Best Practice in Pediatric Blood Culturing

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What do we want?
- High sensitivity
- High specificity
- Rapid detection

Best Practice Questions
- What is the right volume to draw?
- Are anaerobic cultures necessary?
- Rapid diagnostics for positive blood cultures.

Challenges in Pediatric Blood Cultures
- Children are smaller and don’t have as much blood to give.
- Children are difficult draws.
- Perception that children have different courses of blood stream infection.

Have your heard this before?
“Kids have more bacteria in their blood than adults”
“You don’t need as much volume for a pediatric blood culture”

- Limitations of the literature
  - Many great studies done, not so many in the past 20 years.
  - Literature dominated by *H. influenza* and *S. pneumoniae*
  - Patient populations have changed significantly in the past several decades

Concentration of organism in pediatric blood stream infection
- **H. influenza**
  - avg 130 cfu/ml for all cases
  - >100 or 1,000 cfu/ml for those children with invasive disease
- **S. pneumoniae**
  - avg 8 cfu/ml for all cases
  - 18 of 24 patients had <15 cfu/ml
- In both cases those patient with invasive disease had higher bacterial loads.

Pediatric Magnitude of Bacteremia
- 79 previously healthy patients – *H. influenza, S. pneumoniae, N. meningitidis*

<table>
<thead>
<tr>
<th>Infection (%)</th>
<th>CFU &lt;50 (%)</th>
<th>CFU 50-999 (%)</th>
<th>CFU &gt;1,000 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. pneumoniae</em> (25) – URI/Otitis</td>
<td>20 (80)</td>
<td>5 (20)</td>
<td>0</td>
</tr>
<tr>
<td><em>S. pneumoniae</em> (4) – Meningitis</td>
<td>0</td>
<td>2 (50)</td>
<td>2 (50)</td>
</tr>
<tr>
<td><em>N. meningitidis</em> (6) – Sepsis</td>
<td>0</td>
<td>3 (50)</td>
<td>3 (50)</td>
</tr>
<tr>
<td><em>N. meningitidis</em> (6) – Meningitis</td>
<td>1 (17)</td>
<td>4 (66)</td>
<td>1 (17)</td>
</tr>
</tbody>
</table>

Bell et al. 1985. Pediatrics
Bacterial Load in Gram negative Neonatal Sepsis

- 30 episodes of neonatal sepsis (35 positive cx)
- 29 male
- Majority premature
- 1.5 ml cultures
- Only E. coli included

RESULTS
- 50% > 50 cfu/ml
- 37% > 1,000 cfu/ml
- 73% mortality rate in patients with >1,000 cfu/ml

<table>
<thead>
<tr>
<th>CFU/ml</th>
<th># cultures</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>8</td>
<td>23</td>
</tr>
<tr>
<td>5-49</td>
<td>11</td>
<td>31</td>
</tr>
<tr>
<td>50-199</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>200-1,000</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>&gt;1,000</td>
<td>11</td>
<td>31</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
<td></td>
</tr>
</tbody>
</table>


What about Adults?

- Endocarditis studies
  - Weiss and Ottenberg. J Infect Dis. 1932
  - Mollen et al. Amer Heart J. 1947

<table>
<thead>
<tr>
<th>CFU/ml</th>
<th>Streptococci Endocarditis (%)</th>
<th>Staphylococci Endocarditis (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-10</td>
<td>24</td>
<td>41</td>
<td>24</td>
</tr>
<tr>
<td>11-100</td>
<td>59</td>
<td>47</td>
<td>59</td>
</tr>
<tr>
<td>&gt;100</td>
<td>17</td>
<td>12</td>
<td>17</td>
</tr>
</tbody>
</table>

Weinert et al. 1967. JAMA

What about Adults?

- Genitourinary Tract-Associated bacteremia
  - Other studies
  - Kregor et al. 1980. AM J Med

<table>
<thead>
<tr>
<th>Organism</th>
<th># of Positive Cultures</th>
<th>AVG cfu/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterococcus</td>
<td>10</td>
<td>1.4</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>6</td>
<td>84.3</td>
</tr>
<tr>
<td>VGS</td>
<td>2</td>
<td>0.8</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>6</td>
<td>10.3</td>
</tr>
<tr>
<td>E. coli</td>
<td>3</td>
<td>8.2</td>
</tr>
<tr>
<td>S. pyogenes</td>
<td>2</td>
<td>0.8</td>
</tr>
<tr>
<td>S. aureus</td>
<td>2</td>
<td>7.6</td>
</tr>
</tbody>
</table>

Sullivan et al. 1972. Applied Microbiology

Why is a comparison between children and adult bacteremia important?

