

Title:	Guideline for management of Paediatric Sepsis
Version:	Version: 2
Supersedes:	Version 1 Summary of amendments: Removal of 0.9% sodium chloride as bolus fluid—use of balanced crystalloids (Plasmalyte 148 or Hartmann’s solution) recommended Use of adrenaline as preferred first inotrope with peripheral use as an option after intraosseous or central line Clarifications on indications for use of blood products References updated
Application:	For use by any hospital team caring for patients under 16 years age across the Paediatric Critical Care Network in the North West (England) & North Wales region.

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Ratified by:	RMCH (Host Trust): - Paediatric Medicines Management Committee (MMC) - Paediatric Policies & Guidelines Committee
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Responsibility of:	Clinical lead North West & North Wales Paediatric Critical Care Network & NWTS guideline lead consultant

EqIA Registration Number:	36/13
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1. Detail of Procedural Document.

Paediatric Sepsis guideline is for use by clinical teams managing infants, children and young people under 16 years age in the North West (England) & North Wales region.

2. Equality Impact Assessment.

EQIA registration Number (RMCH): 36/13

3. Consultation, Approval and Ratification Process

This guideline was developed with input from:

- North West (England) and North Wales Paediatric Transport Service (NWTS) - medical & nursing
- Representatives from both Paediatric Intensive Care Units (Royal Manchester Children's Hospital and Alder Hey Children's Hospital) - medical, nursing and paediatric intensive care pharmacists
- Representatives from the North West (England) and North Wales Paediatric Critical Care Network (PCCN) - medical, nursing and AHP (paediatrics, anaesthetics, and emergency medicine teams)

For ratification process see appendix 1.

4. Disclaimer

These clinical guidelines represent the views of the North West (England) and North Wales Paediatric Transport Service (NWTS) and the North West (England) and North Wales Paediatric Critical Care Operational Delivery Network (PCCN). They have been produced after careful consideration of available evidence in conjunction with clinical expertise and experience.

It is intended that trusts within the Network will adopt this guideline and educational resource after review and ratification (including equality impact assessment) through their own clinical governance structures.

The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient.

Clinical advice is always available 24/7 from NWTS on a case by case basis via the referral line:

08000 84 83 82

Please feel free to contact NWTS (01925 853 550) regarding these documents if there are any queries.

EARLY RECOGNITION OF SEPSIS

Early recognition and initiation of treatment is vital and can prevent illness progression.

Any life-threatening compromise to the airway, breathing, circulation or level of consciousness must be identified early.

Take parental concerns seriously and assess repeatedly using PEWS tool.

If infection is suspected: any red flag, OR 2 amber flags are recognised as high & intermediate risk for sepsis respectively.

RISK FACTORS FOR SEVERE DISEASE

Neonates (i.e. ≤ 44 weeks post gestational age)

Underlying comorbidities

- ⇒ Cardiovascular or respiratory disease
- ⇒ Oncology diagnosis or bone marrow transplant
- ⇒ Immunodeficiency
- ⇒ Asplenia
- ⇒ Chronic steroid dependency
- ⇒ Complex urogenital anatomy or repair
- ⇒ Recent illness within last 6-8 weeks
- ⇒ Concurrent / recent chicken pox
- ⇒ Influenza A or B
- ⇒ Surgery

Chronic illness patients may be carriers of multi-resistant organisms

Those patients with indwelling catheters / lines / gastrostomy / tracheostomy i.e. breach of skin or long-term ventilated patients

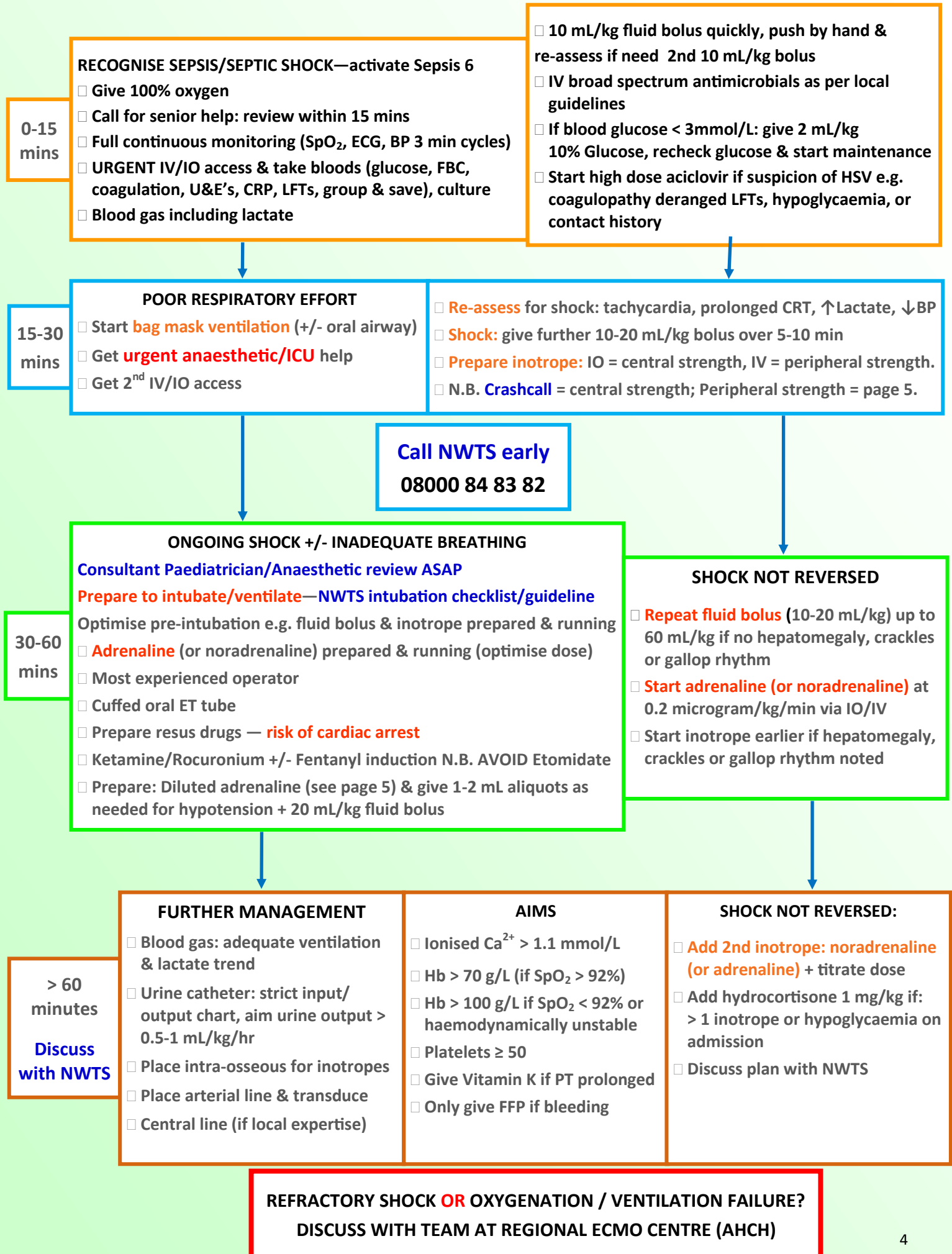
AMBER FLAGS

- ⇒ Abnormal response to social cues/ not smiling/ wanting to play
- ⇒ Reduced activity/ very sleepy/ abnormal behaviour/ parental concern
- ⇒ Moderate tachypnoea/tachycardia (see table)
- ⇒ SpO₂ < 92% in air OR nasal flaring
- ⇒ Capillary refill ≥ 3 seconds
- ⇒ Reduced urine output (<1mL/kg/hr)
- ⇒ Pale or flushed
- ⇒ Leg pain or cold extremities (feet or hands)
- ⇒ Immunocompromised

