Infants and Children and fevers

Phil Bernard, MD

Case scenario #1
- 2 week old presents to your office with fever to 101.5°F during a well-child check. MOC reports he has been asymptomatic. Feeding well, not fussy. GBS status negative.
  - HR 150
  - RR 40
  - BP not-obtained
  - Sats 95%

Questions:
- Chance that this patient is actually sick?
- Most likely organisms?
- What do I do with him?

Minimal changes since....

Why is fever in infants a big deal?
- Toxic kids – later
- Non-toxic appearance
  - 0-28 days 3% SBI 1% meningitis
  - 29-60 days 1.4% SBI 0.4% meningitis
- T-cell lymphocytes non-functional
  - B-cell lymphocytes can't produce IgG's
  - IgG levels rise greatly over the first few months of life

SBI (serious bacterial infection)
- Meningitis
- Bacteremia
- Urinary tract infections
What is a fever?

- 1-90 days
  - RECTAL temperature > 100.4 F (or 38 C)
  - Overbundling is real - recheck in 15 minutes
  - If Mom reports rectal temperature - believe it.
  - 92% children hospitalized had subsequent fever

- 90 days - 3 years
  - > 102.2F (39 C)

Etiology of fever

- Viral
  - RSV
  - Influenza
  - Enterovirus
  - HSV (more later)

epidemiology

- Bacterial Etiology
  - Most common organisms
    - Streptococcus pneumoniae 6%
    - Neisseria meningitidis 15%
    - Haemophilus influenza type B 2%
    - Staphylococcus aureus 24%
    - Staphylococcus epidermidis 19%
    - Fungal infections 15%

Textbooks are old....

Prevnar

Invasive Pneumococcal Disease Rates by Age and Year
Children <5 Years, ABCs, 1996-2003

Various protocols

- Boston
- Rochester
- Philadelphia
**Boston**
- Peripheral white blood cell (WBC) count less than 20,000/microL
- CSF with WBC <10/microL
- UA <10 WBC per high-powered field
- No infiltrate on chest radiograph if one was obtained

**Philadelphia**
- WBC <15,000/microL
- Band-neutrophil ratio <0.2
- UA <10 WBC/hpf and a negative urine Gram stain
- CSF <8 WBC/microL and a negative CSF Gram stain
- Chest radiograph lacking an infiltrate if one was obtained
- Stool without blood and few or no WBCs on the smear

**Rochester**
- WBC 5,000 to 15,000/microL with an absolute band count <1,500/microL
- Urinalysis with <10 WBC/hpf and no bacteria seen
- Stool with <5 WBC/hpf if obtained

**Since HIB immunization**

Bacterial

- Neonatal
  - Group B strep
  - Listeria monocytogenes
  - E. Coli + GNR's
  - Tx: Ampicillin + gentamicin vs. cefotaxime

- Pediatric
  - Staphylococcus
  - Nisseria meningitidis
  - Streptococcus pneumoniae
  - Tx: 3rd generation cephalosporin + Vancomycin (if they are SICK)

Common Pitfalls

- Get a MANUAL DIFF
- < 1 month old = admission
- If you choose to treat with antibiotics
  - Lumbar puncture if < 90 days
- Reflex U/A on any child < 2 years
- Don't consider otitis media source of fever in neonate

Questions:

- Chance that this patient is actually sick? 3%
- Most likely organisms?
  - Hasn't changed for infants
- What do I do with him?
  - Admit him, pan-culture including Lumbar puncture
  - Antibiotics
  - If WBC is low, fever is low, consider observation only

Case scenario #2

- 2 week old presents to the E.R. with fever to 101.5 F during a well-child check. MOC reports he has been feeding poorly for 24 hours and increasingly fussy.
  - HR 185
  - RR 70
  - BP not-obtained
  - Sats unobtainable
  - Skin cold, thready pulses

Questions:

- Chance that this patient is actually sick? 100%
- Chance that he will die?
- Most likely causes
- What do I do with him?