- We have a pretty good idea of what it takes to do a proper blood culture for an adult.
Why is a comparison between children and adult bacteremia important?

• We have a pretty good idea of what it takes to do a proper blood culture for an adult.
  – Volume 20-30 ml
  – Number 2-4 cultures

• What about in pediatrics?
  – Unknown

How much blood should be drawn from a child?

• Cumitech 1C estimates that it is safe to draw 4-5% of patients blood for culture.
  – 6 ml = 80% sensitivity.
  – 2 ml = 50% sensitivity.

What is safe?

Blood Culture Volume at CMC

• Data from PICU
  – Average volume per bottle 0.77 ml
  – Average volume per culture 1.63 ml
  – Average volume per culture event 3.26 ml

• Average age of patient 13.4 years old.
• Average weight 47 kg (103 lbs.)

At 47 kg:
  Max Draw (24 hr) = 90 ml
  Recommended culture volume = 40-60

What is the normal blood culture practice in our hospital?

• Children’s Medical Center Dallas
  – ~550 beds
  – >500,000 annual visits

• Laboratory
  – ~150,000 annual microbiology tests
  – >20,000 blood cultures
Conclusion

Volume is critical for optimizing blood culture sensitivity in BOTH pediatrics and adults.

CAP Requirement:

**MIC.22640**

- **PHASE 1**

  RECOMMENDATIONS FOR THE APPROPRIATE VOLUME OF BLOOD PER CULTURE ARE AVAILABLE TO THOSE COLLECTING THE SPECIMENS

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How do you satisfy this requirement?

**Bottle Weight Variation**

- **BioMerieux Peds Bottle**
  - Varies up to 0.3 grams within and between lots
- **VersaTrek redox 1**
  - Varies by up to 1 gram within a lot
- **Bactec**
  - Varies by less than a gram

**Options for reporting**

- Selective weighing of bottles.
  - Weigh before distributing to floors
  - Weigh often and use a range calculation
  - Weigh bottles for patient care and report a range

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What is the value of anaerobic cultures?

- Need to optimize use of limited blood volume.
- What is the true need for anaerobic cultures?
- Can we predict patients who are at high risk for anaerobic bacteremia?
Anaerobic Blood Cultures in Pediatric Emergency Room Patients

Freedman et al. 2004. Ped Emer Care
- 2,675 paired cultures (595 +)
- 31 (11.2%) were positive in anaerobic medium only.
- No obligate anaerobes were isolated.

Table 1: Number of Clinically Significant Organisms Isolated

| Organism           | Aerobic | Anaerobic | Anaerobic but Obligates
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteroides gracilis</td>
<td>9</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Bacteroides fragilis</td>
<td>10</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Peptostreptococcus</td>
<td>17</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Peptostreptococcus</td>
<td>6</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Peptostreptococcus</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Peptostreptococcus</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Peptostreptococcus</td>
<td>1</td>
<td>1</td>
<td>0</td>
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<td>0</td>
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<td>Peptostreptococcus</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Value of Routine Anaerobic Cultures in Pediatrics

Zaldi et al. 1995. Pediatrics
- 9,360 paired cultures (723 +)
- 11.6% grew in anaerobic bottle only
- 940 total isolates
  - 29 were strict anaerobes
  - Only 13 considered significant
  - From anaerobic bottle only
- From 6 patients
- 5 of 6 had risk factors that would predict anaerobic bacteremia
- The sixth was actually from an autopsy blood culture
- Wilson et al. showed that 4% of autopsy blood cultures had anaerobes and none of them appeared to be significant

Should Children Have Routine Anaerobic Blood Cultures?

Zaldi et al. 1995. Pediatrics
- Some would argue YES. That they are useful in certain patient populations
  1. Patients with abdominal signs and symptoms
  2. Debilitated patients with sacral decubitus ulcers or cellulitis
  3. Patients with poor dentition, severe oral mucositis, or chronic sinusitis
  4. Patients with neutropenia who are receiving high-dose corticosteroid therapy, which may mask abdominal signs and symptoms
  5. Patients with sickle-cell disease
  6. Infants born to mothers with prolonged rupture of membranes or chorioamnionitis
  7. Patients with suspected bacteremia after human bite wounds or crushing trauma

Should Children Have Routine Anaerobic Blood Cultures?