RED FLAGS

- ⇒ Capillary lactate > 2mmol/L
- ⇒ Grunting/Apnoeic/Cyanosed/SpO₂ < 90% in air
- ⇒ Weak, high pitched or continuous cry
- ⇒ V, P, or U on AVPU (Altered mental state)
- ⇒ Looks very ill
- ⇒ Temperature < 36 °C
- ⇒ Non-blanching rash or mottled/ashen/cyanotic
- ⇒ Not passed urine in last 6-12 hours (dry nappies)
- ⇒ Bradycardia < 60 / min
- ⇒ Severe tachypnoea/tachycardia (see chart below)
- ⇒ WCC less than 2 OR more than 30
- ⇒ Hypotension
- ⇒ If under 3 months, temperature > 38 °C

RESP RATE ¹⁹	NORMAL	MODERATE	SEVERE	HEART RATE ¹⁹	NORMAL	MODERATE	SEVERE
37–44 weeks (neonate)	30-59	60-79	≥ 80	Neonate	91-149	150-179	≤ 70 or ≥ 180
<1yr	30-39	40-54	> 54	<1yr	110-149	150-159	<80 or >160
1-2	25-34	35-49	> 50	1-2	100-139	140-149	<80 or >150
3-4	25-29	30-39	> 40	3-4	95-129	130-139	<60 or >140
5-7	20-23	24-28	> 29	5-7	80-109	110-119	<60 or >120
8-11	15-21	22-24	> 25	8-11	60-104	105-114	<60 or >115
> 12 yr	15-21	22-24	> 25	> 12 yr	65-90	91-130	<55 or >130



GOAL = REVERSE SHOCK

Maintain or restore airway, oxygenation & CO₂ clearance

Restore and maintain normal perfusion:

- No difference in central and peripheral pulse quality
- Heart rate and BP within normal limits for age
- Central CRT ≤ 2 seconds

Normal mental status (unless intubated and sedated)

Urine output > 0.5—1mL/kg/hour

Serum lactate < 2 mmol/L

Normal serum glucose (discuss with NWTS if > 10 mmol/L)

**Call NWTS
EARLY
08000 84 83 82**

INDUCTION DRUGS (BOLUS)

- Ketamine 1-2 mg/kg (max 150 mg)
- Rocuronium 1 mg/kg (max 100 mg)
- +/- Fentanyl 1-2 microgram/kg (max 200 microgram)
- Severe sepsis/shock: CAUTION risk of cardiac arrest & use reduced doses of any induction agent

FLUIDS

- Use balanced crystalloid 10-20 mL/kg fluid boluses i.e. Hartmann's or Plasmalyte 148
- Only use 0.9% sodium chloride if other fluids not available
- Give 2 mL/kg 10% Glucose if blood glucose < 3mmol/L
- Re-check blood glucose & run glucose containing maintenance fluids as soon as possible

INOTROPES

N.B.: Crashcall concentrations are for CENTRAL administration only

DILUTE ADRENALINE TAKE 0.1 ML/KG (10 MICROGRAMS/KG) FROM MINIJET SYRINGE 1:10,000 ADRENALINE (USING A 3-WAY TAP). MAKE THIS UP TO 10 ML WITH 0.9% SODIUM CHLORIDE (MAX: 1MG IN 10ML I.E. NEAT). USE 0.5-2 ML BOLUS if ↓BP at induction of anaesthesia

CENTRAL (via IO or CVL) INFUSION ADRENALINE / NORADRENALINE: 0.3 MG/KG MADE UP TO 50 ML 5% GLUCOSE OR 0.9% SODIUM CHLORIDE MAX CONCENTRATION 16 MG/ 50 ML

RATE: 0.05-1.5 MICROGRAM/KG/MIN VIA CENTRAL VENOUS OR IO LINE

RATE = 0.5-15 ML/HR VIA CENTRAL OR INTRA-OSSEOUS LINE

Set up all inotropes with 3-way tap to allow for piggybacking (page 18)

Titrate dose to response, add NORADRENALINE (or ADRENALINE) as SECOND LINE. N.B. may need high dose of both

Discuss with NWTS if patient remains hypotensive

PERIPHERAL INFUSION ADRENALINE / NORADRENALINE:

0.3 MG/KG IN 500 ML 5% GLUCOSE OR 0.9% SODIUM CHLORIDE

ADRENALINE Max = 16 MG IN 500 ML

NORADRENALINE Max = 8 MG IN 500 ML

RATE: 0.05-1.5 MICROGRAM/KG/MIN via peripheral line

FOR RATE IN ML/HR SEE APPENDIX; NB only use PVL if IO not available

OTHER: Discuss all other options with NWTS

- Consider dexamethasone (0.15 mg/kg MAX:10 mg/dose) if > 3 months & suspect meningitis
- Consider 10% calcium gluconate bolus +/- infusion (see Crashcall) (if via PVL dilute by 5 times)
- Consider adding inodilator (milrinone) for those with cardiac dysfunction

SYSTOLIC BP ¹⁸	NORMAL	MODERATE	SEVERE	DIASTOLIC BP	TARGET mean BP
37—44 weeks (neonate)	60-80	50-59	< 50	35-53	40-45
< 4 months	60-80	50-59	< 50	37-56	45-50
4 m—2 yr	70-90	60-69	< 60	42-63	50-55
2—5 yr	90-129	80-89	< 80	46-72	55-60
5-12 yr	90-129	80-89	< 80	57-76	60
> 12 yr	110-130	91-100	≤ 90	64-83	65

AIRWAY

- Cuffed ETT is necessary to ventilate in presence of pulmonary oedema
- Secure endotracheal tube appropriately for transfer (see NWTS guidelines)
- Nasogastric tube placed to decompress the stomach
- CXR to check position: ET tube tip at T2-T4 & above carina by 1 cm & NG tube in stomach
- Include heat & moisture exchanger (HME) & end-tidal CO₂ monitoring in circuit

BREATHING: monitor end-tidal CO₂ & SpO₂ continuously

- Place on ventilator with age appropriate settings, aiming for tidal volume 5-8 mL/kg
- Start with positive end expiratory pressure (PEEP) 5 cmH₂O & titrate PEEP upwards to treat pulmonary oedema or paedrs ARDS (may need PEEP 10-15 cmH₂O)
- Tolerate permissive hypercapnia to pH 7.15 as long as haemodynamically stable and adequate SpO₂
- Hypoxaemia associated paedrs ARDS may need inhaled nitric oxide
- Avoid using furosemide to treat pulmonary oedema in shock

CIRCULATION: monitor NIV BP min every 3-5 mins until stable

- Ensure two good intravenous access (ideally including intra-osseous or central venous access)
- Intraosseous line (IO) can be used as central access: see NWTS guidelines how/where to insert
- Switch to IO access early if peripheral cannulation takes more than 2-3 minutes
- Start inotrope infusions via IO (or peripheral line if IO not possible), aim eventually via central line (CVL)
- Always include 3-way tap in inotrope line to enable infusions to be changed without interruption
- Site arterial line: secure & transduce (if femoral, site preferably on same side as CVL so that the other site is free for renal support catheter)
- Check position on CXR if an internal jugular multi-lumen central venous line is inserted
- Track response to treatment with regular blood gases including lactate
- Site urinary catheter