Defining Septic Shock

Definitions

| SIRS (Systemic Inflammatory Response Syndrome) | At least 2 of 4 (including fever or WBC, tachypnea, tachycardia, hypotension, abnormal mental status) |
| Infection | suspected or proven infection or syndrome associated with high probability of infection |
| Sepsis | SIRS + infection |
| Severe Sepsis | Sepsis plus CV dysfunction or ARDS, etc. or two or more other organ dysfunctions |
| Septic Shock | Sepsis and CV dysfunction |

Offenbacher et al. Pediatric Cases March 2009: © 2010
Definitions
• Warm shock - MS, perfusion, flash cap refill with bounding pulses
• Cold shock - MS, perfusion, cap refill > 3 sec and mottled cool extremities
• Fluid-refractory dopamine-resistant shock - shock despite > 60 cc/kg over 1 hr and dopamine to 10 mcg/kg/min

Sepsis in clinical Practice
• 2000 People/day develop Sepsis
  - Mortality is ~ 30%
• Major category for admission to a Pediatric Intensive Care Unit
  - 11% of our patients admitted primary diagnosis

big deal ??

Table 1. Leading causes of death in U.S. children in 1995

<table>
<thead>
<tr>
<th>Cause</th>
<th>Nb of Deaths</th>
<th>Children 1-4 yr (4)</th>
<th>Nb of Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital anomalies</td>
<td>1,329</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Prematurity</td>
<td>1,329</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sudden infant death, unspecified</td>
<td>2,398</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cancer</td>
<td>1,370</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory distress syndrome</td>
<td>1,509</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>1,494</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Birth defects</td>
<td>1,265</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6 Complications of pregnancy</td>
<td>1,298</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7 Accidents</td>
<td>787</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Number of deaths for some causes are national estimates; numbers for all other causes are from the National Center for Vital Statistics data.

Watson and Carcillo, 2005

Sepsis in Children
• 5-30% of children with sepsis also have shock
• 9-18% mortality
• Confirmed bacteria in ~ 75% of PICU patients
Outcomes

Why are the outcomes changing?

Failed drug trials
- Monoclonal antibody to LPS
- Anti - Tumour-necrosis-factor alpha (TNF-α)
- Antithrombin III (ATIII)
- Tissue-factor-pathway inhibitor (TFPI)

Traditional view of sepsis

Why do Clinical trials fail?

Experimental
- Single genetic profile
- Blood borne
- Short-term survival
- No mechanical ventilation
- Healthy

Reality
- Multiple polymorphisms
- Often with tissue infiltration - Over 1/3rd with cultures negative
- 30-day mortality
- Long-term mech vent injury
- LOTS OF CO-MORBIDITIES

Drotrecogin Alfa (Xigris)

- Activated Protein C
- Approved by FDA for severe sepsis in adults in Nov. 2001 following PROWESS study
- Mortality decreased from 31% to 26%
- Need to treat = 1 in 16 patients
- Specifically not approved for Pediatric use

RESOLVE
(REsearching severe Sepsis and Organ dysfunction in children: a global perspective)

- Largest Pediatric trial ever in critically ill children
- Patients enrolled between Nov 2002 and April 2005
- Ages newborn to 17 years
- Activated Protein C versus controls

RESOLVE-results
- 477 patients enrolled
- Study suspended after second planned interim analysis
What did we learn?

- **Peds**
  - Severe hypovolemia
  - Low cardiac output (hypodynamic)
  - Most have High SVR
- **Adults**
  - Less responsive to fluids
  - CO maintained via tachycardia and ventricular dilation
  - Circulatory collapse

Children are NOT small adults

- More volume
- More inotropy
- More responsive to ECMO

Kids Really are Different

<table>
<thead>
<tr>
<th>Adult</th>
<th>Pediatric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence 751,000 cases/yr</td>
<td>Incidence 42,000 cases/yr</td>
</tr>
<tr>
<td>mortality 28.6%</td>
<td>mortality 10.3%</td>
</tr>
</tbody>
</table>


Why such an improvement?

- Etiology is changing - immunizations
- Care is improving?

Outcomes

- Evidence based medicine for Pediatric Critical Care
  - Very few good trials available
  - Best Guess strategy
  - Supportive Care
**Bacterial**
- Neonatal
  - Group B strep
  - Listeria monocytogenes
  - E. Coli + GNR's
- Pediatric
  - Staphylococcus
  - Niesseria meningitidis
  - Streptococcus pneumoniae
- Tx: Ampicillin + gentamicin vs. cefotaxime

**Viral sepsis**
- Herpes Simplex Virus
  - Systemic
    - Not subtle - Fulminant and overwhelming
    - Skin lesions in only 1/3 of patients
    - Thrombocytopenia, Inc. LFT’s, lymphocytic meningitis
  - Meningoencephalitis
    - Must have focal neurologic signs
    - Bloody tap DOES NOT EQUAL HSV
- Enterovirus
  - Myocarditis

**Herpes Simplex**
- Add Acyclovir only in cases with severe systemic infection, skin manifestations, or seizures
- KCH - rate 1.3% of patients given Acyclovir had HSV; all meningoencephalitis cases had skin lesions or generalized seizures
- Clinical question: Are you concerned about disseminated herpes simplex vs meningoencephalitis?

