PEDIATRIC SEPSIS: IDENTIFICATION, PATHOPHYSIOLOGY AND MANAGEMENT

Katharine C Long, MD

DISCLOSURE

Dr. Long has no financial interests/arrangements to disclose

Objectives

- Recognize early warning signs and symptoms of pediatric sepsis
- Initiate goal-directed resuscitation and management of the septic patient
- Understand the pathophysiology of sepsis
- Identify need for institutional level sepsis bundle

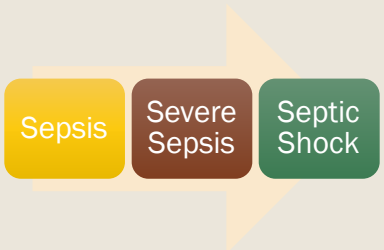
Definition of Shock

- Shock is a syndrome that is characterized by inadequate oxygen delivery and/or extraction to meet metabolic demands of vital organs and tissues
- If untreated, can lead to metabolic acidosis, organ dysfunction, and death

Types of Shock

Shock type	Examples	HR	BP	CO	Cap Refill	SVR
Hypovolemic	Hemorrhage Dehydration	↑	↓	↓	Delayed	High
Cardiogenic	Myocarditis Dysrhythmia	↑	↓	↓	Delayed	High
Distributive	Sepsis Anaphylaxis	↑	↓	↓ or ↑	Flash or delayed	Low or High
Neurogenic	Spinal cord injury	↓	↓	↓	Flash or normal	Low
Obstructive	Tamponade Pneumothorax	↑	↓	↓	Delayed	High
Distributive	Poisoning Sever anemia	↑	Normal or ↑	↑	Normal	Low or Normal

Sepsis Continuum



Severe Sepsis

- Severe sepsis – sepsis + 1 of following
  - *Cardiovascular organ dysfunction*
  - *ARDS defined as Pa_{O_2}/FiO_2 ratio ≤300, bilateral infiltrates on CXR, no evidence of L heart failure*

Septic shock and MODS

- Septic shock – sepsis + cardiovascular organ dysfunction
- Multiple organ dysfunction syndrome (MODS)
  - *Presence of altered organ function, so that homeostasis cannot be maintained without medical management*

Organ dysfunction

- Cardiovascular
  - *Persistent hypotension despite 60 ml/kg*
  - *Need for vasoactive medication*
  - *Signs of impaired perfusion*

Organ dysfunction (cont.)

- Respiratory
  - *PaCO2 > 65, or 20 over baseline PaCO2*
  - *Proven need for > 50% FiO2 to maintain saturation > 92%*
  - *Need for nonelective invasive or noninvasive mechanical ventilation*

Organ dysfunction (more)

- Neurologic
  - *GCS ≤ 11*
  - *Acute change in MS, with decrease in GCS ≥ 3 points baseline*

Pediatric Sepsis

- > 72,000 cases yearly in the United States
- 10-20% Mortality in the US
- Significant Morbidity

The Future….

- Biomarkers to identify patients with serious illness
- Genetic markers to identify immunological profile
- 10-20 years in the future

The Now….

Institutional Initiatives

- 1. Recognition bundle
- 2. Resuscitation and stabilization bundle
- 3. Performance bundle

Recognition Bundle

- Screen patient using institution sepsis trigger tool
- Clinician assessment within 15 min for positive screen
- Initiate Resuscitation Bundle within 15 minutes for those id with trigger tool and clinically confirmed

Resuscitation Bundle

- Attain IV/IO within 5 minutes
- Appropriate fluid resuscitation within 30 minutes
- Initialization broad-spectrum antibiotics within 60 minutes
- Inotrope for fluid-refractory shock within 60 minutes

Stabilization Bundle

- Multimodal monitoring to optimize fluid, hormonal and cardiovascular responses
- Confirm administration of appropriate antibiotics and source control

Performance Bundle

- Measure adherence to Trigger, Resuscitation and Stabilization Bundles
- Perform root cause analysis to id barriers to adherence
- Provide action plan to address and eliminate barriers

Clinical presentation

- Early recognition is important!
- Physical exam focused on tissue perfusion
- Hypotension is a ***LATE*** and ***PREMORBID*** sign

Identifying Serious Illness

- Capillary refill > 2 sec, mottling and pulse quality
- Heart rate > 90th percentile for age
  - *Hypotension is a late finding***
- Mental Status
- Classic physical exam findings

