Key Points in Pediatric Sepsis and Septic Shock
Key Points in Pediatric Sepsis and Septic Shock

• A major killer of global importance
• Recognize early
• Treat aggressively
• Context matters
• A global response
Failure of organ perfusion

Early recognition and treatment

- Pneumonia
- Diarrheal Diseases
- Malaria
- Bacterial sepsis
- Dengue
- Mixed Infections
- Nosocomial Infections

- Myocardial depression
- Endothelial Dysfunction (Capillary leak, vasodilatation)
- Anaemia
- Thrombosis
- Bleeding

Endothelial Dysfuction (Capillary leak, vasodilatation)
Sepsis in Children

• Incidence, mortality and morbidity is unacceptably high worldwide
  • Ruth A et al PCCM 2014 (USA)
  • Thompson and Kissoon CLEP 2014 (Canada)
  • Schlapbach L et al Lancet Infect Dis 2015 (ANZIC)
  • Wang Y et al PCCM 2014 (China)
  • Ganjoo S et al Indian J Pediatr 2014 (India)
  • Folgori L et al Pediatr Infect Dis J 2014 (Europe)
Global Child Deaths

Lozano R et al Global and Regional Mortality... Lancet 2012

xx % percent attributable to sepsis
Key Points in Pediatric Sepsis and Septic Shock

• A major killer of global importance
• **Recognize early**
• Treat aggressively
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### Trajectory of Sepsis and Interventions

<table>
<thead>
<tr>
<th></th>
<th><strong>INFECTION</strong></th>
<th><strong>SEPSIS</strong></th>
<th><strong>SEVERE SEPSIS</strong></th>
<th><strong>SEPTIC SHOCK</strong></th>
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</thead>
<tbody>
<tr>
<td><strong>Prevention</strong></td>
<td>Hand hygiene practices, Vaccinations, NI improvement bundles (VAP, CRBSI, CAUTI, SSI), IC Guidelines, Antibiotic stewardship, Auditing (IC &amp; NSQIP)</td>
<td>PAIRS response process, Antibiotic stewardship, HH, NI bundles, IC bundles</td>
<td>PAIRS response process (ICU consult), Antibiotic stewardship, HH, NI bundles, IC bundles</td>
<td>HH, NI bundles, IC bundles</td>
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<tr>
<td><strong>Recognition/Dx</strong></td>
<td>Sepsis Screening, PEWS &amp; Situational Awareness (PAIRS)</td>
<td>Advanced lab dx, Screening, PAIRS</td>
<td>PAIRS, Advanced lab dx,</td>
<td>PAIRS, Advanced lab dx,</td>
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<tr>
<td><strong>Tx/Follow-up</strong></td>
<td>Sepsis Guideline, Antibiotic stewardship</td>
<td>Order set, Antibiotic stewardship</td>
<td>Order set, Antibiotic stewardship,</td>
<td>Order set, Antibiotic stewardship, Code Blue, ECLS</td>
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- **PAIRS**: Prompt, Assessment, Response, Systematic approach
- HH: Hand hygiene
- NI: Nursing interventions
- IC: Intensive care
- VAP: Ventilator-associated pneumonia
- CRBSI: Central line-related bloodstream infection
- CAUTI: Catheter-associated urinary tract infection
- SSI: Surgical site infection
- PEWS: Paediatric Early Warning Score
- ECLS: Extracorporeal life support
- NSQIP: National Surgical Quality Improvement Program
- **ICU**: Intensive care unit
Sepsis Definitions in Term Neonates

• Clinical findings used in 26/42 (62%) studies
  – Non-specific signs (16), cardiovascular signs (12), respiratory signs (9), abnormal temperature (7), CNS (2), feeding problems (1)

• Test used in 12/42 (29%) of studies
  – C-reactive protein (5), total WBC (4), metabolic acidosis (3), immature to total WBC ratio (3), neutropenia (1), abnormal fibrinogen (1), thrombocytopenia (1), hypoglycemia (1), hyperglycemia (1)
• 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.

• Parents’ concern that the illness was different from their previous experience (OR 36.3, 95% CI 12.3 to 107).
Defining Pediatric Severe Sepsis

PICU – 42 beds, 1729 patients

Consensus guidelines (research criteria) N= 90 (5.2%)

Diagnosis by healthcare professionals (clinical criteria) n= 92 (5.6%)

ICD 9 (administrative criteria) N=103 (6.0%)

Weiss SL et al PCCM 2012
**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></td>
<td>2. Blue or Pale Color Skin</td>
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<td></td>
<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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<tr>
<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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<tr>
<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></td>
<td>10. Severe Breathing difficulty/noise breathing</td>
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<tr>
<td></td>
<td>11. Respiratory rate $&gt;60$ (with any other danger sign)</td>
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<tr>
<td>Umbilical infection</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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<tr>
<td>Not Feeding properly</td>
<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></td>
<td>16. Vomits everything out/projectile vomiting</td>
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</table>
Key Points in Pediatric Sepsis and Septic Shock

- A major killer of global importance
- Recognize early
- Treat aggressively
- Context matters
- A global response
Figure 1: Stepwise management of hemodynamic support in infants and children

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

5 min
- Initial resuscitation: Push boluses of 20 cc/kg isotonic saline or call for up to 60 cc/kg urine output improves or unless rates or hypoperfusion develop.
- Correct hypoglycemia & hypocalcemia. Begin antibiotics.
- Shock not reversed?

