Sepsis: Beyond Fluids and Vasoactive Agents

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

0 min
- Begin high flow O2, Establish IV/IO access.
- Rass, decreased mental status and perfusion.

5 min
- Initial resuscitation: Push bolus of 20 cc/kg isotonic saline or crystalloid up to & over 60 cc/kg until perfusion improves or unless rarely or non-physiologically develop.
- Correct hypoglycemia & hypocalcemia. Begin antibiotics.
- Shock not reversed?

15 min
- Fluid refractory shock: Begin isotonic IV/Ringer.
- Use atropine/entacapone IV/Ringer to obtain central access & airway if needed.
- Reverse cold shock by titrating central dopamine.
- Or, if resistant, initiate central epinephrine.
- Reverse warm shock by titrating central norepinephrine.
- Shock not reversed?

60 min
- Catecholamine resistant shock: Begin hydrocortisone if at risk for absolute adrenal insufficiency.

Monitor CVP in PICU, attain normal MAP, CVP & SevO2 > 70%

Cold shock with normal blood pressure:
1st goal: Tissue epinephrine, SevO2 > 70%, Hgb > 10 g/dL.
2nd goal: Add vasopressor (terlipressin, vasopressin, miconazole, nitroprusside, etc.) with volume loading, consider levsimendan.

Cold shock with low blood pressure:
1st goal: Tissue epinephrine, SevO2 > 70%, Hgb > 10 g/dL.
2nd goal: Add norepinephrine or dobutamine if SevO2 < 70%.
Consider minoxidil, enoximone or levosimendan.

Warm shock with low blood pressure:
1st goal: Tissue norepinephrine, SevO2 > 70%.
2nd goal: Consider vasopressin, terlipressin or angiotensin.
Add dobutamine or low dose epinephrine if SevO2 < 70%.

Persistent catecholamine resistant shock: Rule out and correct pericardial effusion, pneumothorax, & intra-abdominal pressure > 12 mmHg.
- Use pulmonary artery catheter, PICCO monitor, FAST &/or doppler ultrasound to guide fluid, inotrope, vasopressor, vasodilator and hormonal therapies.
- Goal CI > 3.3 & < 5.0 L/min/m²

Shock not reversed?

Refractory shock: ECMO (110 mL/Kg/min) &/or CRRT (> 35 mL/Kg/hr)
High burden of HIV, malnutrition,
Low staff availability
Limited equipment and bed availability
High burden of nosocomial infection

Rudan et al, Bull WHO, 2008
Beyond Fluids and Vasoactive Agents

- Context Matters
- Access to care for sepsis?
- How do we recognize sepsis?
- Adherence to treatment protocols?
- What about post discharge mortality?
- Concluding Remarks
PICU Survival PCP

- Ventilation only
- Oral steroids
- Gancyclovir
- Early ARV

Mortality

90%
20%

Kitchin OP, et al. PCCM 2012
FEAST Exclusion Criteria

Intensive Care

“Mechanical Ventilation, Inotropes, Vasopressors and CRRT prevent increases in early mortality but at a price…..”

COMMENTARY

Totem and Taboo: Fluids in sepsis

Andrew K Hilton¹ and Rinaldo Bellomo²

Crit Care 2011
Fluid Overload and Mortality

Fluid resuscitation in septic shock: A positive fluid balance and elevated central venous pressure are associated with increased mortality*

John H. Boyd, MD, FRCP(C); Jason Forbes, MD; Taka-aki Nakada, MD, PhD; Keith R. Walley, MD, FRCP(C); James A. Russell, MD, FRCP(C)

Fluid overload before continuous hemofiltration and survival in critically ill children: A retrospective analysis*

Jason A. Foland, MD; James D. Fortenberry, MD, FAAP, FCCM; Barry L. Warshaw, MD, FAAP; Robert Pettignano, MD, FAAP, FCCM; Robert K. Merritt, MA; Micheal L. Heard, RN; Kris Rogers, RN; Chris Reid, RRT; April J. Tanner, RN; Kirk A. Easley, MS

Crit Care Med 2011 (VASST Trial)

Crit Care Med 2004
Where Do They Die?

Estimated number of episodes of severe ALRI worldwide in children <5 years in 2010: 19.2 million (15.6–23.8 million)

- 62% of cases that reach hospitals: 11.9 million (10.3–13.9)
  - Case-fatality ratio in admitted cases: 2.1% (1.4–3.1)
  - 19% of deaths were in hospital: 0.27 million (0.16–0.45)

- 38% of cases do not reach hospitals: 7.3 million (5.3–9.9)
  - Case-fatality ratio in communities: 15.4% (10.4–22.5)
  - 81% of deaths occur outside hospital: 1.13 million (1.03–1.19)

Estimated (severe) ALRI deaths in children <5 years in 2010: 1.40 million (1.19–1.64 million)
Pathways of Unnecessary Sepsis

1. Malnutrition, sepsis and elective surgery
2. Sepsis & the implementation of the safe surgery campaign
3. Sepsis and the quality & time of referrals from HDU's
4. Excessive fasting times & sepsis
5. Sepsis related to trauma and high maternal mortality rate
6. Lacking specialist treatment of sepsis in the districts

Severe sepsis (ICU)

Pollach G et al  PCCM 2013
Beyond Fluids and Vasoactive Agents

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Faces of Sepsis - A Social Problem

• Poor care-seeking behavior
  – Education and money
  – Faith in supernatural causes and home remedies,
  – Distance and non-availability of transport,
  – Many stops and long waiting time,
  – Lack of faith in the health system
  – Empowerment