Clinical presentation

Organ system	↓Perfusion	↓↓Perfusion	↓↓↓Perfusion
CNS		Restless, apathetic, anxious	Agitated/confused, stuporous, coma
Respiration		↑Ventilation	↑↑Ventilation
Metabolism		Compensated metabolic acidemia	Uncompensated metabolic academia
Gut		↓Motility	Ileus
Kidney	↓Urine volume, ↑Sp grav	Oliguria (<0.5 ml/kg/h)	Oliguria / anuria
Skin	Delayed cap refill	Cool extremities	Mottled, cyanotic, cold extremities
CVS	↑HR	↑↑HR, ↓peripheral pulses	↓BP, central pulses only

Vitals are Vital

- Patients with poor outcomes within 7 days
  - 71% Unexplained tachycardia
  - 85% Abnormal vital signs upon discharge

Age Group	Respiratory Rate	Heart Rate	Systolic Blood Pressure	Diastolic Blood Pressure	Weight in Kilos	Consider Higher Acuity w/o Presence of Fever
Newborn	30-50	120-160	50-70	30-60	2-3	>180 HR
Infant (1-12 mos)	20-30	80-140	70-100	53-66	4-10	>180 HR
Toddler (1-3 yrs)	20-30	80-130	80-110	53-66	10-14	>140 HR
Preschooler (3-5 yrs)	20-30	80-120	80-110	55-69	14-18	>140 HR
School Age (6-12 yrs)	20-30	70-110	80-120	57-71	20-42	>130 HR
Adolescent (13+ yrs)	12-20	55-105	110-120	66-80	> 50	>110 HR

High Risk Pediatric Populations

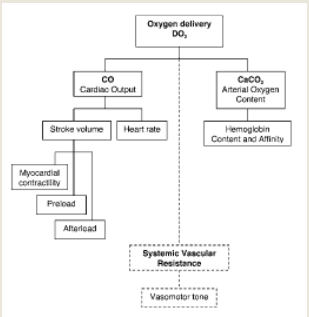
- Malignancy
- Asplenia – including sickle cell disease
- Bone marrow transplant
- Solid organ transplant
- Central line
- Severe MR/CP
- Immunodeficient, immunocompromised or immunosuppressed

Something is Not Right

- Gut feeling
- Based on clinical assessment
- Parental level of concern
- Experienced physicians less common

Pathophysiology

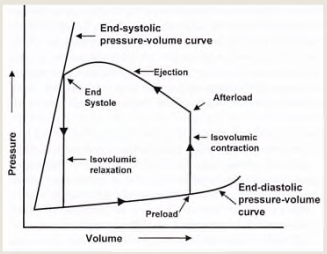
Oxygen Delivery



Arnold DG, et al. *Rogers' Textbook of Pediatric Intensive Care*. 4th ed.

Determinants of Stroke Vol

- Preload
- Afterload
- Contractility
- Heart Rate



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Lack of oxygen

- In aerobic metabolism, ~34 moles of ATP generated per 1 mole of glucose
- With lack of oxygen, switch to anaerobic metabolism
- Pyruvate acid is converted to lactic acid, instead of going through Krebs cycle, only generate 2 moles of ATP
- Have lack of ATP and also metabolic acidosis

Stages of Shock

- Compensated
  - *Normal blood pressure*
  - *Tissue perfusion preserved*
- Uncompensated
  - *Microvascular perfusion becomes marginal*
  - *Organ and cellular function deteriorate*
  - *Hypotension develops*
- Irreversible
  - *Organ and tissues injury that is unresponsive to conventional therapy and leads to death*

Early “Warm” Septic Shock

- Hyperdynamic state
- Clinical signs
  - *Warm extremities with bounding pulses*
  - *Widened pulse pressure, increased cardiac output and mixed venous saturation, decreased SVR*
- Biochemical evidence
  - *Hypocarbia, elevated lactate, hyperglycemia*

Late “Cold” Septic Shock

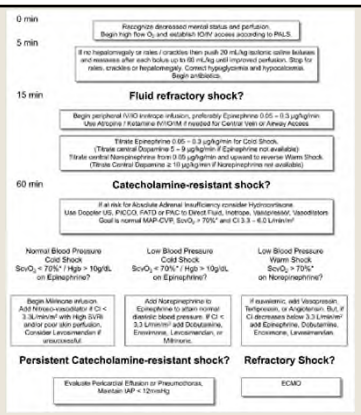
- Uncompensated with drop in cardiac output
- Clinical signs
  - *Cold/clammy skin, rapid, thread pulses, shallow respirations*
- Physiologic parameters
  - *SVR, oliguria, myocardial dysfunction, capillary leak*

Late “Cold” Septic Shock (cont.)

