Objectives

- Review the current burden of disease for viral bronchiolitis in the United States
- Review the current risk of bacteremia, urinary tract infection and meningitis in febrile infants in the post-pneumococcal vaccine era
- Review the available literature on the risk of concomitant serious bacterial infection in the setting of viral bronchiolitis in young infants

The Burden of Disease - RSV

- An estimated 2.1 million children under 5 years of age require medical attention due to RSV yearly
  - About 57,000 hospitalizations per year
  - About 500,000 emergency room visits per year
  - About 1.5 million outpatient visits


Risk of Concomitant Serious Bacterial Illness in Infants with Viral Bronchiolitis

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The enemy...........

Envelope Spikes
G [836]
F [814]

Inner Envelope
M [256]
M2 [194]

Nucleocapsid
N [391]
P [241]
L [nd]

Nonstructural
NS1 [124]
NS2 [139]

Surface of Infected Cells
SN [64]

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Burden of Disease - Bronchiolitis

<table>
<thead>
<tr>
<th>Diagnosis (ICD-9-CM Code)</th>
<th>Infant ID Hospitalizations</th>
<th>All-Cause Infant Hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± S.E.</td>
<td>Mean ± S.E.</td>
</tr>
<tr>
<td>RSV bronchiolitis (486.12)</td>
<td>1 35.5 ± 6.5</td>
<td>2 36.4 ± 2.2</td>
</tr>
<tr>
<td>Acute bronchiolitis, organism not spec (466.99)</td>
<td>2 30.9 ± 6.5</td>
<td>3 37.2 ± 6.5</td>
</tr>
<tr>
<td>Pneumonia, organism not specified (466.99)</td>
<td>3 31.2 ± 6.5</td>
<td>7 38.6 ± 6.5</td>
</tr>
<tr>
<td>Meningitis (326.9)</td>
<td>4 39.6 ± 6.5</td>
<td>1 45.9 ± 6.5</td>
</tr>
<tr>
<td>Pneumonia, nec (466.9)</td>
<td>5 35.9 ± 6.5</td>
<td>0 27.1 ± 6.5</td>
</tr>
<tr>
<td>Pneumonia, nec (466.9)</td>
<td>6 39.9 ± 6.5</td>
<td>7 48.8 ± 6.5</td>
</tr>
<tr>
<td>Tracheitis (493.0)</td>
<td>7 38.5 ± 6.5</td>
<td>4 54.8 ± 6.5</td>
</tr>
<tr>
<td>Tracheobronchitis (493.0)</td>
<td>8 36.4 ± 6.5</td>
<td>2 49.5 ± 6.5</td>
</tr>
<tr>
<td>Infection and/or infection of respiratory system (466.96)</td>
<td>9 35.5 ± 6.5</td>
<td>8 31.5 ± 6.5</td>
</tr>
<tr>
<td>Nonspecified lower respiratory infections (466.9)</td>
<td>10 40.8 ± 6.5</td>
<td>7 45.7 ± 6.5</td>
</tr>
<tr>
<td>Pneumonia, nec (466.9)</td>
<td>11 39.3 ± 6.5</td>
<td>7 45.7 ± 6.5</td>
</tr>
<tr>
<td>Pneumonia, nec (466.9)</td>
<td>12 38.4 ± 6.5</td>
<td>1 42.1 ± 6.5</td>
</tr>
<tr>
<td>Bronchitis (467.9)</td>
<td>13 36.4 ± 6.5</td>
<td>3 44.0 ± 6.5</td>
</tr>
</tbody>
</table>

Conducted using American Academy of Pediatrics

FIGURE 3 Infant ID hospitalizations in the United States in 2003 according to diagnostic group

Burden of Disease - SBI

- 1993 Practice Guideline for fever without localizing signs by Larry Baraff
- 1990 – universal Haemophilus influenzae type B vaccination (Hib)
- 2000 – universal Pneumococcal conjugate vaccine (PCV7)
- Have we been able to alter our clinical practice guidelines based on the impact of these two vaccinations?