Education Policy
Recognition of and Care Seeking Behaviour

• Sensitivity of recognition (median)
  – Diarrhoea (36%), Malaria (37%), Pneumonia (45%)

• Caregivers seeking care outside the home – 73%

• Care seeking from CHW (median)
  – Diarrhoea (5%), Pneumonia (4%), Malaria (1%)

• Use of oral hydration therapy (34%)

Inadequate Knowledge of Danger Signs in Neonates

- 3.07 million deaths with 1/3 in first 24 hours
- Six danger signs
  - Fast or difficulty breathing, fever, difficulty feeding, convulsions, moves only when stimulated and hypothermia
- Knowledge of danger signs
  - At least one (58%), at least two (15%)
- Solution - education of mothers, promotion of birth preparedness

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Recognition

• Recognition an important barrier
  Oliviera Ped Emergency care 2008 24(12): 810
  Kakebeeke et al International Journal of Emergency Medicine 2013 6:4

• 17% recognized early septic shock in UK ED.
  Chronshaw et al Emergency Medicine J 2011;28:670

• 33% underestimated the severity of sepsis in France study.
  Launay et al Pediatr Crit Care Med 2010; 11:469
Recognition

- Early clinical signs non-specific SIRS
  Fever, tachycardia, tachypnea

- Recognition is experience & skills dependent
  Mangia et al. J Pediatric Infectious Diseases 2009 4(2):71-76
  Thompson et al. Lancet 2006 367:397-403

- Failure of supervision of junior staff ↑risk of death in meningococcal sepsis
  Ninis et al. BMJ 2005330:1475
## Suspicion of Sepsis at Health Facility

### Syndromic Sepsis Case Finding Tool - Neonate

**Instruction:** Please look for the danger signs listed below and (✓) Tick in appropriate box

<table>
<thead>
<tr>
<th>Danger Signs</th>
<th>Look/Ask/Feel</th>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td>Hypothermia</td>
<td>1. Cold/Clammy Skin</td>
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<td>2. Blue or Pale Color Skin</td>
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<td>3. Axillary temperature $&lt;96^\circ$ F</td>
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<tr>
<td>Hyperthermia</td>
<td>4. Axillary temperature $&gt;101.3^\circ$ F</td>
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<td>Altered mental status</td>
<td>5. Unconscious /No movement</td>
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<td>6. Lethargic/movement only when stimulated</td>
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<td></td>
<td>7. Difficult to arouse/drowsy</td>
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<td>Convulsion</td>
<td>8. Convulsion- by history (care giver report) or examination</td>
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<td>Respiratory Distress</td>
<td>9. Severe Chest In drawing</td>
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<td>Umbilical infection</td>
<td>10. Severe Breathing difficulty/noise breathing</td>
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<td></td>
<td>11. Respiratory rate $&gt;60$ (with any other danger sign)</td>
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<td>Not Feeding properly</td>
<td>12. Pus/foul smelling discharge from umbilicus</td>
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<td>13. Red and swollen umbilicus with discharge</td>
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<td>14. Stops feeding properly/sudden loss of appetite</td>
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<td>15. Poor or no sucking reflex</td>
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<td>16. Vomits everything out/projectile vomiting</td>
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</tbody>
</table>
Intuition that something was wrong despite the clinical assessment of non-severe illness substantially increased the risk of serious illness (LR 25.5, 95% CI 7.9 to 82.0)

Strongly associated with gut feeling: children’s overall response (drowsiness, no laughing), abnormal breathing, weight loss, and convulsions.

Strongest contextual factor was the parents’ concern that the illness was different from their previous experience (OR 36.3, 95% CI 12.3 to 107).
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Adherence to ACCM guidelines improves outcome

- Community hospital ↓mortality by 30%
  Han et al. Pediatrics 2003 112:793

- ScvO2 >70% ↓mortality by 27%
  Oliveira et al ICM 2008 34:1065

- Boston children's ED ↓LOS 3 days
  Paul Pediatrics 2012;130:e273–e280
Adherence

• 19% adherence, Boston children’s hospital ED.
  – Delay IV fluids & inotropes
    Paul et al. Pediatrics 2012;130:e273–e280

• 36% adherence, pre-PICU UK
  – Delay recognition, IV fluids & inotropes
    Inwald et al. Archives of Diseases in Childhood. 2009;94(5):348

• 12% adherence India
  – Lack of skill & knowledge
    Santhanam et al. J of Indian Critical Care Medicine 2009 13 (2): 54
• Resuscitation Bundle Compliance 24 - 52 %.  
• Management Bundle Compliance 10 - 25 %.  
• Mortality  
  – Resuscitation compliance (OR 0.4, 95% CI, 0.2-0.7)  
  – Management compliance (OR 0.3, 95% CI, 0.1-0.8)
Beyond Ventilation

• Get the basics right
  – antibiotics
  – fluids and nutrition
  – appropriate sedation
  – positioning
  – respiratory secretions clearance
Beyond Ventilation

• Infection Control
  – nosocomial pneumonia
  – staffing
  – hand hygiene

– management of equipment
  • reusable equipment
  • pasteurization process
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Background

Wiens et al. PLOS One. 2013;6(8):e66698
Risk Model Application

- Mobile App
- CHW Referral
- Discharge Kit
Community Referral

Sick Child

CHW Visit

Referral to CHW

Referral to HC/Hospital

Discharge
Beyond Fluids and Vasoactive Agents

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World Sepsis Day: 13 September 2014

A truly global effort to fight sepsis. On every continent. In over 40 countries.
My Sincerest Thanks