SARI CLINICAL CARE TRAINING

SEPSIS AND SEPTIC SHOCK
DELIVER TARGETED RESUSCITATION

World Health Organization

HEALTH EMERGENCIES programme

Learning objectives

At the end of this lecture, you will be able to:

- Describe how to deliver early, targeted resuscitation in patients (adults and children) with sepsis-induced tissue hypoperfusion and shock.
- Understand the special considerations when resuscitating paediatric patients in resource-limited settings.

Five principles of sepsis management (1/2)

1. Recognize patients with sepsis and septic shock:

   – Patients with sepsis have suspected or documented infection **and** acute, life-threatening organ dysfunction.

   – A subset of these patients, may have septic shock and show clinical signs of circulatory failure and hypoperfusion.

   – Patients with sepsis and septic shock **need** treatment and resuscitation immediately!



Five principles of sepsis management (2/2)

2. Give appropriate antimicrobials within **1 hour.**

3. Give a targeted resuscitation during the first **6 hours.**

4. Monitor-record-interpret-respond.

5. Deliver quality care (later lecture).



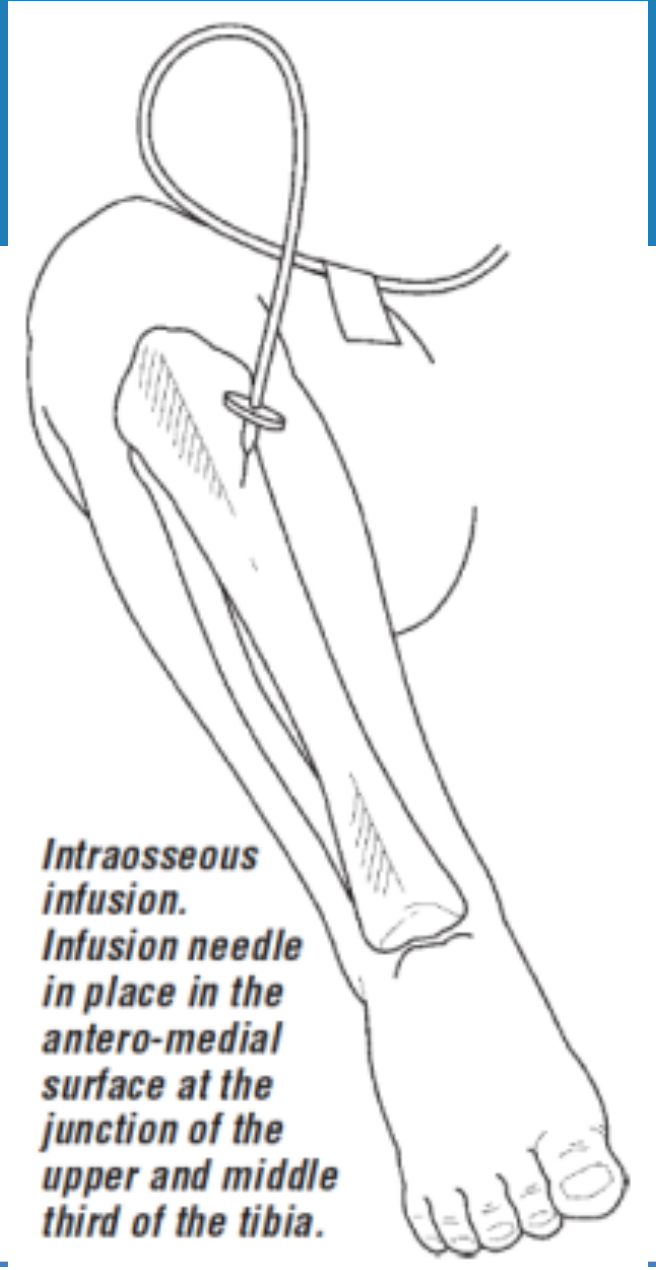
"As soon as sepsis is suspected the clock has started."

Obtain intravenous access

- Patients with sepsis and shock require immediate IV access to initiate fluid resuscitation.
- Peripheral IV catheters are easy to place and adequate for initial resuscitation.
- If unable to place peripheral IV within a few minutes, then consider emergent placement of intraosseous (IO) catheter.

