Community Acquired Pneumonia in Children
An Evidence Based Approach To Evaluation and Management

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Disclosure
I do not have any disclosures or conflicts of interest to reveal

Outline
• Background
• Etiology
• Diagnosis
• Management

Background
• Definition - Pneumonia
  - Inflammation of one or both lungs, usually caused by infection from a bacterium or virus or, less commonly, by a chemical or physical irritant
• WHO Radiographic Definition of Pneumonia
  - A dense opacity that may be a fluffy consolidation of a portion or whole of a lobe or of the entire lung, often containing air-bronchograms and sometimes associated with pleural effusion

World Health Organization Pneumonia Vaccine Trial Investigators’ Group, WHO, 2001

Background
• Community Acquired Pneumonia (CAP)
  - The presence of signs and symptoms of pneumonia in a previously healthy child, due to an infection of the pulmonary parenchyma that has been acquired outside of the hospital.
  - < 7 days from hospital (CAP Guidelines, 1998)
• Hospital Acquired Pneumonia (HAP)
  - 48-72 hours from stay in hospital
• Healthcare-Associated Pneumonia (HCAP)
  - Nursing homes, long term care facilities

Background
• World-wide 150 million new cases in children per year
• 11-20 million hospitalizations
• 4 million annual deaths
• Leading cause of mortality under 5 years of age
  WHO, 2004
Background – National Inpatient

2006 Pneumonia hospital stays for children only

<table>
<thead>
<tr>
<th>Age group</th>
<th>Total number of discharges</th>
<th>LOS days (mean)</th>
<th>In-hospital deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>167,221</td>
<td>3.3</td>
<td>257</td>
</tr>
<tr>
<td>&lt;1</td>
<td>43,103</td>
<td>3.5</td>
<td>51</td>
</tr>
<tr>
<td>1-4</td>
<td>76,912</td>
<td>3.0</td>
<td>89</td>
</tr>
<tr>
<td>5-9</td>
<td>29,781</td>
<td>3.2</td>
<td>16</td>
</tr>
<tr>
<td>10-14</td>
<td>11,728</td>
<td>7.01</td>
<td>4.1</td>
</tr>
<tr>
<td>15-17</td>
<td>3,059</td>
<td>3.59</td>
<td>4.9</td>
</tr>
<tr>
<td>Male</td>
<td>91,518</td>
<td>3.3</td>
<td>125</td>
</tr>
<tr>
<td>Female</td>
<td>74,703</td>
<td>3.1</td>
<td>122</td>
</tr>
<tr>
<td>Missing</td>
<td>1,154</td>
<td>2.5</td>
<td>4</td>
</tr>
</tbody>
</table>

Weighted national estimates for children 0-17 years from HCUP Kids’ Inpatient Database, 2006, Agency for Healthcare Research and Quality (AHRQ)

Burden of Disease

- Prospective cohort in Israel
- 213 children (< 3y) in with CAP
  - Outpatient and inpatient subjects
  - WHO radiographic definitions used
- Febrile 4.9 days
- “Sick” 7-14 days
- Parents work interrupted 4.2 days

- Shoham, et al., Pediatrics, 2005

Outline

- Background
- Etiology
- Diagnosis
- Management

Etiology - limitations

- Difficult to obtain specimens
- Difficult to differentiate between infection and colonization
- Most studies pre-PCV7
- No standard diagnostic criteria
- Age dependent
- Most studies in hospitalized children
- Frequent co-infections

CAP Etiology

<table>
<thead>
<tr>
<th>Age</th>
<th>S. pneumo</th>
<th>M. pneumo</th>
<th>C. pneumo</th>
<th>Virus</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 Yr</td>
<td>24-33%</td>
<td>4-6%</td>
<td>1-3%</td>
<td>28-37%</td>
</tr>
<tr>
<td>5-9 Yr</td>
<td>14-36%</td>
<td>7-30%</td>
<td>9-13%</td>
<td>21-28%</td>
</tr>
<tr>
<td>10-16 Yr</td>
<td>29-31%</td>
<td>14-51%</td>
<td>14-35%</td>
<td>0-4%</td>
</tr>
</tbody>
</table>

- McCracken, PIDJ, 4/2000

Hospitalized CAP

JUVÉN, T et al, PIDJ, 4/2000

- Three year prospective study in Finland
- 254 hospitalized children, mean age 3.8 years
- Acute and convalescent serum available for all subjects
- Possible causative organism identified in 85% of subjects
- Tested for 17 different pathogens (bacteria and viruses)
**Etiology by Age**