INVESTIGATIONS

- Cultures: blood (peripheral + any indwelling lines), PCR (Meningococcal, Pneumococcal & Herpes Simplex as appropriate), urine (with dipstick), stool (if indicated)
- Sputum cultures for M, C & S; NPA for respiratory viral screen; COVID-19 swab or sputum; throat swab (rapid Group A Strep testing) & ASO titre; Pertussis screen (if appropriate)
- Full blood count, coagulation studies, group & save, urea & electrolytes including calcium & magnesium, blood glucose, C-reactive protein, liver function tests. Blood ammonia if reduced level of consciousness
- Arterial (or capillary) blood gas including lactate and intermittent central venous gas including S_{cv}O₂
- CSF cultures, including PCR & virology. **CAUTION:** do **NOT** do an LP if increased work of breathing, unstable blood pressure or persistent tachycardia, altered neurology, coagulopathy or platelets < 50

DRUGS

- Check all antimicrobials given within 1st hour of presentation & time documented
- Maintenance fluids containing glucose to maintain normal blood glucose levels
- Add dexamethasone if suspect meningitis in a child older than 3 months

COMMUNICATION

- Maintain contact with NWTS for on-going advice
- **PARENTS:** outline diagnosis, management and prognosis. Be honest.
- **Document:** history, current management & response to interventions & all blood results
- **Copy current notes** (& any relevant clinic letters), observation, blood results & drug charts for NWTS
- **Send X-rays** or any other imaging via PACS to receiving hospital

BROAD SPECTRUM ANTIMICROBIALS (AS PER LOCAL GUIDANCE) SHOULD BE ADMINISTERED WITHIN THE FIRST HOUR OF PRESENTATION OF SEPSIS (see BNFc for drug doses)

- Under 1 month old or 44 weeks post gestational age: cefoTAXime +/- amoxicillin (to cover Listeriosis)
- Over 1 month age: cefTRIAxone
- If history of cephalosporin anaphylaxis — use teicoplanin, ciprofloxacin and gentamicin
- Add clindamycin especially if toxic shock or necrotising fasciitis suspected (usually due to invasive Group A Strep. or Staph. Aureus) OR if refractory shock (BP not responding to volume, and requiring 2 or more inotropes)
- Add aciclovir if abnormal neurology or encephalopathy, coagulopathy, abnormal LFTs, hypoglycaemia, or contact history of Herpes simplex—all age groups
- Add macrolide (clarithromycin or erythromycin) if Mycoplasma or Pertussis suspected or suspected meningoencephalitis
- Discuss with surgeons and consider adding metronidazole if surgical cause suspected
- Immunosuppression/neutropenia (even in absence of haem/onc diagnosis) → follow regional febrile neutropenia guidelines
- Carriers of multi-resistant organisms— check previous sensitivities; follow local guidelines and discuss with local microbiology team
- If recently overseas or prolonged or multiple antibiotic exposure within 3 months consider adding vancomycin or teicoplanin
- Patients with permanent access devices in situ (e.g. VP shunt, Broviac or Hickman line, Portacath etc.) - follow local guidelines if available / add vancomycin or teicoplanin
- For patients with suspected Gram-negative sepsis (e.g. UTI, abdominal sepsis, Galactosaemia) add gentamicin (stat dose then check levels before next dose if evidence of renal impairment/AKI)

TRIGGERS FOR INTUBATION / ANAESTHETIC REVIEW

- Decreased consciousness level (i.e. GCS ≤ 8; AVPU ≤ P) OR fluctuating consciousness level
- Increasing respiratory failure, signs of exhaustion
- Impending cardiovascular collapse – e.g. persistent tachycardia despite appropriate fluid boluses, borderline/ low normal mean BP; low diastolic blood pressure
- Fluid refractory shock
- 40-60 mL/kg resuscitation fluid given within the first 1-2 hours without reversal of shock
- Increasing size of liver
- Requirement for inotrope/vasopressor infusions

See NWTS intubation guidelines for further details on intubation, ideal drugs and equipment

- Ensure both fluid bolus and vasoactive agent - syringe DILUTE ADRENALINE (RESUS DOSE I.E. 0.1 ML/KG OF 1:10,000 MADE UP TO 10ML MAX: 1MG IN 10ML I.E. NEAT) - are ready before induction drugs are given

WARNING: INDUCTION AGENTS

- Inhalational anaesthetics present a significant risk of cardiovascular depression and cardiac arrest. Only consider using if the risk of a difficult airway outweighs this.
- Thiopentone, propofol & benzodiazepines all carry a similar risk of significant cardiovascular depression and cardiac arrest
- Avoid using etomidate as there is a significant risk of causing adrenal insufficiency

FLUID BOLUSES

- Assess fluid responsiveness and look for signs of fluid overload after each bolus
- **Check for fluid responsiveness:** assess the effect of sustained direct upwards (towards head) pressure on the liver (hepato-jugular response)
 - ⇒ BP improves +/- pulse rate falls: patient still fluid responsive, therefore give more fluid
 - ⇒ BP does not improve or worsens (i.e. evidence of myocardial impairment) start an inotrope
- **Check for signs of volume overload/cardiac failure:**
 - Gallop rhythm
 - Hepatomegaly (new or worsening)
 - On examination of chest: evidence of pulmonary oedema (crepitations or crackles)
 - All above may be associated with or without hypotension.
- **If any are present start inotropes/vasopressors**
- **Aim** for a serial reduction of lactate by 10% every hour or normalisation of lactate
- **Fluid bolus in mL/kg should be dosed as ideal body weight**
- **Use balanced crystalloid** e.g. Plasmalyte 148 or Hartmann's solution (if available) instead of 0.9% sodium chloride. N.B. 0.9% sodium chloride is associated with hyperchloraemic acidosis, AKI and higher mortality when compared to balanced crystalloids¹⁶.
- **Albumin (4.5% human albumin solution)** has not been shown to be a superior initial resuscitation fluid, but there is no definite negative impact or difference in outcomes¹⁵. Recommendation to use balanced crystalloids rather than albumin relates to cost and potential barriers to ready access of albumin compared to crystalloids.
- N.B. if fluid bolus is more than 60 mL/kg consider switching to 4.5% human albumin solution.
- **AVOID** gelatin containing fluids (causes coagulopathy) or starches in acute resuscitation¹⁶
- **High mixed venous oxygen saturation levels do not exclude fluid responsiveness in critically ill septic patients**¹⁶

BLOOD PRODUCTS¹⁶

- **Packed cells** (10-20 mL/kg) only if **Hb < 70 g/L** in **haemodynamically stable** patient.
- Higher target threshold **Hb 100 g/L** **haemodynamically unstable** patient or severe hypoxaemia¹⁶
- **Coagulopathy/Thrombocytopenia:**
 - ◆ Only consider treatment with 10-20 mL/kg Fresh Frozen Plasma (FFP) if active bleeding
 - ◆ Low platelet counts in the absence of active bleeding should not be supplemented unless $< 20 \times 10^9/L$
 - ◆ If bleeding or invasive procedures are planned, aim to keep platelets $> 50 \times 10^9/L$
 - ◆ Low fibrinogen ($< 0.75g/L$) is suggestive of DIC – consider giving 5-10 mL/kg Cryoprecipitate