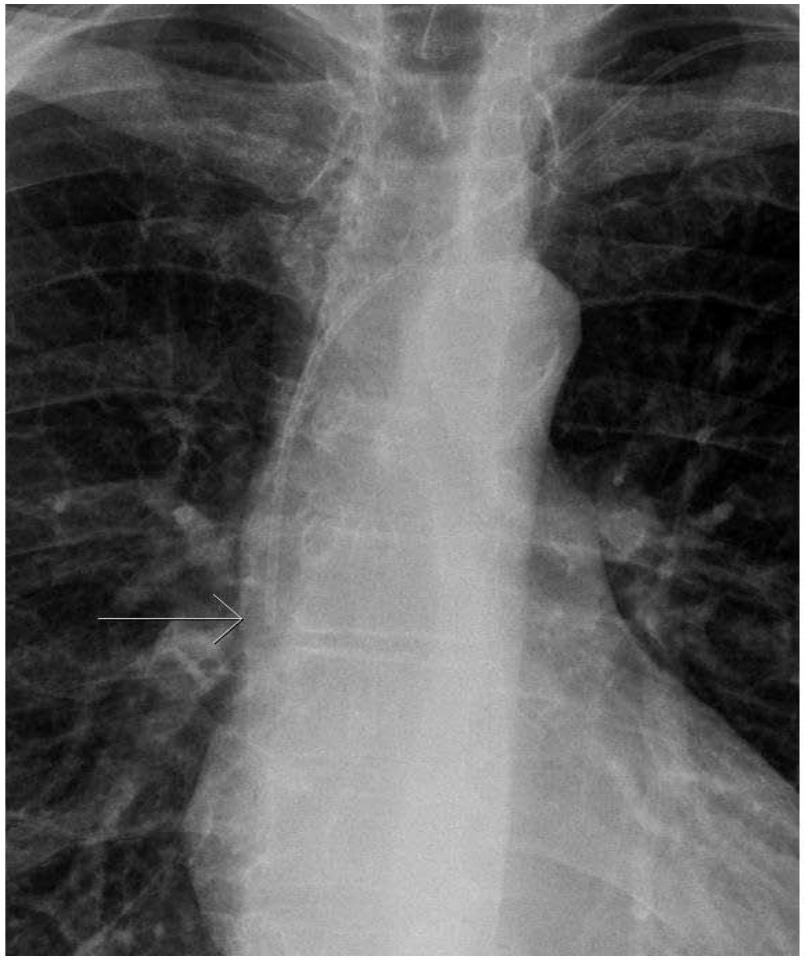
IOs

- Can be easily placed in adults and children during emergency situations.
- Can be used to infuse fluid therapy, vasopressors, antimicrobials and blood transfusions at rapid rate.
- Can be used to take blood samples.



Intraosseous infusion. Infusion needle in place in the antero-medial surface at the junction of the upper and middle third of the tibia.

Central venous catheter (CVC)



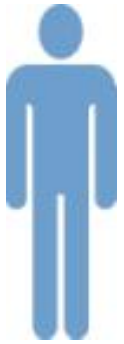
- CVC may be needed in the subset of patients with septic shock that need vasopressors.
- CVC should be placed under complete sterile conditions, using ultrasound guidance when possible.
- CVC should be removed as soon as no longer needed to minimize risk of infection.

Interventions to improve tissue perfusion

- crystalloid fluids
- vasopressors
- inotropes
- packed red blood cell (PRBC) transfusion.

EARLY resuscitation combined with EARLY appropriate antimicrobial therapy saves lives in patients with sepsis and shock.
Surviving Sepsis Campaign, 2016

Resuscitation of adult patients with sepsis



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Resuscitation targets (1/2)



Improved BP:
- mean arterial pressure (MAP) ≥ 65 mmHg
- SBP > 100 mmHg.

Adequate urine output:
- ≥ 0.5 mL/kg/hr.

Skin examination:
- capillary refill < 2–3 sec if < 65 years; < 4.5 if > 65 years
- absence of skin mottling
- well felt peripheral pulses
- warm dry extremities.

Improved sensorium

Normalized lactate levels (if initial level high)

MAP = [SBP + (2 *DBP)] ÷ 3

MAP is driving the driving pressure of perfusion

Resuscitation targets (2/2)



- Invasive haemodynamic parameters (i.e. CVP and $ScvO_2$) are not superior to clinical targets of perfusion.

- However, can be used as adjuncts to guide patient care understanding their limitations and meaning.

