Current trends in pediatric sepsis resuscitation

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Objectives

By the end of this session the learner will be able to:
• Identify common clinical features of septic shock in children
• Understand priorities in acute septic shock resuscitation
• Understand priorities for ongoing management and monitoring in septic children
Signs and Symptoms

- Fever or hypothermia (esp. neonates, brain injured children)
- Irritability → lethargy
- Decreased urine output
- Tachycardia, tachypnea
- Peripheral pulses diminished or bounding
- Cap refill prolonged or instantaneous

Lab:
- High or low WBC count, increased band count
- Acute phase response (↑ fibrinogen, CRP, serum amyloid protein)
- DIC (↓ fibrinogen, ↑ PT/PTT, D-dimer)
- ↑ lactate, IL-6, IL-8, procalcitonin (bacterial disease)

Differential diagnosis

- Non-infectious causes of SIRS
  - Trauma
  - Burns
  - Cardiopulmonary bypass
  - Autoimmune disease
  - Pancreatitis

- Hemophagocytic lymphohistiocytosis
  - Familial or acquired hyperinflammatory disease
  - NK cell defect leading to an inability to turn off the innate immune response
  - Lots of overlap with signs/sx of sepsis
  - Treatment is radically different from sepsis:
    - Immune suppression, BMT
    - Genetic tests, NK function tests, levels of sCD25, sCD163, ferritin can be helpful in making the diagnosis.

Castillo, PCCM, 2009
• 100 children with severe sepsis
• Sampled on day 2 of sepsis
• Risk stratified on the basis of systemic inflammation (CRP) and MAS-like phenotype (ferritin)

But what about hypotension?

Vascular resistance

Don’t wait for hypotension!

Cardiac output

Blood pressure

Percent of volume deficit

Percent of control
• Airway
  – Think about intubating for decreasing GCS
• Breathing and Circulation
  – Provide O2 to optimize systemic saturations
  – Place IV

Revision of the ACCM guidelines for pediatric septic shock resuscitation
Brierley et al, Crit Care Med, 2009

• Next step:
  • Correct hypoglycemia and hypocalcemia and
  GIVE FLUID FAST!!!!

Revision of the ACCM guidelines for pediatric septic shock resuscitation
Brierley et al, Crit Care Med, 2009

Carcillo et al JAMA 266, 1991

Fig 1.—The distribution of survivors and nonsur- vivors within fluid resuscitation groups (see text for definition of groups). The asterisk indicates a significant difference in survival between group 2 and groups 1 and 2 individually and combined.
• Repeated 20 ml/kg fluid boluses may be administered in excess of 60 ml/kg in the first hour and 120 ml/kg in the first 6 hours if, pulses, mental status, urine output, and BP suggest that systemic perfusion is decreased.

How do I administer fluid to a child with shock?

• Traditional IV pump:
  o Max rate 999 ml/hr
  o Set at max rate; this pump can only deliver 20 ml/kg within 5 minutes to a child weighing less than:

  4.16 kg
How do I administer fluid to a child with shock?

Rapid Infuser
($8,700 + $28 for tubing)

Pressure Bag
($90)

How do I administer fluid to a child with shock?

Push-pull System
(< $ 10)
Pull from IV bag  Turn stopcock  Push to patient

Repeat

---

Don’t forget about….

PALS guidelines removed upper age limit for use of IO access!
Airway
- Think about intubating for decreasing GCS

Breathing and Circulation
- Provide O₂ to optimize systemic saturations
- Think about positive pressure to take away work of breathing and allow cardiac output to be redirected…… as much as 20% of it!

Intubating a child with septic shock:
- Watch preload!
  - Increased intra-thoracic pressure may = decreased venous return and decreased cardiac output.
- Sedatives can lower BP
  - Ketamine is first line
  - Be careful with doses of other drugs
  - Avoid etomidate
    - Adrenal suppression with one dose

Fluid refractory shock:
- If shock persists after 60 ml/kg of fluid resuscitation (and normal CVP) it’s time to start thinking about a vasoactive drug…

But which one?
The hallmark of adult sepsis is a high-output, low SVR state.