CHOICE OF INOTROPE AND COLD/ WARM SHOCK

- **START an inotrope after 40-60 mL/kg** fluid boluses if there is evidence shock has not reversed i.e. persistent tachycardia, prolonged CRT, raised lactate (i.e. lactate ≥ 2 mmol/L), reduced urine output, poor peripheral perfusion (core: peripheral temperature difference; poor peripheral pulses)
- **Start an inotrope earlier** if evidence of cardiac dysfunction i.e. new or worsening hepatomegaly, pulmonary oedema (crepitations or crackles on chest examination) or gallop rhythm noted
- **HYPOTENSION** is a late sign and is not needed for diagnosis of sepsis or septic shock. If present, it confirms severe septic shock.
- **START adrenaline (cold shock) or noradrenaline (warm shock) - see page 9.** Only use dopamine if adrenaline or noradrenaline are not readily available.
- **Use a peripheral inotrope whilst waiting for intra-osseous or central access** – N.B. This is for **short term use only** and must be changed to intra-osseous or central access as soon as possible. See appendix for peripheral inotrope concentrations and rate calculations.
- Monitor carefully for signs of extravasation when using peripheral or intra-osseous access.
- **Maximum duration for peripheral inotropes is 12-24 hours.** Regular inspection of PVL site must occur at least every hour. N.B. Extra-vigilance must be taken after 6 hours for both adrenaline and noradrenaline infusions via PVL - it is important to switch to central line if still required between 12-24 hours.

Previously the paediatric Surviving Sepsis international guidelines recommended clinical assessment to differentiate “warm” versus “cold” shock. The 2020 update recommends moving away from this due to poor correlation of clinical assessment versus advanced monitoring. These categories are included for use in circumstances where advanced haemodynamic monitoring is not available.

	COLD SHOCK	WARM SHOCK
SIGNS	<ul style="list-style-type: none"> Capillary refill time >3 seconds Reduced peripheral pulses Cool & mottled extremities Core/peripheral temperature gap >3°C Narrow pulse pressure 	<ul style="list-style-type: none"> Flash capillary refill time Bounding peripheral pulses Warm to edges with flushed appearance Low diastolic Wide pulse pressure
	<p>First line inotrope: ADRENALINE</p> <p>Second line: Cold shock with low BP</p> <p>Titrate Adrenaline + consider adding Noradrenaline</p> <p>Consider Milrinone (inodilator) - d/w NWTS</p> <p>Second line: Cold shock with normal/ high BP</p> <p>Consider adding Milrinone (always d/w NWTS)</p>	<p>First line inotrope: NORADRENALINE</p> <p>Second line: Warm shock with low BP</p> <p>Titrate Noradrenaline + consider adding Adrenaline</p> <p>May consider adding Vasopressin—d/w NWTS</p> <p>May also consider adding Milrinone to ensure good cardiac output (always d/w NWTS)</p>

- **Vasopressin** (vasopressin-receptor agonist) (vials may be labelled as: argipressin or vasopressin USP or pitressin = synthetic vasopressin) may be used if vasodilation and hypotension persists in spite of starting noradrenaline and adrenaline infusions OR the clinical team may decide not to start vasopressin and continue to titrate noradrenaline and adrenaline infusions according to response. N.B. In adults, renal replacement therapy was required less often in those treated with vasopressin. See Crashcall for dose
- **Milrinone** = inodilator (selective inhibitor of phosphodiesterase type 3). It improves cardiac output by inotropic effect (cAMP mediated) and may reduce afterload (by vasodilation). It also improves myocardial relaxation in diastole. Be aware that blood pressure may drop with milrinone (vasodilation) and further fluid bolus may be required or a reduced dose of milrinone infusion. Milrinone should be considered in those patients with evidence of persistent hypoperfusion and cardiac dysfunction despite other vasoactive agents. Cardiac dysfunction is defined as difference in oxygen saturation between arterial and mixed venous blood (AVO₂) at least 30% or an increase in serum lactate more than 2 mmol/L. Do NOT give a loading dose of milrinone. Caution: up to 85% milrinone is excreted renally; use 50-75% normal dose if estimated GFR less than 50 mL/min/1.73 m². See Crashcall for dose
- **HYDROCORTISONE 1 MG/KG (MAX 100 MG)**: add if patient remains haemodynamically unstable on 2 inotropes OR in presence of hypoglycaemia. Ideally check blood cortisol level first (may be done on previously sent biochemistry sample).

CORRECT HYPOGLYCAEMIA & ELECTROLYTES

- **Hypoglycaemia**: Glucose containing maintenance fluids must be initiated early in combination with 10% glucose boluses to maintain blood glucose > 2.4 mmol/L
- Treat **Hypocalcaemia**: 10% calcium gluconate bolus (see Crashcall) +/- infusion. N.B. If giving via PVL 10% calcium gluconate must be diluted by 5 times (i.e. Dilute each 1mL of 10% solution with 4mL of diluent to give a final concentration of 0.045 mmol/mL).
- Aim to maintain ionised calcium > 1.1 mmol/L
- Treat **Hypomagnesaemia**: use supplemental dose on Crashcall. N.B. this causes vasodilation and may cause hypotension, so give slowly over 20 minutes with an additional fluid bolus if necessary
- If giving via PVL dilute Magnesium Sulfate 50% by 5 times to a concentration of 0.4mmol/ml

CORTICOSTEROIDS

- **If meningitis suspected** (& more than 3 months old), give **dexamethasone 0.15 mg/kg/dose (max 10 mg/dose) IV 6 hourly** (ideally within 6 hours but not more than 12 hours of starting antibiotics)
- **If actual or suspected primary adrenal insufficiency** (i.e. Hyponatremia with hyperkalemia) treat with sick day dose of hydrocortisone (20 mg/m²/DAY in 4 divided doses). Ideally check blood cortisol level first. N.B. Up to 25% children in septic shock may have adrenal insufficiency

BICARBONATE USE

- Not recommended for treatment of hypoperfusion-induced lactic acidaemia & pH ≥ 7.15
- However, bicarbonate may be considered if pH < 7 despite continued fluid resuscitation and inotropes or if known renal failure

EXTRA-CORPOREAL MEMBRANE OXYGENATION (ECMO)

Consider referral to regional ECMO team on PICU at Alder Hey Children's Hospital for children with sepsis induced paediatric acute respiratory distress syndrome and refractory hypoxia OR septic shock refractory to all other treatments.

DRUG DOSES

Use **www.crashcall.net** for emergency drug doses and **BNFc** for all other doses.

Always seek local microbiology advice – patient specific antimicrobials

Antimicrobial Paediatric Guidelines: UK Paediatric Antibiotic Stewardship. <http://www.uk-pas.co.uk>

PROPHYLAXIS

- Prophylaxis depends on the suspected (or confirmed) causative agent and level of exposure. The local Public Health England health protection team will be able to give advice over the phone 24/7.
- Should be arranged by local team for family and staff contacts after informing local Public Health England team
- Meningococcus: patient will also need prophylaxis unless treated with ceftriaxone
- Consider prophylaxis for the team if PPE not utilised during resuscitation especially those involved in any aerosol generating procedures if Meningococcus or Pertussis suspected.
- Always check with local Public Health England health protection team for up-to-date guidance.

OUTCOMES FOR PAEDIATRIC SEPSIS

Outcomes are improved when best practice guidelines are followed^{6,9,10,11}.