Resuscitation: fluid type



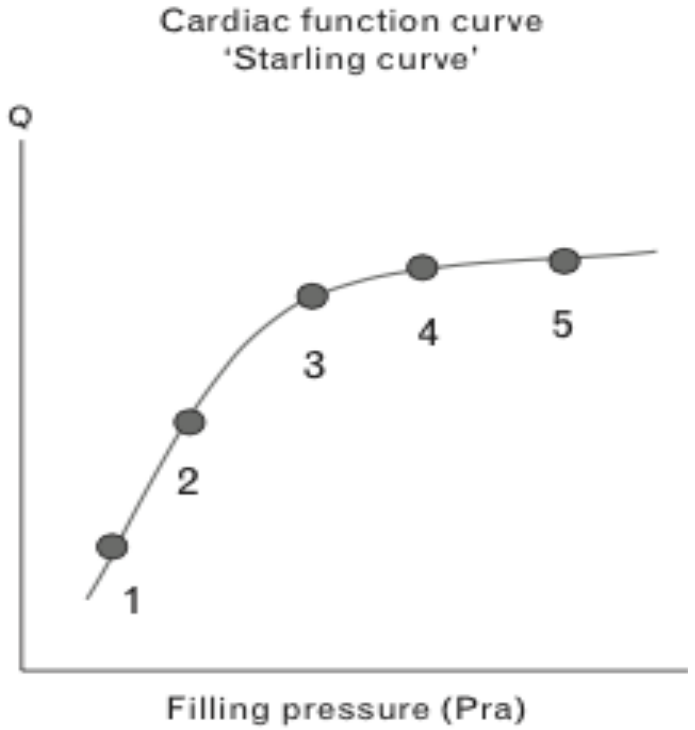
- Crystalloid fluid is preferred:
  - Lactate Ringers (LR*), Ringer's Acetate (RA), PlasmaLyte (PL) or normal saline (NS)
    - NS is associated with hyperchloremic acidosis. Balanced solutions minimize this risk. Avoid hyperchloraemia.
  - Albumin as effective as crystalloids in septic shock
    - Use in addition to crystalloid, when substantial crystalloids are needed for intravascular volume repletion.
  - Do NOT give hypotonic fluid.
  - Do NOT give semisynthetic colloids
    - i.e. starch-based colloids (HES, dextrans) have been associated with increased acute kidney injury, renal replacement therapy and mortality. Gelatin safety unknown.

Resuscitation: fluid challenge



- Give fluid for resuscitation as a fluid challenge (also termed bolus or loading).
- Give initial fluid challenge of 20–30 mL/kg over 30–60 minutes (or faster).
- Perform sequential evaluations to assess clinical response.
- If shock persists, continue to give additional fluid challenges (i.e. 250–500 mL) over 30 minutes as long as there is a clinical response.

Resuscitation: Fluid responsive



- Fluid challenge aims to correct the hypovolaemia associated with sepsis.
- By improving hypovolaemia, stroke volume and cardiac output improve; and thus perfusion parameters also improve.
- A fluid responsive patient shows signs of improved perfusion with the fluid challenge.

Predicting fluid responsiveness

- Administering fluid challenges when patient is no longer fluid responsive can be harmful:
  - i.e. organ oedema, prolonged days of MV.

- However, predicting fluid responsiveness is a challenge:
  - Single, static parameters, such as CVP or inferior vena cava (IVC) size do **not** reliably predict volume responsiveness in isolation.

- Dynamic variables may more reliably predict responsiveness, however cut-off points, sensitivity and specificity remain in question.

Passive leg raise (PLR)

- Passive leg raise technique is a way to "mimic" fluid loading by moving 300 mL of blood from the lower extremities to the right heart to predict if further fluid loading may be helpful.
- Requires real-time, direct measurement of cardiac output to assess effect.
- Patient must not be stimulated, coughing or in discomfort as this may increase sympathetic stimulation and alter cardiac output effects.

Dynamic parameters: cardiac ultrasound



- Left ventricular outflow tract velocity time integral (VTI) change of > 18% with PLR manoeuvre suggests fluid responsive.
- ΔIVC max-min/mean, during respiratory cycle,
  - when ≥ 12% suggests fluid responsiveness.
- Validated only on patients on controlled, mechanical ventilation (and set TV 8 mL/kg).
- Requires advanced ultrasound expertise.

Dynamic parameters: CVP



- CVP response to fluids:
  - If cardiac output and BP do not improve, and CVP remains unchanged, OK to try more fluids.
  - But if CVP did increase then unlikely to respond to more fluid.

Ongoing fluid resuscitation should be guided on individual basis, based on reassessment of clinical signs of perfusion, fluid responsiveness and risks of fluid overload.

If MAP remains < 65 mmHg, start vasopressors



- Vasopressors maintain a minimum perfusion pressure and adequate flow during life-threatening hypotension.

- Vasopressors are potent vasoconstrictors and increase myocardial contractility to a lesser extent:
  - Administer through a CVC.
  - Give at a strictly controlled rate, titrate to desired effect.
  - Discontinue when no longer needed to minimize risks.