The vasoconstrictive response in children can be profound. Kids are different [Ceneviva, Pediatrics, 1998]:
- 50 children with septic shock refractory to > 60 ml/kg volume with PCWP > 8 and functioning PAC
- 58% had a low CI (< 3.3 L/min/m²) and high SVRI (> 1600 dyne-sec/cm²). COLD SHOCK
- Only 20% had a high CI and low SVRI. WARM SHOCK

Warm Sepsis vs. Cold Sepsis
- WARM SHOCK: Erythroderma, bounding pulses, wide pulse pressure
- Staph (MRSA, MSSA), strep
- Tampons (still a problem), cutaneous infections
- Criteria:
  - Fever
  - Hypotension
  - Erythroderma → desquamation (1 – 2 weeks)
  - 3 or more: GI (V/D), muscular (myalgia, ↑CK), mucous membranes, renal failure, ↑ transaminases, ↓ platelets, ↓ mental status
  - No other sx growth/serologies
  - Vancomycin (initial), nafcillin (if MSSA), clindamycin (inhibit toxin production); IVIG (binds toxin)

But which one?
- COLD:
  - Cool extremities, prolonged cap refill, diminished peripheral pulses, narrow pulse pressure
  - Target β₁ receptors:
    - Dopamine 5 – 10 μg/kg/min
    - Epinephrine 0.05 – 0.1 μg/kg/min
- WARM:
  - Warm extremities, flash cap refill, bounding peripheral pulses, wide pulse pressure
  - Target α₁ receptors:
    - Dopamine > 10 μg/kg/min
    - Epinephrine > 0.1 μg/kg/min
    - Norepinephrine > 0.05 μg/kg/min
Catecholamine resistant shock:
Consider adrenal insufficiency!
Persistent shock:
- Measure CVP, ScvO2, Hgb
  - Target ScvO2 > 70%
  - Hgb > 10 g/dL
- Volume load to CVP 8-12 mm Hg
- COLD shock, normal BP:
  - Afterload reduce (nitravasodilators, dobutamine, milrinone)
- COLD shock, low BP:
  - Consider norepinephrine
  - Consider afterload reduction later
- WARM shock, low BP:
  - ↑ norepinephrine
  - Vasopressin

Very persistent shock:
- Rule out and correct
  - Pneumothorax
  - Pericardial effusion
  - Intra-abdominal hypertension
- GOAL:
  - CI 3.3 – 6 L/min/m²
  - ScvO2 > 70%
If all else fails….ECMO

Goal is to normalize….
- Heart rate
- Perfusion
- Blood pressure
- Urine output
- Lactate (base deficit?)
- ScvO2

What if these are not normalizing?
SvO₂ measurement

The difference between systemic saturations (pulse ox) and SvO₂ should be < 30%.

PA catheter

Using thermodilution, one can measure or calculate:
Cardiac output/index, SVR

The “gold standard” place to measure SvO₂ is in the pulmonary artery.
PA catheter

The “gold standard” place to measure SvO2 is in the pulmonary artery.

PA catheters have largely fallen out of use in children due to:

- High complication rate
- Difficulty with placement in infants/small children
- Still useful in cases where measuring PA pressures is important

PiCCO
(Pulse Contour Cardiac Output)

PiCCO catheters are essentially arterial lines which contain a thermister. A computer can analyze the arterial line waveforms to provide estimates of stroke volume and SVR. You can use transpulmonary thermodilution to calculate cardiac output/index.

This is the standard invasive cardiac output measurement technique in the PICU at Nationwide Children’s Hospital.

PiCCO
(Pulse Contour Cardiac Output)

Downsides:
- Arterial line must be central.
- Arterial line waveforms are notoriously artifactual in kids (spasm, size).
- Part of catheter lumen is occupied by thermister (increased clot risk?).
- Requires CVL above the diaphragm for some measurements (but not CI, SVRI).
NIRS regional saturation

What if you could do the same thing non-invasively?

Near infrared spectroscopy has the potential to do this...

Invos monitor, Somanetics, Inc.