FOLLOWING FACTORS ARE INDEPENDENTLY ASSOCIATED WITH INCREASED MORTALITY^{5,7,9}:

- **Failure to be looked after by senior paediatrician & failure of sufficient supervision of junior staff**
- **Persistent evidence of shock (2-fold increase in mortality per hour patient remains in shock)**
- **Failure to administer adequate inotropes/vasopressors or resuscitation volume (even if inotropes/vasopressors started)**
- **Delays in administration of antibiotics⁵ (every hour's delay increases mortality by around 7.6%)**
- **Lack of guidelines for recognition and management of children with septic shock**

Studies have shown improvements in mortality, length of hospital stay, development of new or progressive multiple organ dysfunction and duration of organ dysfunction when each of these factors are corrected.

Compliance is difficult and **failure to meet Sepsis 6 is highlighted repeatedly in the literature for both paediatric and adult sepsis**. Regular audit can improve adherence⁴ & by inference outcomes from sepsis.

AUDIT: NWTS uses the following criteria when reviewing management of sepsis:

- 1) High flow O₂ commenced at time of referral
- 2) IV/IO access obtained at time of referral
- 3) Lactate measured on admission, and regularly during stabilisation
- 4) Antibiotics given in first hour; If HSV suspected, acyclovir given and HSV PCR taken
- 5) Adequate fluid resuscitation received; and inotropic support initiated when indicated
- 7) Dexamethasone given suspected bacterial meningitis
- 8) Time of admission and first contact with NWTS

N.B. Failure to deliver antibiotics in the first hour is the most common failure in this pathway

It would be achievable to repeatedly audit Sepsis 6 at DGH level. Regular plan-do-study-act cycles have been shown to improve adherence⁴ to guidelines

CALCULATION WORKSHEET: PERIPHERAL ADRENALINE OR NORADRENALINE INFUSION

N.B. Crashcall amount for inotrope infusion is for CENTRAL use only

1

To make up a suitable concentration for a peripheral adrenaline or noradrenaline infusion you will need:

500 mL bag of either 0.9% sodium chloride or 5% glucose

Adrenaline or noradrenaline 1:1,000 (1mg/mL) vials

2

To calculate the amount of adrenaline/noradrenaline required to add to 500 mL bag
Amount (mg) = 0.3 mg x weight in kg

AMOUNT REQUIRED = 0.3 x _____ (kg) = _____ mg

N.B. ADRENALINE MAXIMUM concentration = 16 mg in 500 mL

N.B. NORADRENALINE Maximum concentration = 8 mg in 500 mL

It is recommended that an inotrope infusion is always delivered via a dedicated peripheral line and that the line includes a 3-way tap

3

VOLUME ADRENALINE OR NORADRENALINE INJECTION REQUIRED

using adrenaline or noradrenaline 1:1,000 (1 mg/mL)

Amount in mg = volume required (mL)

CALCULATION EXAMPLES FOR PERIPHERAL ADRENALINE / NORADRENALINE INFUSION

EXAMPLE 1: PATIENT WT = 14 KG

Amount adrenaline or noradrenaline required = 0.3 mg x 14 kg = 4.2 mg

Using adrenaline or noradrenaline vials 1:1,000 (1 mg/mL) volume drug required = 4.2 mL

Add adrenaline or noradrenaline 4.2 mL to 500 mL 5% glucose

EXAMPLE 2: PATIENT WT = 58 KG

Amount **AD**renaline or **NOR**adrenaline required = 0.3 mg x 58 kg = 17.4 mg

BUT ADrenaline **MAX** concentration = 16 mg in 500 mL

NORadrenaline **MAX** concentration = 8 mg in 500 mL

Using **AD**renaline 1:1,000 (1 mg/mL) volume drug required = 16 mL

Using **NOR**adrenaline 1:1,000 (1 mg/mL) volume drug = 8 mL

Add either **AD**renaline 16 mL or **NOR**adrenaline 8 mL to 500 mL bag 0.9% sodium chloride

Infusion Rate Calculations **Peripheral ADRenaline or NORadrenaline
Inotrope: microgram/kg/min**

What does 1 mL/hr of infusion equal in microgram/kg/min?

How do I calculate the infusion rate in mL/hr to deliver specific dose microgram/kg/min

Step 1: Convert total amount of drug in mg added to the bag to micrograms by multiplying by 1,000

Step 1: Convert total amount of drug in mg added to the bag to microgram by multiplying by 1,000

Step 2: Divide this by patient's weight (in kg)

Step 2: Multiply the specified dose (in microgram) by the patient's weight (kg)

Step 3: Divide this number by 60 (mins)

Step 3: Multiply this number by 60 (mins)

Step 4: Divide this number by volume in bag (in mL)

Step 4: Divide this number by the drug amount in micrograms in the bag.

Step 5: Multiply this by the rate of the infusion (mL/hr)

Step 5: Multiply this by total volume in bag (in mL)

This result gives the dose in micrograms/kg/min delivered

This calculated number will be the rate required in mL/hr to provide an infusion at a rate of specific dose micrograms/kg/min

EXAMPLE: DOSE FROM RATE

Patient wt = 16 kg

To calculate peripheral ADRENALINE infusion dose delivered

Dose = 0.3 mg x 16 kg = 4.8 mg

4.8 ml added to 500 mL bag 5% glucose

Rate running = 12 mL / hr

Step 1: Total dose = 4.8 mg x 1000 = 4,800 micrograms

Step 2: 4,800 micrograms ÷ 16 kg = 300 micrograms / kg

Step 3: 300 micrograms / kg ÷ 60 mins = 5

Step 4: 5 ÷ 500 mL = 0.01

Step 5: 0.01 x 12 mL = 0.12 micrograms / kg /min

EXAMPLE: RATE FROM DOSE REQUIRED

Patient wt = 28 kg

To calculate infusion rate: peripheral NORADRENALINE

Dose = 0.3 mg x 28 = 8.4 mg
(N.B. MAX noradrenaline conc = 8mg/500mL)

Dose required = 0.2 micrograms / kg /min

Step 1: 8 mg x 1000 = 8,000 micrograms

Step 2: 0.2 micrograms x 28 kg = 5.6 micrograms

Step 3: 5.6 micrograms x 60 mins = 336 micrograms

Step 4: 336 micrograms ÷ 8,000 micrograms = 0.042

Step 5: 0.042 x 500 = 21 mL/ hr

ADRENALINE infusion for PERIPHERAL administration

Amount ADRenaline to add to 500 mL bag 0.9% sodium chloride / 5% glucose = 0.3 mg x weight (kg)
MAXIMUM concentration = 16 mg in 500 mL. (Patients >100kg, dose at 100kg)

DOSE: 0.05-1.5 MICROGRAMS/KG/MIN VIA PERIPHERAL LINE (FOR RATE ML/HR SEE TABLE BELOW)

IF STARTING AN ADRENALINE INFUSION ALWAYS DISCUSS WITH NWTs TEAM. OBTAIN FURTHER NWTs ADVICE IF >1.5MCG/KG/MIN REQUIRED. LARGE VOLUMES REQUIRE NWTs REVIEW WITHIN 1 HOUR OF COMMENCING.