15 min
- Fluid refractory shock: Begin isotonic IV/Ringer's lactate to obtain central access & airway if needed.
- Reverse cold shock by titrating central dopamine.
- 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 & ScvO₂ > 70%.

Cold shock with normal blood pressure:
- 1st goal: Titrate epinephrine, ScvO₂ ≤ 70%, Hgb > 10 g/dL.
- 2nd goal: add vasodilator (vasodilators, miconazole, bromocriptine, milrinone, & ephedrine) with volume loading. Consider levosimendan.

Cold shock with low blood pressure:
- 1st goal: Titrate norepinephrine, ScvO₂ ≥ 70%, Hgb > 10 g/dL.
- 2nd goal: Add more epinephrine or add dobutamine if ScvO₂ < 70%.
- Consider milrinone, enoximone or levosimendan.

Warm shock with low blood pressure:
- 1st goal: Titrate norepinephrine, ScvO₂ > 70%.
- 2nd goal: Consider vasopressor, terlipressin or angiotensin.
- Add dobutamine or low dose dopamine if ScvO₂ < 70%.

Shock not reversed?

Persistent catecholamine resistant shock: Rule out and correct pericardial effusion, pneumothorax, & intraperitoneal pressure >12 mm Hg.
Use pulmonary artery catheter, PICCO monitor, FAPD & Doppler ultrasound to guide fluid, inotrope, vasopressor, vasodilator and hormonal therapies.
Goal C.I. > 3.3 & < 5.0 L/min/m²

Shock not reversed?

Refractory shock: ECMO (110 mL·kg⁻¹·min⁻¹) &/or CRRT (> 35 mL·kg⁻¹·hr⁻¹)
Stepwise management of hemodynamic support in infants and children

1. Recognize decreased mental status and perfusion. Begin high flow O₂ and establish IV/IO access.

2. **Initial resuscitation:**
   - Push boluses of 20 cc/kg isotonic saline or colloids up to and over 60 cc/kg until perfusion improves or unless rates or hypovolemia develop.
   - Correct hypoglycemia & hypocalcemia. Begin antibiotics.
   - If shock not reversed, consider ECMO (110 mL/kg/min) &/or CRRT (>35 mL/kg/hr).

3. **Fluid refractory shock:**
   - Begin inotrpe IV/IO.
   - Use atropine/ketamine IV/IM/MM to obtain central access & airway if needed.
   - Reverse cold shock by titrating central dopamine or, if resistant, titrate central epinephrine.
   - Reverse warm shock by titrating central norepinephrine.
   - If shock not reversed, consider ECMO (110 mL/kg/min) &/or CRRT (>35 mL/kg/hr).

4. **Catecholamine resistant shocks:**
   - Begin hydrocortisone if at risk for absolute adrenal insufficiency.

5. **Monitor CVP in PICU, maintain normal MAP + CVP & ScvO₂ > 70%**

- **Cold shock with normal blood pressure:**
  - 1st goals: Titrate epinephrine, ScvO₂ > 70%, Hgb > 10 g/dL.
  - 2nd goals: Add vasodilators & renal vasodilators, milrinone, nitroprusside, & others with volume loading, consider levosimendan.

- **Cold shock with low blood pressure:**
  - 1st goals: Titrate norepinephrine, ScvO₂ > 70%, Hgb > 10 g/dL.
  - 2nd goals: Add dobutamine if ScvO₂ < 70%, consider milrinone, enoximine, or levosimendan.

- **Warm shock with low blood pressure:**
  - 1st goals: Titrate norepinephrine, ScvO₂ > 70%.
  - 2nd goals: Consider vasopressin, terlipressin or angiotensin.
  - Add dobutamine or low dose epinephrine if ScvO₂ < 70%.

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

- **Shock not reversed?**
Figure 1: Stepwise management of hemodynamic support in infants and children

0-5 min

- 0 min
  
  Recognize decreased mental status and perfusion.
  
  Begin high flow O₂. Establish IV/IO access.
Initial resuscitation: Push boluses of 20 cc/kg isotonic saline or colloid up to & over 60 cc/kg until perfusion improves or unless rales or hepatomegaly develop. Correct hypoglycemia & hypocalcemia. **Begin antibiotics.**
**Fluid refractory shock:** Begin inotrope IV/IO.
use atropine/ketamine IV/IO/IM
to obtain central access & airway if needed.