<table>
<thead>
<tr>
<th>Age</th>
<th>Total</th>
<th>Viral</th>
<th>Bacterial</th>
<th>Mixed</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2</td>
<td>108</td>
<td>86</td>
<td>51</td>
<td>37</td>
</tr>
<tr>
<td>2 to 5</td>
<td>84</td>
<td>49</td>
<td>47</td>
<td>28</td>
</tr>
<tr>
<td>&gt;5</td>
<td>62</td>
<td>23</td>
<td>36</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>254</td>
<td>158</td>
<td>134</td>
<td>77</td>
</tr>
</tbody>
</table>

- 62% viral infection
- 53% bacterial
- 30% mixed

**Hospitalized CAP**

Michelow et al., Pediatrics 2004

- Prospective cohort, Dallas, 1999-2000
- 6wk-18y/o
  - Inclusion: Fever, clinical signs and infiltrate
  - Exclusion: Bronchiolitis, immune issues
- 154 subjects
  - Identified etiology in 80%
  - Extensive etiologic evaluations
    - Blood, pleural bacterial cx
    - Pneumococcal PCR
    - Viral cx and DFA (RSV/Paraflu/Adeno/Flu)
    - Serology for Chlamydia pneumoniae and trachomatis, Mycoplasma pneumoniae and viruses listed above

**Etiology Type**

**Virus**

- RSV: 73 (29)
- Rhinovirus: 58 (24)
- Parainfluenza: 25 (10)
- Adenovirus: 19 (7)
- Influenza: 10 (4)
- Coronavirus: 7 (3)
- HHV-6: 7 (3)
- EBV: 1
- VZV: 1

**Bacteria**

- S. pneumoniae: 52 (20)
- H. influenzae: 22 (9)
- M. pneumoniae: 17 (7)
- M. catarrhalis: 10 (4)
- C. pneumoniae: 7 (3)
- S. pyogenes: 3 (1)
- C. trachomatis: 2 (1)

**Hospitalized CAP: Etiology by Age**

- 37% Viral
- 23% Bacterial
- 19% Mixed
- 21% Unknown

**Hospitalized CAP Etiology**

- Bacterial: 23%
- Mixed: 19%
- Viral: 37%
- Unknown: 21%

**Hospitalized CAP Etiology**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>No. of Episodes</th>
<th>Bacterial</th>
<th>Viral</th>
<th>Mixed</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>H. influenzae</em></td>
<td>28</td>
<td>6</td>
<td>15</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
<td>21</td>
<td>10</td>
<td>4</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td><em>S. pyogenes</em></td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><em>M. pneumoniae</em></td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><em>M. catarrhalis</em></td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><em>C. pneumoniae</em></td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>C. trachomatis</em></td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><em>V. vulnificus</em></td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Note:** The categories of co-infections with bacteria and with viruses are not mutually exclusive.
**Hospitalized CAP Etiology**

2m – 5 years 99 patients 86% etiology

- Mixed/Multiple 29%
- Viral 14%
- Bacterial 12%
- 5 years 2m – 5 years 99 patients 86% etiology


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**“Atypical” Bacteria**

- *M. pneumoniae and C. pneumoniae*
- Children older than 5 yrs significant burden
- Emerging disease in children ≤ 5 yrs
  - Esposito et al, Eur Resp J 2000
  - Principi et al, CID, 2001
  - Esposito et al, CID, 2002
  - Thumere et al, Pediatr Pulm, 2003
  - Michelow et al, Pediatrics, 2004

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**Hospitalized CAP – Atypical Bacteria**

Esposito et al, CID, 2002

- 196 children hospitalized with CAP age 2 – 5 years
  - PCR and acute and convalescent serology
    - C. pneumonia
    - M. pneumonia
    - S. pneumonia
  - Comparison between typical and atypical pathogens:
    - Clinical presentation
    - Radiographic findings
    - Laboratory data
    - Treatment and outcomes

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**Bacterial CAP 2-5 y/o**

Table 1. Characteristics of 196 children evaluated in a study of community-acquired pneumonia.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>99 (50.5)</td>
</tr>
<tr>
<td>Age, mean years ± SD</td>
<td>3.70 ± 0.875</td>
</tr>
<tr>
<td>Acute bacterial infection</td>
<td>98 (50.3)</td>
</tr>
<tr>
<td>Acute atypical bacterial infection</td>
<td>44 (22.5)</td>
</tr>
<tr>
<td>Due to <em>M. pneumoniae</em></td>
<td>30 (15.3)</td>
</tr>
<tr>
<td>Due to <em>C. pneumoniae</em></td>
<td>6 (3.1)</td>
</tr>
<tr>
<td>Due to mixed <em>M. pneumoniae</em> and <em>C. pneumoniae</em></td>
<td>10 (5.1)</td>
</tr>
<tr>
<td>Mixed <em>S. pneumoniae</em>-atypical bacterial infection</td>
<td>16 (8.2)</td>
</tr>
<tr>
<td>Due to <em>S. pneumoniae</em> and <em>M. pneumoniae</em></td>
<td>14 (7.1)</td>
</tr>
<tr>
<td>Due to <em>S. pneumoniae</em> and <em>C. pneumoniae</em></td>
<td>2 (1.0)</td>
</tr>
<tr>
<td>Undiagnosed cases</td>
<td>98 (43.9)</td>
</tr>
</tbody>
</table>