WEIGHT (KG)	AMOUNT (MG) TO ADD TO 500 ML BAG	RATE (ML/HR) = 0.05 MICROGRAM/KG/MIN	RATE (ML/HR) = 0.1 MICROGRAM/KG/MIN	RATE (ML/HR) = 0.2 MICROGRAM/KG/MIN	RATE (ML/HR) = 0.5 MICROGRAM/KG/MIN	RATE (ML/HR) = 1 MICROGRAM/KG/MIN	RATE (ML/HR) = 1.5 MICROGRAM/KG/MIN
3 kg	0.9 mg	5 mL/hr	10 mL/hr	20 mL/hr	50 mL/hr	100 mL/hr	150 mL/hr
3.5	1 mg	5	10	20	50	100	150
4	1.2 mg	5	10	20	50	100	150
5	1.5 mg	5	10	20	50	100	150
6	1.8 mg	5	10	20	50	100	150
7	2.1 mg	5	10	20	50	100	150
8	2.4 mg	5	10	20	50	100	150
9	2.7 mg	5	10	20	50	100	150
10	3 mg	5	10	20	50	100	150
12	3.6 mg	5	10	20	50	100	150
15	4.5 mg	5	10	20	50	100	150
17	5.1 mg	5	10	20	50	100	150
20	6 mg	5	10	20	50	100	150
25	7.5 mg	5	10	20	50	100	150
30	9 mg	5	10	20	50	100	150
35	10.5 mg	5	10	20	50	100	150
40	12 mg	5	10	20	50	100	150
45	13.5 mg	5	10	20	50	100	150
50	15 mg	5	10	20	50	100	150
55	16 mg	5.1	10.3	20.6	52	103	155
60	16 mg	5.6	11.2	22.5	56	113	169
65	16 mg	6.1	12.2	24.3	61	122	183
70	16 mg	6.6	13	26	66	131	197
75	16 mg	7	14	28	70	140	211
80	16 mg	7.5	15	30	75	150	225
85	16 mg	8	15.9	32	80	159	239
90	16 mg	8.4	16.9	34	84	169	253
95	16 mg	8.9	17.8	36	89	178	267
100	16 mg	9.4	18.8	37.5	94	188	281

NORADRENALINE infusion for **PERIPHERAL** administration

Amount NORadrenaline to add to 500 mL bag 0.9% sodium chloride / 5% glucose = 0.3 mg x weight (kg)

MAXIMUM concentration = 8 mg in 500 mL. (Patients >100kg dose at 100kg)

DOSE: 0.05-1.5 MICROGRAMS/KG/MIN VIA PERIPHERAL LINE (FOR RATE ML/HR SEE TABLE BELOW)

DISCUSS WITH NWTs TEAM IF STARTING NORADRENALINE INFUSION. OBTAIN FURTHER NWTs ADVICE IF >1.5MCG/KG/MIN REQUIRED. LARGE VOLUMES REQUIRE NWTs REVIEW WITHIN 1 HOUR OF COMMENCING.

WEIGHT (KG)	AMOUNT (MG) TO ADD TO 500 ML BAG	RATE (ML/HR) = 0.05 MICROGRAM/KG/MIN	RATE (ML/HR) = 0.1 MICROGRAM/KG/MIN	RATE (ML/HR) = 0.2 MICROGRAM/KG/MIN	RATE (ML/HR) = 0.5 MICROGRAM/KG/MIN	RATE (ML/HR) = 1 MICROGRAM/KG/MIN	RATE (ML/HR) = 1.5 MICROGRAM/KG/MIN
3 kg	0.9 mg	5 mL/hr	10 mL/hr	20 mL/hr	50 mL/hr	100 mL/hr	150mL/hr
3.5	1 mg	5	10	20	50	100	150
4	1.2 mg	5	10	20	50	100	150
5	1.5 mg	5	10	20	50	100	150
6	1.8 mg	5	10	20	50	100	150
7	2.1 mg	5	10	20	50	100	150
8	2.4 mg	5	10	20	50	100	150
9	2.7 mg	5	10	20	50	100	150
10	3 mg	5	10	20	50	100	150
12	3.6 mg	5	10	20	50	100	150
15	4.5 mg	5	10	20	50	100	150
17	5.1 mg	5	10	20	50	100	150
20	6 mg	5	10	20	50	100	150
25	7.5 mg	5	10	20	50	100	150
27	8mg	5.1	10.1	20.3	51	101	152
30	8mg	5.6	11.3	22.5	56	113	169
35	8mg	6.6	13.1	26.3	66	131	199
40	8mg	7.5	15	30	75	150	225
45	8mg	8.4	16.9	33.8	84	169	253
50	8mg	9.4	18.8	37.5	94	188	281
55	8mg	10.3	20.6	41.3	103	206	309
60	8mg	11.3	22.5	45	113	225	338
65	8mg	12.2	24.4	48.8	122	244	366
70	8mg	13.1	26.3	53	131	263	394
75	8mg	14.1	28.1	56	141	281	422
80	8mg	15	30	60	150	300	450
85	8mg	15.9	31.9	64	159	319	478
90	8mg	16.9	33.8	68	169	338	506
95	8mg	17.8	35.6	71	178	356	534
100	8mg	18.8	37.5	75	188	375	563

CALCULATION WORKSHEET: PERIPHERAL DOPAMINE INFUSION

N.B. Crashcall amount for dopamine infusion is for CENTRAL use only

1

To make up a suitable concentration for a peripheral dopamine infusion you will need:

50 ml of either 0.9% sodium chloride or 5% glucose

Dopamine 200 mg/5mL (i.e. 40 mg/mL) vial

2

To calculate the amount of dopamine required make up to 50 mL infusion

Amount (mg) = 3 mg x weight in kg

AMOUNT DOPAMINE REQUIRED = 3 x _____ (kg) = _____ mg

N.B. MAXIMUM concentration = 160 mg in 50 mL

It is recommended that an inotrope infusion is always delivered via a dedicated peripheral line and that the line includes a 3-way tap

3

VOLUME DOPAMINE INJECTION REQUIRED using dopamine 200 mg/5 mL (40 mg/mL)

Volume = amount in mg ÷ drug concentration mg/mL

CALCULATION EXAMPLES FOR PERIPHERAL DOPAMINE INFUSION

EXAMPLE 1: PATIENT WT = 16 KG

Amount dopamine required = 3 mg x 16 kg = 48 mg

Using dopamine 200 mg/5 mL vial (40 mg/mL) drug volume required = 48 mg ÷ 40mg = 1.2 mL

To make up to total 50 mL add dopamine 1.2 mL to 48.8 mL 5% glucose

EXAMPLE 2: PATIENT WT = 56 KG

Amount dopamine required = 3 mg x 56 kg = 168 mg

BUT MAX concentration = 160 mg in 50 mL

Using dopamine 200 mg/5 mL vial (i.e. 40 mg/mL) volume drug required for 160 mg = 4 mL

IE To make up to total 50 mL add dopamine 4 mL to 46 mL 5% glucose

Infusion Rate Calculations Peripheral Dopamine Inotrope: micrograms/kg/min

What does 1mL/hr of infusion equal in micrograms/kg/min?

Step 1: Convert total amount of drug in mg added to the bag to micrograms by multiplying by 1,000

Step 2: Divide this by patient's weight (kg)

Step 3: Divide this number by 60 (mins)

Step 4: Divide this number by volume (mL) in syringe

Step 5: Multiply this by the rate of the infusion (mL/hr)

This result gives the dose in micrograms/kg/min being delivered

EXAMPLE: DOSE FROM RATE

Patient wt = 16 kg

To calculate peripheral dopamine infusion dose delivered

Dose = 3 mg x 16 = 48 mg

Add 1.2 ml dopamine (40 mg/mL) to 48.8 mL 5% glucose

Rate running = 4.6 mL / hr

Step 1: Total dose = 48mg x 1000 = 48,000 micrograms

Step 2: 48000 micrograms ÷ 16kg = 3000 micrograms

Step 3: 3000 micrograms ÷ 60 mins = 50 micrograms / min

Step 4: 50micrograms ÷ 50 mL = 1

Step 5: 1 x 4.6 mL = 4.6 micrograms / kg / min

How do I calculate the infusion rate in mL/hr to deliver specific dose micrograms/kg/min

Step 1: Convert total amount of drug in mg added to the bag to micrograms by multiplying by 1,000

Step 2: Multiply the specified dose (in micrograms) by the patient's weight (kg)

Step 3: Multiply this number by 60 (mins)

Step 4: Divide this number by the amount of drug in micrograms in the syringe.