- Start vasopressors after initial fluid bolus:
  - But can be given early, during ongoing resuscitation when shock is severe and diastolic pressure is low.
  - **Do not delay administration.**

Vasopressors



- Norepinephrine (first choice, titrate):
  - potent vasoconstrictor with less increase in HR.
- Epinephrine (alternative, titrate):
  - potent vasoconstrictor, and also has inotropic effects
  - can add as additional agent to achieve desired effect
  - can use as an alternative to norepinephrine (if not available).
- Vasopressin (fixed dose 0.03 U/min):
  - can be used to reduce norepinephrine dose
  - can add as additional agent to achieve effect
  - caution if patient not yet euvolemic.
- Restrict dopamine use because it may be associated with increased mortality and increase in tachyarryhthmia.

Titrate vasopressors to desired effect



- Titrate to target MAP range ≥ 65–70 mmHg.
- Can individualize MAP target based on patient's clinical characteristics:
  - i.e. consider higher MAP (i.e. ≥ 80 mmHg) in patients with chronic hypertension to reduce risk of AKI, if patient responds better to higher MAP.
- Titrate vasopressors to improve markers of perfusion:
  - **i.e. mental status, urine output**, **normalization of lactate* and skin examination.**
- Titrate down vasopressors if blood pressure in above target range.

Inotropes for septic shock



- Add inotropes if patient shows continued signs of hypoperfusion despite achieving adequate fluid loading and use of vasopressors to reach target MAP.
    - Measured or suspected low cardiac output (i.e. echocardiogram).

- Dobutamine is first choice inotrope. If not available, then epinephrine:
    - Start at 2.5 µg/kg/min (max 20), titrate to improve clinical markers of perfusion and cardiac output.
    - Do **not** aim to increase cardiac output to supranormal levels.
    - Risks include tachyarrhythmias and hypotension.

PRBCs for shock



- Give PRBCs transfusion when there is severe anaemia:
  - Hb ≤ 70g/L (7.0 g/dL) in absence of extenuating circumstances such as myocardial infarction, severe hypoxaemia, or acute haemorrhage.

- Targeting higher thresholds (≥ 90–100 g/L) does not lead to better outcomes in patients with sepsis.

Peripheral administration of vasopressor

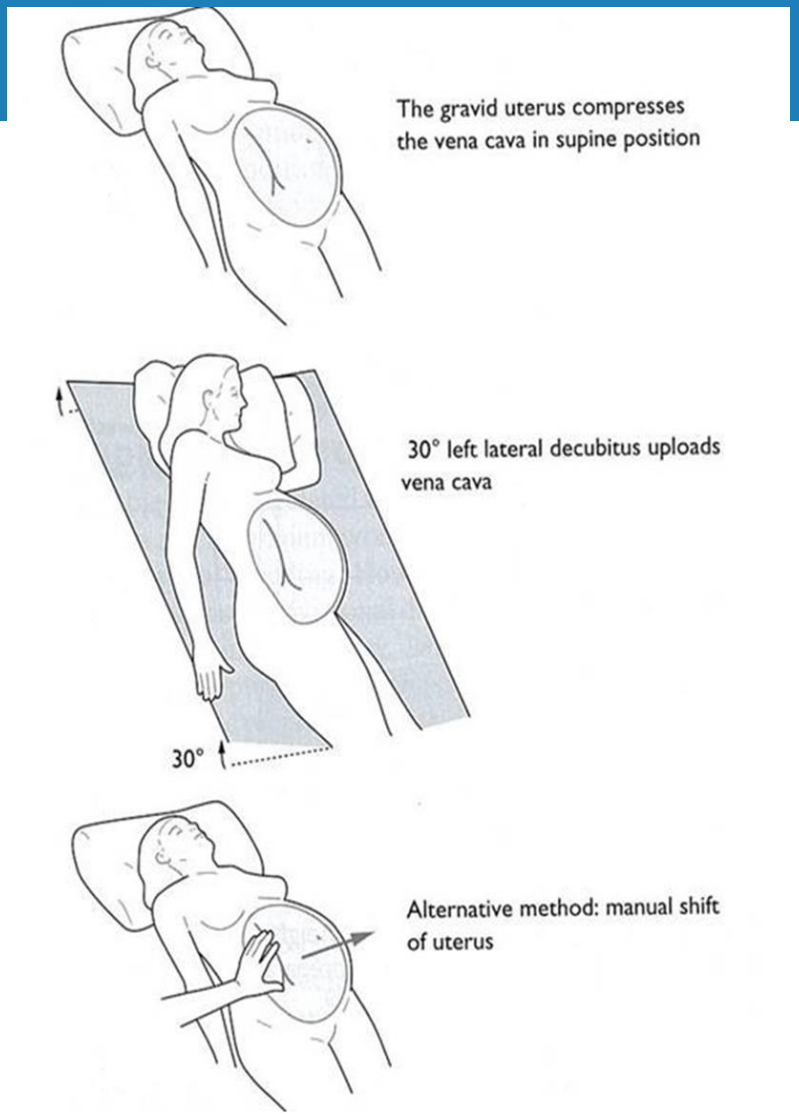
- Though preference is for central delivery, norepinephrine, dopamine or epinephrine can be given via peripheral IV.
- **Caution:** Risk of peripheral infusion is extravasation of medication and local tissue necrosis.
- Requires close nursing care to check infusion site:
  - If necrosis, stop infusion and consider injection of 1 mL phentolamine solution subcutaneously.
  - Phentolamine is a vasodilator
  - 5–10 mg in 10 mL of NS.