Dunne et al. 1994. PDI
- Some would argue NO. That anaerobic bacteremia is rare in pediatrics and that blood would be better used in an aerobic bottle.
  - 116 clinically relevant positive blood cultures from paired bottles
  - 1 anaerobe isolated
  - Found no difference between yield of aero/aero pairs and aero/anaero pairs
  - Aero/aero identified more episodes of bacteremia

Final Thoughts on Pediatric Anaerobic Cultures

- Pediatric blood volume is limited
- Certain patient populations are at higher risk for anaerobic BSI
- True anaerobic BSI is rare (<5% of pediatric BSI)
- Isn’t it better to optimize for isolation of staphylococci, non-fermenters and candida?
  - In adults Morris et al. showed that they could increase yield of blood cultures by 6% by prioritizing aerobic cultures in lieu of anaerobic cultures
  - Anaerobes have predictable susceptibility pattern which is likely to be covered by empiric treatments

The Need For Improving Blood Culture Diagnostics

Munson et al. 2003. JCM
- Figure 1: Percentage of all antimicrobial interventions covering only the enterobacteriaceae, enterococci, enterococcus, coagulase
  - 60%
  - 30%
  - 15%
Technology for Blood Culture Diagnostics

These Technologies Can Make a Difference

Rapid Identification of Yeast is Important
- Antifungals are toxic drugs
- Antifungals are expensive
  - Ambisome (Amphotericin) $\ldots$
  - Caspofungin $\ldots$
  - Fluconazole $\ldots$
- Organism identification very important for guiding therapy
  - \textit{C. albicans} = Fluconazole
  - Everything else = Ambisome or Caspofungin until susceptibility known

A common clinical dilemma...
1. One blood culture positive.
2. Lab reports Gram positive cocci in clusters.
3. Now what?

Is it a contaminant?..... No antibiotics...Discharge?
Is it \textit{S. aureus}?.......... Antibiotics...ICU?
Is it MRSA?................. Vancomycin.

Impact beyond the Laboratory

- OSU study using PCR GeneXpert to detect and differentiate MRSA and MSSA
- PCR resulted in a significant reduction in ICU and overall hospital costs.
  - 1.7 day shorter time to change from vancomycin to cefazolin or nafcillin.
  - Shortened length of stay by 6 days

PNA-FISH Clinical Impact on Yeast Identification

**Results**
- **Identification**
  - \textit{C. albicans} $\times$ 34.5 hr improved turn-around-time
  - Non-\textit{C. albicans} $\times$ 51.3 hr improved turn-around-time
- **Antifungal cost**
  - \textit{C. albicans} $\times$ $1,978$ decrease cost/patient
  - Non-\textit{C. albicans} $\times$ $1,680$ decrease cost/patient
- No difference in mortality

Forrest et al. 2006. JCM

Bauer et al. 2010. CID
The next step – Multiplex panels

Conclusions about Pediatric Blood Cultures

• Children appear to have higher magnitudes of bacteremia in some cases….but not all
• Sensitivity improves with volume.
  – 6 ml = 80% sensitivity
• Reporting blood culture volumes may be an opportunity to improve practice in pediatric blood cultures.
• Decide for yourself about the utility of anaerobic cultures
• New technology rapidly emerging to improve blood culture diagnostics

Thank you for your attention!

Outpatient Blood Cultures: Time to positivity

Pathogens

• Avg 18.4 hours
  – 87% Positive by 24 hours
  – 92% Positive by 36 hours
  – 99.7% Positive by 72 hours

Outpatient Blood Cultures: Time to positivity

Contaminants

• Avg 32.8 hours  P <0.0001
• Children <1 more likely to have contaminated cultures.

Organism (N) | Avg Time (hr) | 95% CI (hr)
---|---|---
CONS (219) | 27 | 23-31
S. pyogenes (23) | 20 | 17-23
SPN (145) | 14 | 13-14
VGS (44) | 22 | 19-24
GAS (10) | 25 | 19-33
GBS (13) | 12 | 11-12

Gram + Pathogen 15.5  P < 0.0001
Gram + Contaminant 25.0