Step 5: Multiply this by total volume in syringe (mL)

This calculated number will be the rate required in mL/hr to provide an infusion at a rate of specific dose micrograms/kg/min

EXAMPLE: RATE FROM DOSE REQUIRED

Patient wt = 38 kg

Calculating infusion rate (mL/hr) for peripheral dopamine

Dose = 3 mg x 38 kg = 114 mg

Dose required = 10 micrograms / kg / min

Step 1: 114 mg x 1000 = 114,000 micrograms

Step 2: 10 micrograms x 38 kg = 380 micrograms

Step 3: 380 micrograms x 60 mins = 22,800 micrograms / hr

Step 4: 22,800 microgram/hr ÷ 114,000 micrograms = 0.2

Step 5: 0.2 x 50 mL = 10 mL / hr

DOPAMINE infusion for **PERIPHERAL** administration:

Amount of DOPAMINE to make up to 50 mL syringe 0.9% sodium chloride or 5% glucose
= 3 mg x weight (kg)

N.B. MAXIMUM concentration = 160 mg made up to 50 mL

DOSE: 5-10 MICROGRAMS/KG/MIN VIA PERIPHERAL LINE (FOR RATE ML/HR SEE CHART BELOW)

WEIGHT (KG)	AMOUNT (MG) MADE UP TO 50 ML	RATE (ML/HR) = 5 MICROGRAM/KG/MIN	RATE (ML/HR) = 7.5 MICROGRAM/KG/MIN	RATE (ML/HR) = 10 MICROGRAM/KG/MIN
3 kg	9 mg	5 mL/hr	7.5 mL/hr	10 mL/hr
3.5	10.5 mg	5	7.5	10
4	12 mg	5	7.5	10
5	15 mg	5	7.5	10
6	18 mg	5	7.5	10
7	21 mg	5	7.5	10
8	24 mg	5	7.5	10
9	27 mg	5	7.5	10
10	30 mg	5	7.5	10
12	36 mg	5	7.5	10
15	45 mg	5	7.5	10
17	51 mg	5	7.5	10
20	60 mg	5	7.5	10
25	75 mg	5	7.5	10
30	90 mg	5	7.5	10
35	105 mg	5	7.5	10
40	120 mg	5	7.5	10
45	135 mg	5	7.5	10
50	150 mg	5	7.5	10
55	160 mg	5.2	7.8	10.3
60	160 mg	5.6	8.4	11.3
65	160 mg	6	9.1	12.2
70	160 mg	6.6	9.8	13.1
75	160 mg	7	10.5	14
80	160 mg	7.5	11.3	15
85	160 mg	8	12	16
90	160 mg	8.4	12.7	16.9
95	160 mg	8.9	13.4	17.8
100	160 mg	9.4	14	18.8

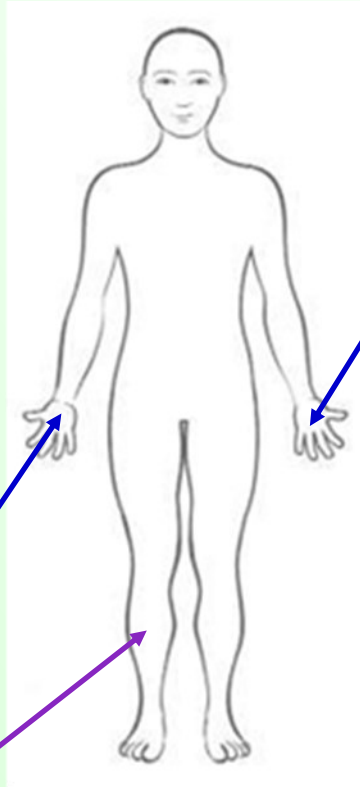
MILRINONE infusion for PERIPHERAL administration:

WEIGHT (kg)	AMOUNT mg in 50 ml	RATE (mL/hr) = 0.5 microgram/kg/min
< 5 kg	5 mg	Wt (kg) x 0.3
> 5 kg	10 mg	Wt (kg) x 0.15

WEIGHT (KG)	AMOUNT (MG) MADE UP TO 50 ML	RATE (ML/HR) = 0.25 MICROGRAM/KG/MIN	RATE (ML/HR) = 0.5 MICROGRAM/KG/MIN	RATE (ML/HR) = 0.75 MICROGRAM/KG/MIN
3 kg	5 mg	0.45	0.9	1.35
3.5	5	0.5	1	1.5
4	5	0.6	1.2	1.8
5	10	0.4	0.75	1.1
6	10	0.45	0.9	1.35
7	10	0.5	1	1.6
8	10	0.6	1.2	1.8
9	10	0.7	1.4	2
10	10	0.75	1.5	2.25
12	10	0.9	1.8	2.7
15	10	1.1	2.25	3.4
17	10	1.3	2.6	3.8
20	10	1.5	3	4.5
25	10	1.9	3.8	5.6
30	10	2.3	4.5	6.8
35	10	2.6	5.3	7.9
40	10	3	6	9
45	10	3.4	6.8	10.1
50	10	3.8	7.5	11.3
55	10	4.1	8.3	12.4
60	10	4.5	9	13.5
65	10	4.9	9.8	14.6
70	10	5.3	10.5	15.8
75	10	5.6	11.3	16.9
80	10	6	12	18
85	10	6.4	12.8	19.1
90	10	6.8	13.5	20.3
95	10	7.1	14.3	21.4
100	10	7.5	15	22.5

INTRAVENOUS INFUSIONS: PRACTICAL TIPS

- **IDEALLY** aim for 2 good peripheral venous lines (PVL) or one PVL plus one intra-osseous line.
- Using the 2 intravenous / intra-osseous lines it is possible to give all infusions and bolus drugs required safely, see example below.