Permission C. Gomersall
http://www.aic.cuhk.edu.hk/web8/Dopamine_extravasation_1.jpg

Management of pregnant woman with shock

- Maternal positioning:
  - Lateral tilt (elevating either hip 10–12 cm) or manual displacement of uterus to left will augment venous return to heart.
  - Enlarging gravid uterus compresses pelvic and abdominal vessels, inhibiting venous return when patient is supine, thus tilting displace uterus.
  - Maternal position should **not** be flat on back after 24 weeks.



- Even before maternal haemodynamics are compromised, blood may shunt away from placenta.
- Monitor woman and fetus.
- Once maternal BP or SpO_2 are reduced, then fetus will become rapidly distress.
- Early recognition and resuscitation are essential.
- During pregnancy, there is an overall increase in blood volume, HR and cardiac output, and reduction in oncotic pressure.

Management of pregnant woman with shock

- Ensure adequate hydration, use IV fluids as necessary:
  - Close attention to fluid balance to prevent fluid overload and pulmonary oedema.
  - Oncotic pressure decreases throughout pregnancy and in the postpartum period.

- Vasopressors – use cautiously with appropriate available monitoring:
  - May decrease uterine perfusion.
  - Administer with IV fluids – uteroplacental flow will not be adequate with vasopressors alone.
  - Must monitor fetus when administering.

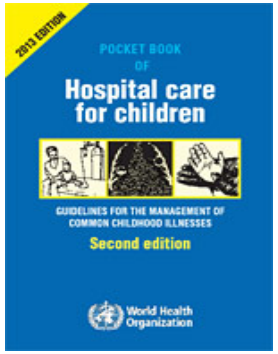
Resuscitation of paediatric patients with SARI and sepsis



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Special considerations for children with shock