**Fungal**
- Candida (17% survival)
  - Immunocompromised
- Treatment
  - Fluconazole
  - Amphotericin B

**Non infectious issues**

**Congenital heart disease**
- 8 in 1000 live births (1/3 are cyanotic)
- Ductal-dependent lesions
- Answer: prostaglandins
Non-accidental Trauma
- Must be suspected in order to be recognized
- On average, a child presents to an ER THREE times prior to the dx being made
- Risk factors include:
  - Young, single parents
  - Lower education
  - EthOH/drug abuse
  - prematurity

Questions:
- Chance that this patient is actually sick? 100%
- Chance that he will die?
  - Relatively Low if from bacterial sepsis
  - 50% if from disseminated HSV
- Most likely causes
- What do I do with him?...

What do I do with him?
- Ampicillin
- Gentamicin
- Acyclovir
- Prostaglandin 1 (PGE1)
- PALS

Updates to PALS Guidelines

Septic Shock

Fluids

First hour: Rush repeated 20 mL/kg boluses of lactated Ringer's up to 3, 4, or more based on patient response.
- Additional therapies:
  - Correct hypoglycemia and hyperglycemia
  - Administer inhaled antipseudomonal (PSE)
  - Consider ordering DSAI vasopressor drip and stress-low hydrocortisone
Early Reversal of Pediatric-Neonatal Septic Shock by Community Physicians Is Associated With Improved Outcome

Yong Y. Han, Joseph A. Carcillo, Michelle A. Dragotta, Debra M. Bills, R. Scott Han et al

91 patients

65 survivors

26 nonsurvivors

Prism score 13

Prism score 26

Patient survival vs whether shock was reversed

Patient survival vs resuscitation a/s PALS

63

64

Does it matter?

• Every hour patient went without resuscitation increased mortality risk by 100%
• Every hour patient went without transfer increased mortality risk by 50%

What’s New in PALS
Get an Airway

- Don't necessarily intubate in the field (esp. if transport time is short)
- Landmark study by Gausche showed intubation in field trended towards worsening outcomes
- Success related to:
  - the length of training,
  - Supervised operating room and field experience
  - Rapid sequence intubation (RSI)

Etomidate

- NOT recommended

- Instead
  - Ketamine
  - Atropine

Cuffed ETTs

- Extubation Rates the same
- Post-extubation stridor the same
- Caveat: keep cuff pressure < 20 mmHg
- New rule: cuff size = (age in years/4) + 3

LEAN

- ETT route is route of last resort
- ? Accurate doses
- Vasopressin effective via ETT (but at what dose?)
  - should we be even using it kids?
- Epinephrine via ETT may give more β effects and therefore may increase myocardial ischemia

Compression-only CPR

- Bystanders Only
- Adult guidelines
- NOT FOR
  - Pediatrics
  - EMS providers
  - Arrest from non-cardiac origin

Shockable Rhythms

- AED’s are now recommended for children 1 year and up
- Provide CPR before and immediately after shocking
- NO MORE SHOCK. SHOCK. SHOCK. Epi. SHOCK

LEARN

- Never pause CPR
- Give 1 shock
- Minimum: 40 J/kg
- AED > 1 year of age
- Resumes CPR immediately
  - EPI: 0.02 mg/kg
  - (1/1000: 0.1 mg/kg)
  - (1/100: 0.1 mg/kg)
  - (1/10: 0.1 mg/kg)
  - (1/1: 0.1 mg/kg)
  - (1:1 0.1 mg/kg)
  - Repeat every 3 to 5 minutes
Epinephrine

- High dose epi is NOT recommended
- May be useful in rare circumstances (like β-blocker ingestion)

Cooling

- Adult studies: cooling may improve outcomes
- Neonatal studies: cooling may improve outcomes
- Pediatric studies???
  - Consider cooling to 32-34°C for patients who remain comatose following cardiac arrest

Advanced Support

- Nitric oxide
- Continuous renal replacement therapy
- Extracorporeal Membrane Oxygenation

Conclusion

- DESPITE RUMOURS TO THE CONTRARY--
  - MOST OF OUR KIDS GO BACK TO THEIR HOMES!
- Golden Hour of Sepsis
- Multi-disciplinary Multi-tiered approach