Esposito et al, CID, 2002

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**Etiology Summary**

- Overall, viruses are the most common cause of CAP
- Children hospitalized with CAP have a high incidence of bacterial CAP
- *S. pneumoniae* is still the most important bacterial pathogen
- Atypical bacteria are a significant cause of pneumonia even in young children (<5 y/o)
- Mixed infections are common in children hospitalized with CAP

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**Table 1. Infections caused by viruses and atypical bacteria diagnosed in 75 children (age 5-14 years) hospitalized with community-acquired pneumonia.**

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>No. (%) of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viruses</td>
<td></td>
</tr>
<tr>
<td>Paramyxovirus</td>
<td>6 (8)</td>
</tr>
<tr>
<td>Type 1</td>
<td>4</td>
</tr>
<tr>
<td>Type 2</td>
<td>1</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>9 (12)</td>
</tr>
<tr>
<td>Influenza virus</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Subtype H1N1</td>
<td>3</td>
</tr>
<tr>
<td>Subtype H3N2</td>
<td>3</td>
</tr>
<tr>
<td>Respiratory syncytial virus</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Human metapneumovirus</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Human rhinovirus</td>
<td>34 (45)</td>
</tr>
<tr>
<td>Bacteria</td>
<td>50 (60)</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>5 (7)</td>
</tr>
<tr>
<td><em>Mycoplasma pneumoniae</em></td>
<td>16 (21.3)</td>
</tr>
<tr>
<td><em>Chlamydia pneumoniae</em></td>
<td>2 (2.7)</td>
</tr>
<tr>
<td>Total diagnosed cases</td>
<td>75 (100)</td>
</tr>
</tbody>
</table>

Tsolia et al, CID, 2004
Viruses are the most common etiology in children < 5 years of age, RSV #1
In the SW United States data confirm the importance of S. pneumonia, M. pneumonia and C. pneumonia as causes of bacterial CAP
Mixed etiology for 30-50% of cases of pneumonia in children

CAP Diagnosis - Things to know
No gold standard
Combination
- Clinical data
- Radiographic data
- Laboratory data
Confirmation of etiology
- Seldom done
- Burdensome
- Limited clinical utility
- Low yield

Texas Children's Hospital Community-Acquired Pneumonia (CAP) Clinical Guideline

Clinical Data
Several studies attempt to predict pneumonia using clinical findings
Overall - high sensitivity low specificity
Classic study
  - Prospective study of 136 patients in ED
  - Studied 29 different signs and symptoms
  - Tachypnea best single predictor
  - The absence of tachypnea, nasal flaring, grunting, rales, decreased BS is high neg predictive value

Clinical Data
Lynch, et al., Pediatrics, 3/04
- Clinical predictors of positive CXR
- Prospective cohort - ED
- 570 patients
- Clinical presentation compared to CXR
  - Predictive signs and symptoms (p < 0.05)
    - Fever, decreased BS, crackles, retractions, grunting
    - Tachypnea p = 0.001
    - Fever + any above sign
    - Sensitivity > 90%
    - Best combination - fever and tachypnea
      - Specificity 19.4%

Clinical Data
Mahabee et al, Clin. Pedia., 2005
- 510 patient
- 2-59 months
- Any sign/symptom of respiratory infection got CXR
- Predictive factors:
  - Older age p = .005
  - Tachypnea p = .001
  - O2 sat ≤ 95% p = .001
  - Nasal flaring p < .001
  - Fever, crackles, retractions, grunting not predictive

Outline
- Background
- Etiology
- Diagnosis
- Management
Clinical Data atypical vs. *S. pneumoniae*