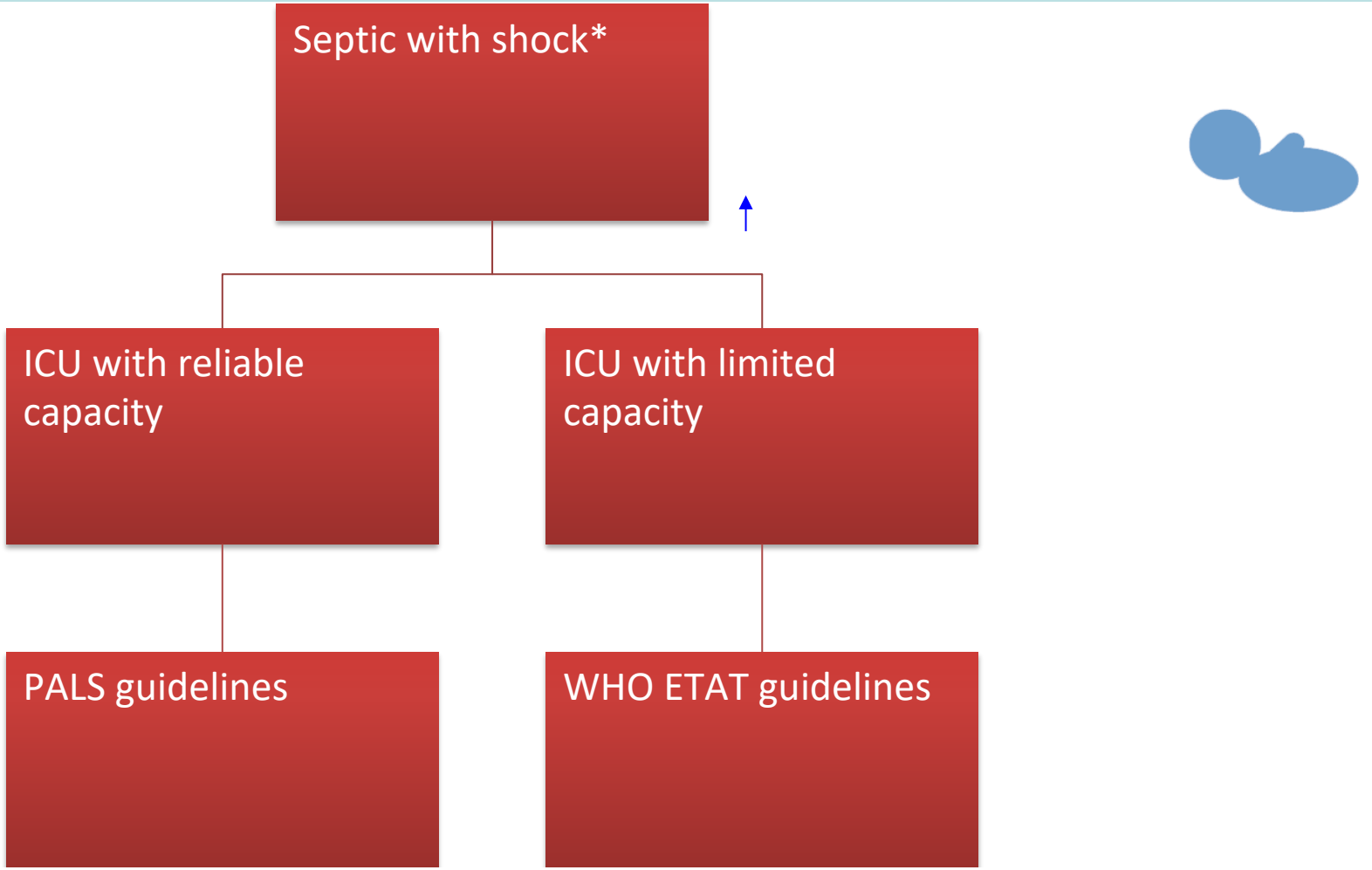


- See WHO *Pocket Book of Hospital Care for Children* for detailed management if child has:
  - severe acute malnutrition
  - severe malaria with profound anaemia (i.e. Hb < 5)
  - diarrhoea and severe dehydration
  - severe dengue shock syndrome.

ICU capacity

- **Consider local resources to delver intensive care to children, availability of the following:**
  - **advanced respiratory support, ventilators**
  - **haemodynamic monitoring**
  - **skilled and experienced staff (i.e. paediatric intensivists).**
  - **If any of the above are limited, consider using WHO guidance over PALS guidance for treatment of septic child with shock.**

Considerations for fluid resuscitation in the paediatric septic patient



* WHO shock definition is more strict than PALS definition.

WHO ETAT shock definition

- **Presence of all of the following three clinical criteria required to diagnose shock:**
  - **delayed capillary refill ≥ 3 sec**
  - **cold extremities**
  - **weak and fast pulse.**

- **Or frank hypotension.**

Age	< 1mo	1-12mo	1-12 yr	>12yr
SBP	< 50	<70	70 +(2 × age)	<90

Reach resuscitation targets within 6 hours

Improved sensorium

Skin examination:
- capillary refill ≤ 2 sec
- absence of skin mottling
- well felt peripheral pulses
- warm dry extremities.

Threshold heart rates:
- up to 1 year: 120–180 bpm
- up to 2 years: 120–160 bpm
- up to 7 years: 100–140 bpm
- Up to 15 years: 90–140 bpm.

Adequate urine output:
- ≥ 1.0 mL/kg/hr.

Normal calcium and glucose levels

Improved BP:
- age-appropriate SBP and MAP.

BP is less reliable endpoint because children have potent vasoconstrictor response. If the child is hypotensive, cardiovascular collapse may occur soon.

