Principles of management of suspected septic shock

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Note: This document applies to acute late-onset hemodynamic instability presumed to be due to sepsis.
The document has been subdivided into broad monitoring and management topics and each topic is subdivided into 3 sections, domain, recommendation, and strength of recommendation following the EPIQ bundle format.

A. MONITORING OF CLINICAL VARIABLES

Domain	Recommendation	Strength of recommendation & certainty of evidence
What clinical variables should be monitored?	**Recommended:** ***Non-invasive:*** Blood pressure (systolic, mean, diastolic) Heart rate Capillary refill time Urine output Continuous pre and post ductal oxygen saturation monitoring ***Invasive:*** Arterial line should be used for BP monitoring (when possible) CVP monitoring may be helpful [Low values (<5 cm H_2O) suggest hypovolemia; trending may be helpful]	Strong recommendation [based on group consensus; low to very low certainty of evidence] Weak recommendation [based on group consensus; low to very low certainty of evidence]
What BP thresholds should be used to define hypotension?	Target Blood Pressure systolic / diastolic and mean BP above the 3rd centile for gestational age (Zubrows)- or mean BP > CGA as per standard local protocol. May use patient specific BP threshold where tissue oxygen delivery is deemed compromised based on clinical judgement	Weak recommendation [low certainty of evidence]
What should be the frequency of non-	BP should be measured q 15 min until patient is hemodynamically stable following which q 1 hour pre-ductal BP	Weak recommendation [based on group

invasive BP monitoring?	should be preferred in non-invasive BP measurement	consensus; very low certainty of evidence]
How should urine output be monitored?	Routine UOP monitoring q 4-8 h based on local practice. A urine output of <0.5 ml/kg/hr or greater than 50% drop from baseline urine output with optimized intravenous fluids may suggest hemodynamic compromise – may consider more frequent monitoring. Monitoring using in dwelling urinary catheter may be used in anuria or suspected retention [eg. from opioids or muscle relaxant]	Weak recommendation [based on group consensus; very low certainty of evidence]
Should NIRS be routinely used?	Clinicians may use NIRS as an adjunct in centres where NIRS monitoring is available and local practice guidelines have been developed. Insufficient evidence to suggest thresholds for intervention	Weak recommendation [low certainty of evidence]

B. FLUIDS

What type of fluid?	Normal Saline (NS)	Strong recommendation [based on group consensus; low certainty of evidence]
Volume of each bolus	10-20ml/kg over 15-20 min (Consider underlying pathophysiology [such as underlying cardiac dysfunction/significant pulmonary edema] while considering the volume of bolus)	Weak recommendation [based on group consensus; low certainty of evidence]
Maximum volume of initial resuscitation	In patients with suspected hypovolemia consider giving 1-2 NS boluses (maximum 30-40 ml/kg)	Weak recommendation [based on group consensus; low to very low certainty of evidence]

C. VASOPRESSOR/INOTROPE

When to consider: Fluid unresponsive/CI

In neonates with acute late-onset hemodynamic instability, early use of echocardiography (TNE where available) is recommended to confirm diagnosis, establish severity and guide hemodynamic management. In the absence of echocardiography (or when not feasible), the first choice of cardiotropic agent should be informed by clinical suspicion of vasodilatory shock or vasoconstrictive shock. • Vasodilatory shock: Increased heart rate, low peripheral vascular resistance, vasodilatation (warm, bounding & wide pulses, normal to flash cap refill), low BP with widened pulse pressure • Vasoconstrictive shock: Increased heart rate, vasoconstriction (poor pulses, cold extremities, mottled skin, prolonged cap refill, low BP with narrowing pulse pressure Careful assessment for treatment response is warranted.	Strong recommendation [based on group consensus; low to very low certainty of evidence]

How to decide if you need vasopressor vs. inotrope?	Vasodilatory shock → vasopressor Vasoconstrictive shock → inotrope	Weak recommendation [based on group consensus; low to very low certainty of evidence]
NB: If vasopressor or inotrope will be started through a central line, line should be flushed as appropriate – ensure timely delivery to the patient by overcoming the dead space		
Vasopressors		
What is the first line vasopressor?	Norepinephrine or Dopamine are suggested as first line agents	Weak recommendation [based on group consensus; low to very low certainty of evidence]