PERIPHERAL VENOUS LINE:

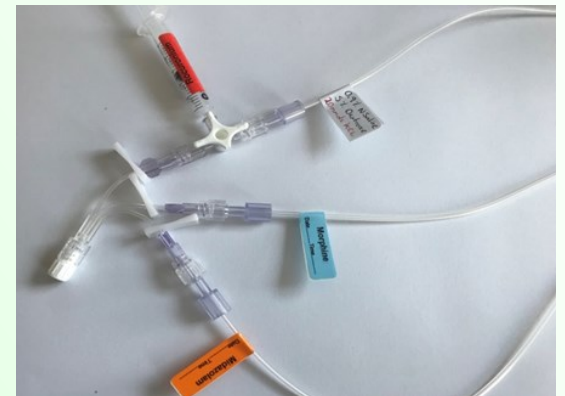
SEDATION + MAINTENANCE + BOLUS

Attach triple tail extension

Lumen 1: morphine or fentanyl infusion

Lumen 2: midazolam

Lumen 3 (with 3 way tap): maintenance fluids plus bolus drugs e.g. rocuronium



2ND PERIPHERAL VENOUS LINE OR INTRAOSSEOUS LINE

INOTROPE SET-UP

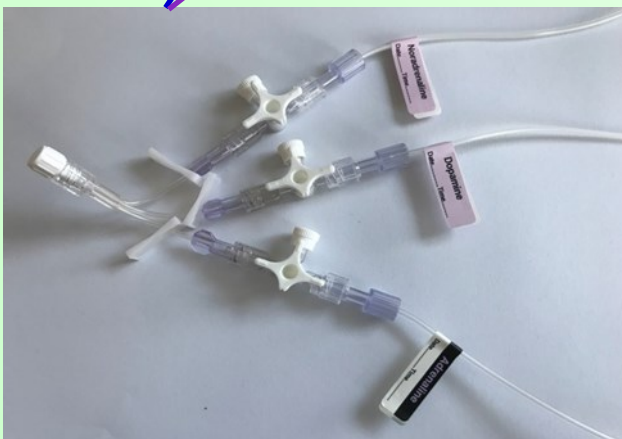
Attach a triple tail extension with 3-way tap on each lumen

Lumen 1: Adrenaline

Lumen 2: Noradrenaline

Lumen 3: Vasopressin or Milrinone

This enables inotrope infusions to be changed safely using the piggyback technique ie avoiding any interruption in infusions.



REMEMBER that the **PREFERRED** route for **INOTROPES** is **CENTRAL** ie via intraosseous or central line

ONLY deliver inotropes via peripheral venous lines if there are no other options

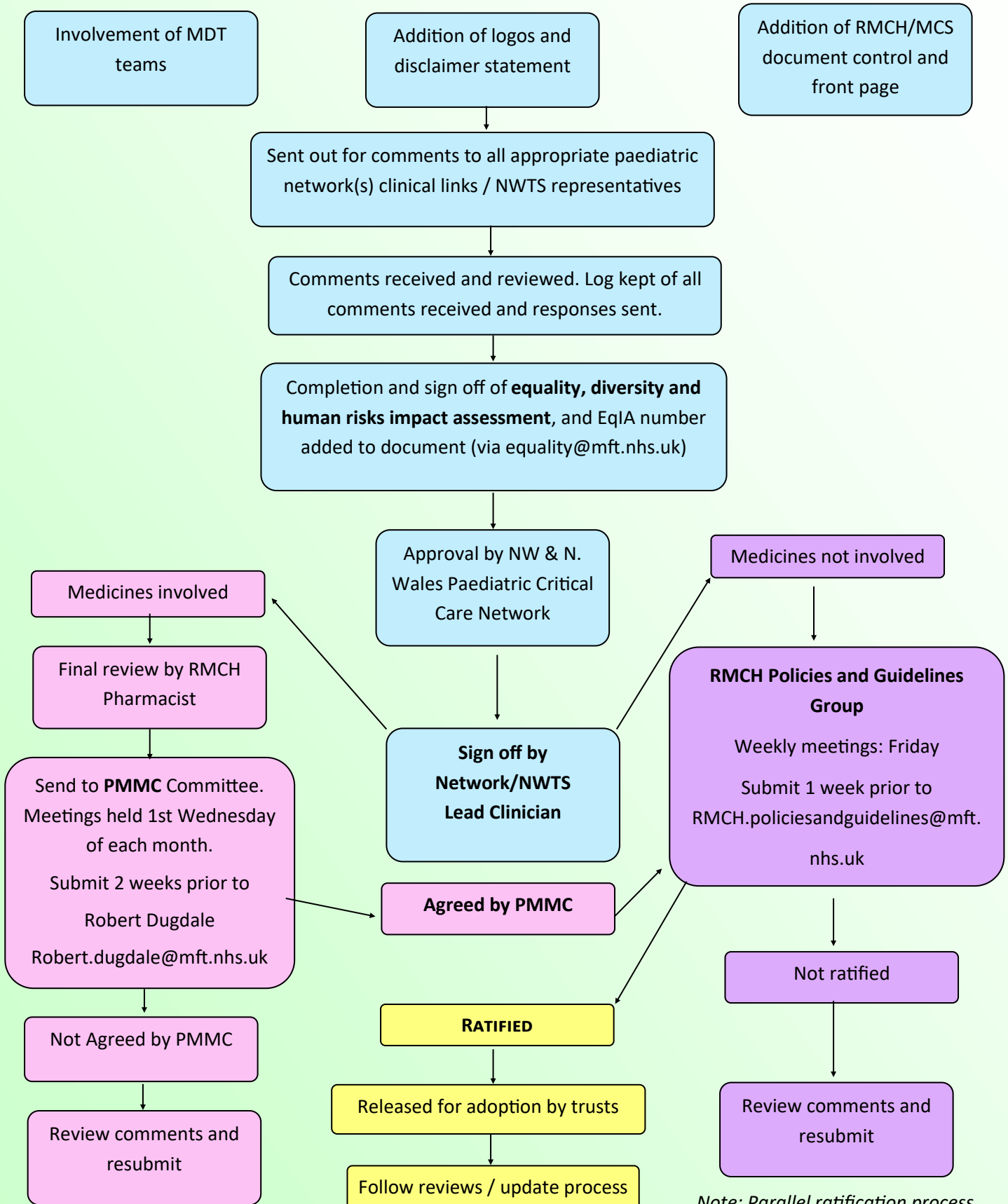
NEVER DELAY STARTING INOTROPES WHEN INDICATED

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- ¹⁷UK Paediatric Antibiotic Stewardship—website: <http://www.uk-pas.co.uk/>
- ¹⁸MANCHEWS2— RMCH paediatric early warning score
- ¹⁹Sepsis six (paediatrics)

Appendix 3: ratification pathway for NWTS / Network guidelines

Ratification of Guidelines with Host Organisation (MFT)



Note: Parallel ratification process with AHFT (see below)

Appendix 2 continued



Involvement of MDT teams

Addition of document control and front page

Addition of logos and disclaimer statement

Sent out for comments to all paediatric network(s) clinical links / NWTS representatives

Comments received and reviewed. Log kept of all comments received and responses sent.

Completion and sign off of **equality, diversity and human risks impact assessment**, and EqIA number added to document (via equality@mft.nhs.uk)

Approval by NW & N. Wales Paediatric Critical Care Network

Sign off by Network/NWTS Lead Clinician

Send to **CDEG** (Clinical Development & Evaluation Group which includes clinical pharmacist) at Alder Hey

Meetings held 3rd Friday of every month, papers submitted by 1st Friday of the month via Liz McCann
liz.mccann@alderhey.nhs.uk

Not ratified

Review comments and resubmit

RATIFIED

Released for adoption by trusts

Follow reviews / update process

Resources

www.Crashcall.net - for intubation drugs / sedation regime
UK Paediatric Antibiotic Stewardship—website: <http://www.uk-pas.co.uk/>
BNFc for drug doses

Contact numbers:

North West (England) & North Wales Paediatric Transport Service (NWTS)

- NWTS REFERRAL LINE: 08000 84 83 82
- NWTS Office: 01925 853 550

Regional Paediatric Intensive Care Unit Alder Hey Children's Hospital : 0151 252 5241

Regional Paediatric Intensive Care Unit Royal Manchester Children's Hospital : 0161 701 8000

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North West (England) and North Wales Paediatric Critical Care Network

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PICU, Alder Hey Children's Hospital

Next Review Due: November 2024

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For the most up to date version of this guideline visit: www.nwts.nhs.uk