First: fluid loading

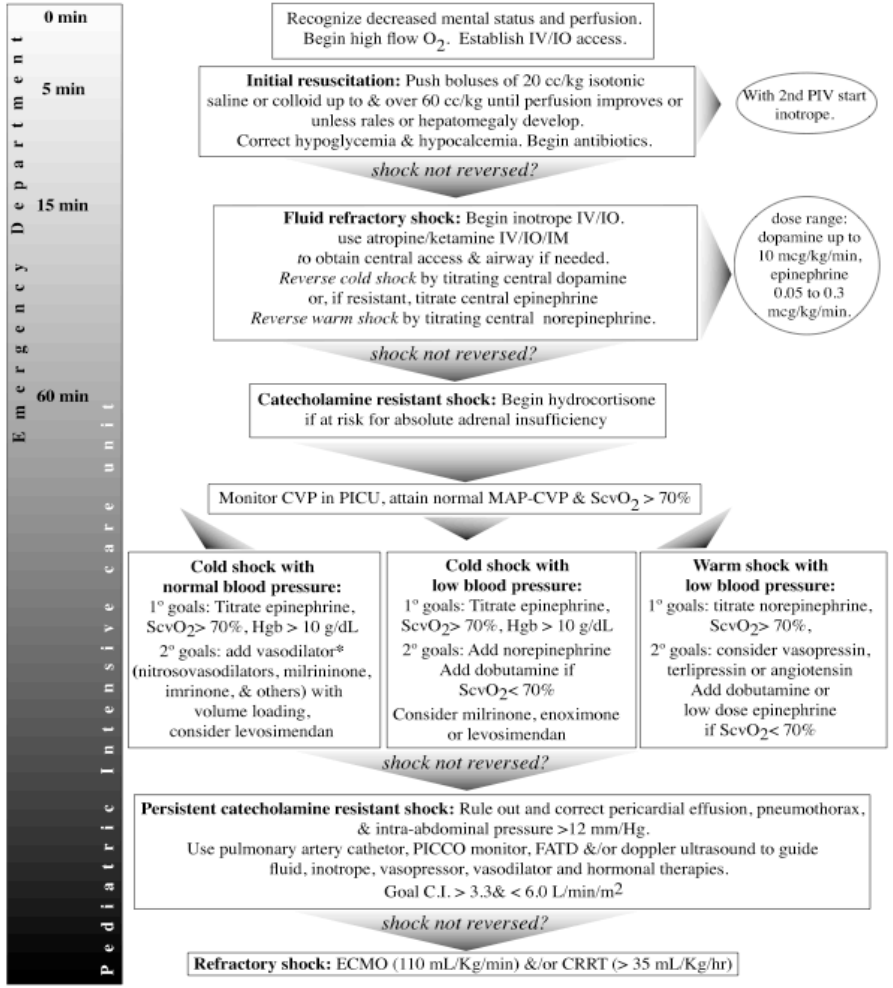
	WHO ETAT 2016	PALS Guidance 2015
Initial bolus	10 –20 mL/kg over 30–60 minutes (faster if profound hypotension).	20 mL/kg over 5–10 minutes.
Reassessment	Reassess perfusion indicators between fluid challenges. Examine for fluid overload.	
Second bolus	If after first bolus, child is still in shock, repeat fluid bolus. 10 mL/kg over 30 minutes providing no signs of fluid overload.	If after first bolus, child still in shock, give another 20 mL/kg challenge over 15–20 minutes. Can be repeated.
Max fluid at 1 hour	**30 mL/kg**	**60 mL/kg**
When to stop fluid therapy	Fluid therapy should be stopped once shock resolves (targets are met) or there are signs of fluid overload or cardiac failure.	

Second: inotropes and vasopressors



- If child remains in shock after initial fluid load then start inotrope/vasopressors:
  - titrate epinephrine, 0.05–0.5 mcg/kg/min (IV or IO) or dopamine
  - if child has hypotension (warm shock) add norepinephrine, 0.05–0.3 mcg/kg/min.
- Monitor child frequently and regularly:
  - children may cycle between these shock states as their illness evolves.

Figure 1: Stepwise management of hemodynamic support in infants and children



- For those working in ICU with reliable capacity, then PALS guidelines can be adapted to your setting.

When to stop fluid therapy

- Stop fluids once resuscitation targets have been met to avoid harmful effects of fluid overload.