*Reverse cold shock* by titrating central dopamine
or, if resistant, titrate central epinephrine

*Reverse warm shock* by titrating central norepinephrine.

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dose range:
dopamine up to 10 mcg/kg/min,
epinephrine 0.05 to 0.3 mcg/kg/min.
GLOBAL NEWBORN AND CHILD SEPSIS INITIATIVE

Bundles A-D
A Child mortality > 30 / 1,000
B Child mortality < 30 / 1,000
C Developing nation
D Developed nation

Sao Paolo reports reduction in mortality from 40% to 12%
In Septic Shock with ScvO₂
Guided to 70% with fluid, Inotropes, pRBCs

Thailand reports 60% drop in mortality with NP high flow O₂
for Pneumonia

Rotterdam and St Mary’s Report 1-2% mortality with Meningococcal Septic Shock
with 1st hour resuscitation and transport (was 20-22%)

Kenya reports 4% mortality with Malaria,
Vietnam reports 0-1% mortality with Dengue Shock
with IV fluid resuscitation (was 24-60%)

Gandchiroli, India reduced neonatal mortality from 16% to 2% with HCW + IM Abx

Immunizations, Potable Water, Nutrition
Zinc, Vitamin A
IM Antibiotics available to All through HCW

1st Hr IV Antibiotics Fluid Resuscitation
Inotrope infusion
Mechanical Ventilation Available to All (PICU)

1st Hr IV Fluids and Antibiotics
O₂ / np CPAP
Available in Emergency Clinic

Extra Corporeal Support TRANSPORT

A Child mortality > 30 / 1,000
B Child mortality < 30 / 1,000
C Developing nation
D Developed nation
AIMS

• We sought to determine whether the GPSI which contains 21 shared elements for Group C (Developing) and Group D (Developed) industrialized nations could be simplified to 3 element bundles for
  • ED management
  • PICU Management
  • Shock Reversal
New Three Element Bundles (GROUPS C + D)
ED 1st hour Management

1) Reverse shock and restore capillary refill < 2 seconds with normal blood pressure
2) Administer antibiotics
3) Give D10 with Na containing maintenance fluid to prevent hypoglycemia

Rationale – Derived from analysis of GPSI vanguard (Group C n = 147; Group D n = 365)
Bundle compliance associated with improved survival OR 3.272 [95% CI 1.814-5.903]
Shock Reversal Checklist

• Fluid resuscitation in 20 ml/kg boluses up to 60 ml/kg if patient does NOT have signs of fluid overload eg. hepatomegaly, rales cardiomegaly, or severe chronic anemia

• Peripheral epinephrine for fluid refractory shock

• Transition to central epinephrine for cold shock and central norepinephrine for warm shock

Restored NL MAP-CVP and SCVO2 > 70% & Restored CR < 2 secs, NL BP, NL MAP-CVP, and SCVO2 > 70% & Restored NL MAP-CVP and SCVO2 > 70%
New Three Element Bundles (Groups C + D)  
PICU Management

1) Reverse shock: Maintain normal MAP-CVP and SCVO2 > 70%
2) Confirm Source Control: Ensure appropriate (sensitive) antibiotics administered and if applicable surgical nidus removal
3) Attain Effective Tidal Volume 6-8 mL/kg if mechanically ventilated for ARDS

Rationale – Derived from GPSI vanguard (Group C n = 147; Group D n = 365)  
Bundle compliance associated with improved survival OR 2.288 [95% CI 1.427-3.669]
New Three Element Bundles GROUP B
Endemic Malaria Belt

1) Establish intravenous access and begin maintenance intravenous fluids containing Dextrose and Sodium

2) Treat with anti-malarials and antibiotics

3) Administer a blood transfusion if Hgb ≤ 5 g/dL

Rationale: FEAST trial demonstrated a mortality of 7.26 % (95% CI 5.78-9.03%) compared to 10.57% (95% CI 8.78-12.58%) with bolus.
New Three Element Bundles GROUP B
Endemic Dengue Belt

1) Establish intravenous access and begin fluid bolus with physiologic intravenous solution such as Ringers or Hartmanns.
2) Titrate to normalizing hemoconcentration or pulse pressure
3) Begin High Flow nasal cannula oxygen or NPCPAP for acute respiratory distress

Rationale: Three randomized trials showed reduction to 0.19 % mortality (95% CI < 0.06 – 1.08 %) in infants and children with Dengue Shock
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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 Bellomo*²

Crit Care 2011
Key Points in Pediatric Sepsis and Septic Shock

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WHA endorsement will achieve:

• Sepsis linked tightly to infection prevention & AMR campaigns
• Rising public awareness in Member States
• Improved access to basic aspects of care
• Increasing number of national Registries
• Greater funding allocated to research and improvement
• More data, more funds, more TALKING SEPSIS.

http://www.world-sepsis-day.org
World Sepsis Day: 13 September 2014

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