What is the dose of first line vasopressor and the rate of titration?	*[All dosages mentioned below are suggested starting dosages; for maximum dose and drug interactions consult local formulary]* Norepinephrine: 0.05mcg/kg/min, increase by 0.05mcg/kg/min q30 minutes Max dose: 0.4mcg/kg/min Dopamine: 5mcg/kg/min, increase by 2.5mcg/kg/min q30 minutes Max dose: 15 mcg/kg/min	Weak recommendation [based on group consensus; low to very low certainty of evidence] Weak recommendation [based on group consensus; low to very low certainty of evidence]
What is the second line vasopressor?	Dopamine/Norepinephrine Vasopressin	Weak recommendation [based on group consensus; low to very low certainty of evidence]
What is the dose of second line vasopressor and the rate of titration?	Dopamine/Norepinephrine as mentioned before Vasopressin: 0.0003 u/kg/min, increased by 0.0001-0.0003 u/kg/min q 30 min Max dose: 0.002 u/kg/min	Weak recommendation [based on group consensus; low to very low certainty of evidence]
Inotropes		
What is the first line inotrope?	If hypotension: Epinephrine Dobutamine If hypertension – milrinone	Weak recommendation [based on group consensus; low to very low certainty of evidence]

What is the dose of first line inotrope and the rate of titration?	Epinephrine: 0.01 to 0.1 mcg/ kg/min. Increase by 0.01-0.02 q 30-60 minutes, up to 0.1 mcg/ kg/min Dobutamine: 5mcg/kg/min, increase by 5mcg/kg/min q30 minutes Milrinone: starting dose 0.33mcg/kg min, may be increased up to 0.66 mcg/kg/min, no loading dose	Weak recommendation [based on group consensus; low to very low certainty of evidence]
What additional biochemical monitoring should be used?	Specific additional Biochemical parameters: Blood gas, serum lactate, glucose (epinephrine), Na (if vasopressin)	Strong recommendation [based on group consensus; low to very low certainty of evidence]

D. **ADJUNCT THERAPIES**

Is there any indication for the routine use of sodium bicarbonate infusions?	Use of sodium bicarbonate in the context of PPHN is not routinely recommended However, to optimize the pH milieu for a minimal critical threshold to prevent inactivation of vasopressor/inotropes bicarbonate may be used in selected cases	Strong recommendation [based on group consensus; low certainty of evidence] Weak recommendation [based on group consensus; very low certainty of evidence]
Is there any indication for the use of corticosteroids?	No available evidence to support use of steroids in the context of septic shock. For catecholamine resistant shock (i.e., reaching max dose cardiotropes as above with no/inadequate clinical response) its use may be considered. ***Choice of corticosteroid:*** Hydrocortisone 0.5-1.0 mg/kg – frequency as per local protocol (No evidence exploring benefit of loading dose in this population)	Weak recommendation [based on group consensus; very low certainty of evidence]

Should a serum cortisol level guide therapy?	Serum cortisol level should not guide whether to use corticosteroids	Strong recommendation [based on group consensus; low certainty of evidence]

Suggested role of TNE guided care in neonates with suspected septic shock

At any point, a TNE can be requested by the clinical team as per local resources and protocol. Inadequate response to therapy and progressive escalation of therapy are situations where TNE should be **strongly considered.** [Strong recommendation; based on group consensus]	
TNE findings of hyperdynamic heart with normal cardiac output? [compensated vasodilatory shock]	Vasopressor – norepinephrine first line
TNE findings of hyperdynamic heart with low cardiac output? [decompensating vasodilatory shock]	Reassess fluid status Increase vasopressor
TNE findings of elevated PVR with normal cardiac output? [sepsis with acute pulmonary hypertension]	Consider changing vasopressor to vasopressin Inotropy with milrinone (in normotensive patients) or epinephrine
TNE findings of elevated PVR with low cardiac outputs? [sepsis with acute pulmonary hypertension and cardiogenic shock]	Change vasopressor to vasopressin Inotropy with epinephrine
TNE findings of cardiac dysfunction with normal cardiac output? [compensated vasoconstrictive shock]	Epinephrine Milrinone
TNE findings of cardiac dysfunction with low cardiac output? [decompensating vasoconstrictive shock]	Epinephrine

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