- Biochemical abnormalities
  - *Metabolic acidosis, hypoxia, coagulopathy, hypoglycemia*
- Rapidly progress to MOSF or death if untreated
  - *MOSF: Coma, ARDS, CHF, renal failure, ileus, GI hemorrhage, DIC*
  - *More organ systems involved = worse prognosis*

Management

- General principles
- Increase oxygen delivery
- Decrease oxygen demand
- Treat underlying cause



General Principles

- IV, Oxygen, Monitor
- Airway – intubate if unable to maintain
- Breathing – 100% oxygen to start
  - *Airway obstruction and breathing abnormalities can cause shock*
- Circulation – rapid IV access, frequent VS reassessment

Initial therapeutic endpoints

- CR ≤ 2 sec
- BP normal for age
- Normal pulses, with no differential between peripheral and central pulses
- Warm extremities
- Normal mental status

Increase oxygen delivery

- Remember $DO_2 = CaO_2 \times CO$
- or $DO_2 = [(1.34 \times Hgb \times Sat) + (0.003 \times PaO_2)] \times SV \times HR$
- Increase carrying capacity by increasing Hgb and saturation
- Stroke volume determined by preload, afterload, and contractility

Volume resuscitation

- Early volume resuscitation is important!
- Obtain early IV access
  - *The best access is **short** and **wide**!*
  - *Pouiselle's law*

$$F = \frac{\pi p r^4}{8 \mu l}$$

  - *Large bore PIV, IOs, and cordis are better than a thin, long central line*

Importance of Early Resuscitation

Carcillo, JAMA 1991

- Retrospective review of 34 pediatric patients with culture positive septic shock from 1982-89.
- Three groups
  - *1 – 20 ml/kg in 1st hour*
  - *2 – 20-40 ml/kg in 1st hour*
  - *3 – greater than 40 ml/kg in 1st hour*
- No difference in ARDS between groups

Volume resuscitation

- Optimize preload with NS or LR (crystalloid)
- 10-20 ml/kg aliquots
- Hand-push at bedside
- After 40-60 ml/kg, reassess and consider
  - *Ongoing losses, adrenal causes, intestinal tissue ischemia, obstructive shock*
  - *Further fluid therapy can be guided by response, labs, CVP measurements, CXR*

Blood products Plasma therapies

- If SvO_2 < 70% can target Hgb > 10
- After stabilization and recovery of shock, target Hgb > 7
- Transfuse platelets if:
  - *≤ 10k*
  - *≤ 20k and significant risk of bleeding*
  - *≤ 50k and active bleeding*
- Use plasma therapies for coagulopathic dz

Vasoactive medications

- Used when there is cardiogenic or distributive component of shock
- Failure to improve perfusion despite adequate oxygenation, ventilation, heart rate, and volume expansion

Adrenergic agonists

- Dopamine – D1, α1, β1
- Epinephrine - α1, β1, β2
  - *More affect on HR and contractility*
- Norepinephrine - α1 >>> β1
  - *Mostly vasoconstriction, increased SVR*
- Dobutamine - β1
  - *Increases contractility, HR*
  - *May decrease SVR*

Corticosteroids

- Give Hydrocortisone if:
  - *Fluid refractory*
  - *Catecholamine resistant shock*
  - *Suspected or proven absolute adrenal insufficiency*

Decrease oxygen demand

- Intubate and use mechanical ventilation
  - *Will decrease work of breathing*
  - *Use lung protective strategies*
- Sedation and paralysis
  - *Sedation decreases metabolic demands of brain, which will decrease overall oxygen demand*

Antibiotics and Source Control

- Administer within 1 hour
- Blood cultures first, but don't delay antibiotics
- Early and aggressive source control
  - *Nec fascitits, abscess, septic joint*

ECMO

- Consider ECMO in refractory septic shock and respiratory failure

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