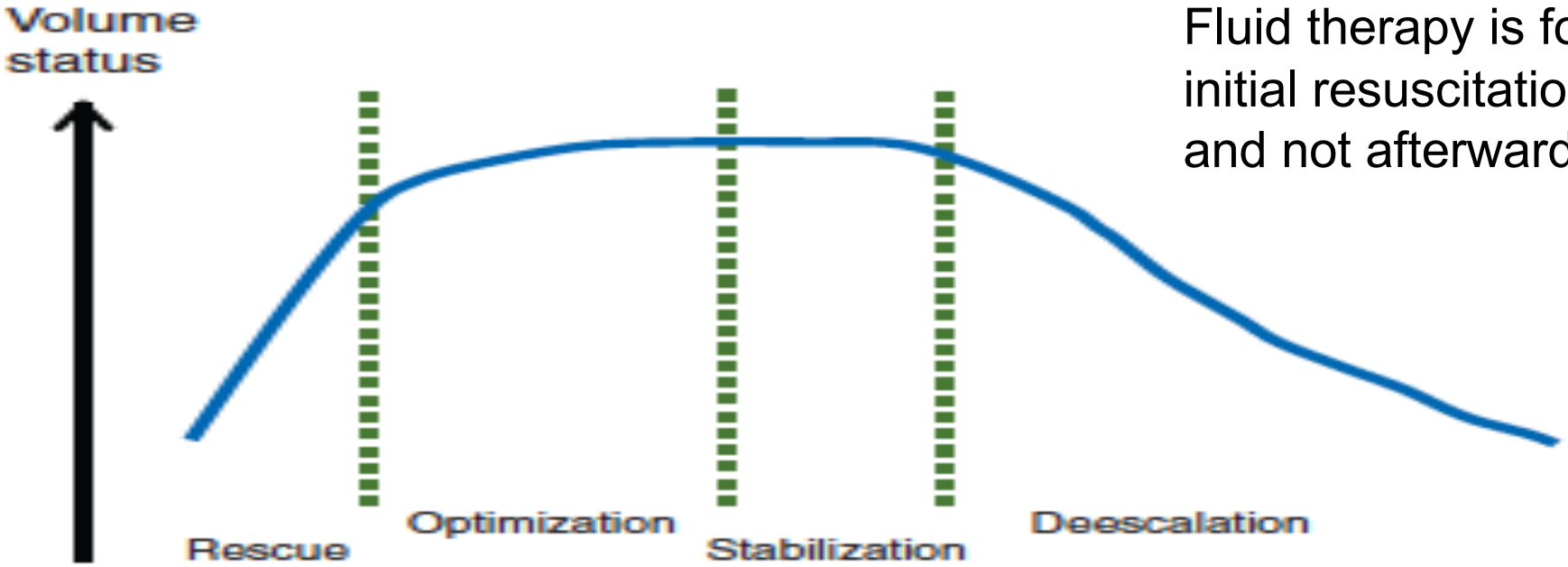
- Stop fluids if patient is no longer fluid responsive and develops signs of fluid overload:
  - Very high CVP (interpreted in context of high intra-thoracic pressures, pulmonary hypertension and RV dysfunction).
  - Pulmonary oedema (e.g. crackles on auscultation, chest X-ray or ultrasound).
  - Hepatomegaly and cardiac failure are also a signs of overload.



Risks of excess fluid therapy

- Increased tissue oedema.
- Worsened hypoxaemia.
- Worsens cardiac function in patients with cardiac failure.
- Increased length of stay.
- Increased morbidity and may increase mortality.

Fluid therapy over time



Fluid therapy is for initial resuscitation and not afterward

Principles	Lifesaving	Organ rescue	Organ support	Organ recovery
Goals	Correct shock	Optimize and maintain tissue perfusion	Aim for zero or negative fluid balance	Mobilize fluid accumulated
Time (usual)	Minutes	Hours	Days	Days to weeks
Phenotype	Severe shock	Unstable	Stable	Recovering
Fluid therapy	Rapid boluses	Titrate fluid infusion conservative use of fluid challenges	Minimal maintenance infusion only if oral intake inadequate	Oral intake if possible Avoid unnecessary i.v. fluids

Corticosteroids and shock

- Consider **low dose** IV hydrocortisone, if adequate fluid resuscitation and vasopressors fail to restore hemodynamic stability:
  - 50 mg every 6 hours or continuous for adults for (i.e. 5 days)
  - 50 mg/m^2/24 hours (1–2 mcg/kg 6 hourly) in children
  - taper when vasopressors no longer needed
    - i.e. 50 mg twice daily for days 6–8; 50 mg once daily days 9–11.
  - risks are hyperglycaemia and hypernatraemia.

- Precaution:
  - **Do not** administer high doses steroids (i.e. > 300 mg daily).
  - **Do not** use in sepsis without shock.
  - **Do not** use to treat influenza pneumonitis alone, but can be used for other respiratory indications.

Hyperglycaemia and sepsis

- Initiate a protocolized approach to blood glucose management when two consecutive measurements >10 mmol/L (180 mg/dL):
  - target glucose of < 180 mg/dL
  - avoid intensive insulin for tight glucose control (4.5–6 mmol/L, 80–110 mg/dL), this approach causes harm
  - avoid wide swings in glucose levels.

- Frequently monitor blood glucose, every 1–2 hours until stable, then every 4 hours, to prevent hypoglycaemia.

- Major risk is severe hypoglycaemia:
  - caution: point of care measurement can be falsely high in shock, interpret with caution.

Useful website

For access to Surviving Sepsis Campaign Guidelines and bundles, please visit:

www.survivingsepsis.org

Summary

- Early targeted resuscitation combined with **early** appropriate antimicrobial therapy saves lives in patients with sepsis and septic shock.
- Early resuscitation with crystalloid fluid and vasopressors are the most common intervention for septic shock.
- Resuscitation targets include improved blood pressure **and** other markers of tissue perfusion (mental status, urine output, skin, pulses, lactate).
- Modify resuscitation strategies for **children** with shock if child has severe malaria with anaemia or severe malnutrition; or is being cared for in setting with limited ICU capacity.

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