
    - Central nervous system: disorientation or altered conscious level
- Evidence against an alternative diagnosis

Diagnosis:

- History and examination
- Laboratory findings:
    - Leukocytosis
    - Elevated prothrombin time
    - Hypoalbuminemia
    - Hypocalcemia
    - pyuria

Management:

- Identification and decontamination of the site of toxin production
- Aggressive fluid resuscitation
- Administration of antistaphylococcal/antistreptococcal antibiotics:
    - Clindamycin 13mg/kg IV 8 hourly
    - Liaise with ID team re need for additional antibiotics
    - Probably already getting Cefotaxime
- Supportive care
- Administration of pooled human immunoglobulins:
    - use intranet doses, liaise with ID team
- Consider the presence of MRSA (might need Linezolid)

References:

1. Goldstein B *et al.* International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics. Pediatr Crit Care Med 2005; 6: 2-8.
2. Carcillo JA, Fields AI. Clinical practice parameters for hemodynamic support of pediatric and neonatal patients in septic shock. Crit Care Med 2002;30: 1365-78.
3. Bryce J *et al.* WHO estimates of the causes of death in children. Lancet 2005;365:1147-52.
4. Inwald DP, *et al*. Emergency management of children with severe sepsis in the United Kingdom: the results of the Paediatric Intensive Care Society sepsis audit. Arch Dis Child 2009;94:348-353.
5. Brierley J *et al.* Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. Crit Care Med 2009;37:666-688.
6. Han YY *et al*. Early reversal of paediatric-neonatal septic shock by community physicians is asscociated with improved outcome. Paediatrics 2003;112:793-799.
7. Adavnced paediatric life support, fourth edition.
8. De Oliveira CF, de Oliveira DS, Gottschald AF et al: ACCM/PALS haemodynamic support guidelines for paediatric septic shock: An outcomes comparison with and without monitoring central venous oxygen saturation. Intensive Care Med 2008; 34:1065-1075.
9. Meyer DM, Jessen ME. Results of extracorporeal membrane oxygenation in children with sepsis. The Extracorpeal Life Support Organisation. Ann Thorac Surg 1997; 63:756-761
10. Booy R, et al. Meningococcal Research Group: Reduction in case fatality rate from meningococcocal disease associated with improved healthcare delivery. Arch Dis Child 2001; 85:386-390
11. Maat M et al. Improved survival in children with sepsis and purpura: Effects of age, gender and era. Crit Care 2007; 11:172
12. Guidelines for the management of adults with hospital acquired ventilator associated and healthcare associated pneumonia. Am J Respir Cri Care Med 2005; 171: 388-416
13. Lachman P et al. Using care bundles to prevent infection in neonatal and paediatric ICUs. Curr Opin Infect Dis. 2009:22(3):224-8
14. www.patientsafetyfirst.nhs.uk/content.aspx?path=/interventions/criticalcare/
15. Dellinger RP, Levy MM, Rhodes A et al: Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013; 41:580-637
16. www.toxicshock.com
17. www.**cdc**.gov/nhsn/pdfs/pscmanual/6psc**vap**current.pdf
18. Bigham MT, Amato R, Bondurrent P et al. Ventilator associated pneumonia in the pediatric intensive care unit: characterizing the problem and implementing a sustainable solution. J Pediatr 2009; 154:582-587.

19. Brierley J, Highe L, Hines S, Dixon G. Reducing VAP by instituting a care bundle using improvement methodology in a UK Paediatric Intensive Care Unit. Eur J Pediatr 2012; 171:323-330
20. Brilli RJ, Sparling KW, Lake MR et al. The business case for preventing ventilator associated pneumonia in pediatric intensive care unit patients. Jt Comm J Qual Patient Saf. 2008; 34:629-638
21. Bizzarro MJ, Sabo B, Noonan M et al. A quality improvement initiative to reduce central line associated bloodstream infections in a neonatal intensive care unit. Infect Control Hosp Epidemiol 2010; 31: 241-248
22. Schulman J, Stricof R, Stevens TP et al. Statewide NICU central line associated bloodstream infection rates decline after bundles and checklists. Pediatrics 2011; 127:436-444