Meningitis

- Again, consensus growing that risk of meningitis in 3 – 36 months age group has declined to the degree that routine LP may not be necessary in most cases. Rate= <1%
- Under 30d the rate remains above 1% (Caviness, J Peds Aug 2008)
- Baker and Bell (Archives 1999) rate was 1.6%
- Schwartz (ADC 2009) rate was 1.1% or 3.4% depending

Finally – the question at hand

- What is the conditional probability of SBI given bronchiolitis (in the youngest infants, least likely to be protected by newer vaccinations)?
- Or, are these actually dependent variables? Does RSV increase the risk for SBI and, if so, in what settings?
- CB Hall (J Peds 1988) first suggested that risk of SBI in RSV infection was low
- However, people continue to publish 20 to 40% rates of bacterial co-infection with RSV generally tracheal aspirates or acute and convalescent titeres for pneumococcus, and seasonal peaks of invasive pneumococcal disease have a strong correlation with RSV seasons in multiple geographic locations

Bacteremia

- Consensus growing that the risk of occult bacteremia in infants over 2 to 3 months of age does not merit the use of routine blood cultures in well-appearing children (rates from 0.25% – 0.8% with contaminant rates of 2% – 4%)
- But what about under 2-3 months? Different pathogens, unvaccinated......
  - Baker and Bell (1999) – bacteremia <28days = 3.1%
  - PROS febrile infant study (JAMA 2004), practice-based evaluation of fever in infants under 3 months, bacteremia found in 1.8% of infants (2.4% of those tested)
  - Few recent studies of the under 28d crowd: Kadish (2000) 3.2%; Schwartz (2009) 1.6%

Pooled Prevalence of UTI in Infants by Age and Sex

<table>
<thead>
<tr>
<th>Table 1. Pooled Prevalence of UTI in Infants by Age and Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>No. of studies</td>
</tr>
<tr>
<td>Prevalence of UTI</td>
</tr>
<tr>
<td>% (95% CI)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; UTI, urinary tract infection.


JAMA

Systematic Review

- Studies addressing the question of SBI in infants with either clinical bronchiolitis or RSV disease providing both culture results by age and total number of cultures drawn and enrolling all comers
  - Fever
  - Prospective or retrospective
  - Site of study (ED, clinic, inpatient)
  - Length of follow-up
  - Exclusion criteria
Results

- Using our most inclusive sample:
  - Rate of UTI = 5% (CI 4.1% - 6.3%)
  - Rate of Bacteremia = 0.3% (CI 0.1% - 0.8%)
  - Rate of Meningitis = 0 (CI 0.0001 - 0.4%)
**Evidence for actual UTI?**

- Usually lacking, i.e. no evidence of inflammation on urinalysis.

- When available there are specific statements to the effect of “over-calling” so as not to appear to underestimate the incidence of SBI, i.e. what do you do with a urine cx with 30,000 cfu of viridans strep?

- For example, Melendez provided UA and culture results and 5 of 6 positive cultures had 0 WBC per hpf.

**Other Factors?**

<table>
<thead>
<tr>
<th>UTI</th>
<th>Febrile</th>
<th>Afebrile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liebelt</td>
<td>0/35 (0)</td>
<td>0/13 (0)</td>
</tr>
<tr>
<td>Oray-Schro</td>
<td>5/69 (7.2%)</td>
<td>0/16 (6.3%)</td>
</tr>
<tr>
<td>Purcell 2007</td>
<td>20/175 (11.4%)</td>
<td>9/65 (9.2%)</td>
</tr>
</tbody>
</table>

**Take home?**

- It’s probably not as simple as a math problem using probabilities but its getting closer.

- No good evidence that RSV increases the risk of concomitant SBI at the time of presentation (i.e. ED, on admit), rather there is evidence that SBI and bronchiolitis function as independent probabilities and therefore most patients will have one disease and do not require a strategy of universal screening as in fever without source. It may be more important to have clinical bronchiolitis than documented RSV.

- The idea that UTI co-travels is likely to be a result of overuse of screening urine cultures and finding asymptomatic bacteruria.

- No doubt that during the course of illness, secondary bacterial infection occurs in certain settings: mechanical ventilation, re-occurrence of fever late in the illness, clinical deteriorations, etc but these events should not guide a primary strategy of screening for SBI on presentation but should inform patient specific evaluation strategies.

Thanks and recognition go to Ami Waters, MS4 and Vanessa Hill, MD who did part of the work that went into this analysis.