NIRS regional saturation

An adhesive patch containing a NIR light source and sensor is placed on the target region.

Based upon the light absorbance of the underlying tissue, a % saturation for the vascular bed under the patch is calculated.

Correlates well with SvO₂.

Remember though.....if you don’t have fancy technology you can still do it the old-fashioned way......
What about antibiotics?

Empiric antibiotics

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Mortality if you got the right empiric abx</th>
<th>Mortality if you got the wrong empiric abx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibrahim et al, Chest, 2000</td>
<td>482</td>
<td>28%</td>
<td>62%</td>
</tr>
<tr>
<td>MacArthur et al, Clin Inf Dis, 2004</td>
<td>2,634</td>
<td>33%</td>
<td>43%</td>
</tr>
<tr>
<td>Kumar et al, Crit Care Med, 2006</td>
<td>2,731</td>
<td>Each hour in delay of correct abx in the first 6 hours of hypotension = an average decrease in survival of 7.6% !</td>
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Empiric antibiotics

- Intubated children with CAP
  - Delays as short as 2 – 4 hours were associated with adverse outcomes in children with severe CAP

- Obtain cultures, then....

- Use a de-escalating approach with prompt, broad coverage early with subsequent management dictated by culture results and clinical course.

- Know what your patient (and your unit) has grown in the past!

An Empiric Antibiotic Protocol Using Risk Stratification Improves Antibiotic Selection and Timing in Critically Ill Children

- Single center analysis of time to correct antibiotics before and after implementation of a CPOE-based protocol that stratifies subjects by low or high risk for healthcare-associated organisms.

- N = 491
Ongoing management - MODS

- **Respiratory:**
  - High PEEP, low tidal volume ventilation (6ml/kg) for ALI/ARDS
  - Keep FiO2 < 60%, Pea < 30 mmHg
- **Renal:**
  - Consider early CRRT for kids who are > 10% fluid overloaded after shock is stabilized.
  - Remember to dose meds (including abx) for CRRT.
- **Heme:**
  - Consider plasma exchange for thrombocytopenia-associated multiple organ failure (TAMOF)
    - Restores vWF cleaving protease (ADAMTS13)
  - Transfusion threshold of 7 g/dL may be acceptable once shock has stabilized…remember the TRIPICU study….

Ongoing management - MODS

- **Glycemic control:**
  - Looks like tight glycemic control is not a management priority
- **Activated Protein C:**
  - Initially looked good in adults…bad in kids
  - Off the market
- **Source control**
  - Particularly in the setting of refractory culture positive sepsis, think about:
    - Infected devices
    - Abscesses
    - Osteomyelitis
    - Empyema
    - Endocarditis
    - IVIG
      - No role for empiric sepsis tx
      - Indicated for TSS
      - Indicated for ↓ IgG levels
**Nosocomial Sepsis**

- The longer a child stays in the ICU, the greater the nosocomial sepsis risk.
- Must cover for:
  - MRSA
  - Coag-negative staph
  - Nosocomial Gram negatives:
    - Pseudomonas
    - Enterobacter
    - Klebsiella
    - Acinetobacter?
    - Stenotrophomonas?

**Sepsis QI**

- Standardization and timeliness of resuscitation:
  - ACCM guidelines
  - Surviving sepsis
  - WFPCCS pediatric global sepsis initiative
- Care bundles
    - Hospital-wide QI project aimed at sepsis recognition, IV access, IVF, antibiotics, vasoactives
  - Han et al, *PCCM* 2014
    - Global sepsis initiative “resource rich” group
    - A multi-element sepsis bundle was associated with more rapid shock reversal.

**Conclusions**

- Kids are likely to be cold rather than warm (except for TSS)...don’t wait for hypotension!
- Guidelines exist that can help you streamline your approach to pediatric septic shock.
- You can (and should) still give a lot of fluid to kids with septic shock.....FAST.
- Monitor the success of therapy (hemodynamics, lactate).
- Early, correct empiric antibiotic therapy is essential.
- Institutional sepsis bundles are effective at improving sepsis outcomes.
Questions?