Table 1. Clinical characteristics of 152 children at the time of enrollment in a study of pediatric community-acquired pneumonia.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Haemophilus influenzae</th>
<th>Other atypical pathogens</th>
<th>Mixed atypical pathogens</th>
<th>Undiagnosed causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean years ± SD</td>
<td>3.66 ± 3.69</td>
<td>5.76 ± 4.60</td>
<td>8.76 ± 4.00</td>
<td>9.66 ± 4.98</td>
</tr>
<tr>
<td>Cough</td>
<td>23 (47.0)</td>
<td>36 (66.0)</td>
<td>6 (16.0)</td>
<td>48 (85.0)</td>
</tr>
<tr>
<td>Adenoid</td>
<td>21 (42.1)</td>
<td>20 (36.0)</td>
<td>6 (16.0)</td>
<td>40 (71.0)</td>
</tr>
<tr>
<td>Signs of infection</td>
<td>8 (16.0)</td>
<td>11 (19.6)</td>
<td>7 (18.0)</td>
<td>15 (27.0)</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>31 (64.0)</td>
<td>33 (58.0)</td>
<td>11 (28.0)</td>
<td>40 (76.0)</td>
</tr>
<tr>
<td>Severe disease</td>
<td>15 (30.0)</td>
<td>16 (28.0)</td>
<td>6 (16.0)</td>
<td>21 (38.0)</td>
</tr>
<tr>
<td>Fever</td>
<td>13 (26.0)</td>
<td>10 (18.0)</td>
<td>8 (22.0)</td>
<td>21 (38.0)</td>
</tr>
<tr>
<td>Nausea</td>
<td>41 (83.0)</td>
<td>41 (74.0)</td>
<td>16 (44.0)</td>
<td>79 (141.0)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>6 (12.0)</td>
<td>7 (13.0)</td>
<td>2 (5.0)</td>
<td>11 (20.0)</td>
</tr>
</tbody>
</table>

**NOTE:** Cells show no. (% of patients, unless otherwise noted.

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**TEXAS CHILDREN’S HOSPITAL COMMUNITY-ACQUIRED PNEUMONIA (CAP) CLINICAL GUIDELINE**

- A complete physical examination should be performed. A combination of clinical findings, including vital signs and pulse oximetry, is most predictive in determining CAP.

- A small percentage of children < 5 years of age may present with abdominal pain or with fever and no signs of respiratory illness.

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**Imaging - Chest X-Ray (CXR)**

- “Gold Standard” for Dx of pneumonia
- Significant intra and inter-observer variation in interpretation
  - Davies et al, Pediatr Infect Dis J, 1997
- Limited correlation with etiology
  - Virksi et al, Thorax, 2002
- Poor correlation with clinical criteria
- Does not affect clinical outcomes

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**CXR**

- Alveolar, lobar infiltrate
- Interstitial Infiltrate
CXR Virus vs. Bacteria

Virkki et al, Thorax, 2002
- Evaluated 254 cases of suspected CAP
- Etiology found in 85% of cases
- Compared to CXR findings

Results:
- **Alveolar** and especially **lobar** - 78% bacterial (p=0.001)
- **Interstitial** - 50% bacterial, 50% viral

CXR Findings

Atypical vs. S pneumonia

<table>
<thead>
<tr>
<th>Finding</th>
<th>Streptococcus pneumonia (n=48)</th>
<th>Atypical bacteria (n=48)</th>
<th>Mixed S. pneumonia and atypical bacteria (n=18)</th>
<th>Unligated cases (n=39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>6 / 10.4</td>
<td>6 / 0.3</td>
<td>12 / 17.2</td>
<td>17 / 12.3</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>3 / 9.2</td>
<td>4 / 0.7</td>
<td>4 / 15.3</td>
<td>9 / 13.0</td>
</tr>
<tr>
<td>Parinal lung infiltrates</td>
<td>15 / 31.3</td>
<td>20 / 0.3</td>
<td>10 / 54.3</td>
<td>16 / 48.6</td>
</tr>
<tr>
<td>Retrorenal hilar infiltrates</td>
<td>13 / 27.1</td>
<td>21 / 0.5</td>
<td>3 / 15.3</td>
<td>21 / 0.5</td>
</tr>
<tr>
<td>Alveolar or lobe consolidation</td>
<td>16 / 37.5</td>
<td>12 / 0.6</td>
<td>5 / 15.5</td>
<td>27 / 11.4</td>
</tr>
<tr>
<td>Bilateral consolidations</td>
<td>7 / 13.7</td>
<td>4 / 0.7</td>
<td>2 / 15.3</td>
<td>15 / 11.0</td>
</tr>
<tr>
<td>Flail pleurisy</td>
<td>3 / 6.3</td>
<td>3 / 0.5</td>
<td>1 / 6.3</td>
<td>4 / 0.7</td>
</tr>
</tbody>
</table>

*NOTE: Data are no. (% of patients). Significant difference was significant. Individual radiographic characteristics were marked as presented by a radiologist.*

Esposito et al, CID, 2002

Who needs a CXR?

Outcomes
- 522 children age 2 month or older who met (WHO) clinical def. of severe pneumonia were randomized into CXR and no CXR (control)
- Primary outcome: Time to recovery
- Secondary outcomes:
  - Diagnosis
  - Management
  - Subsequent use of health facilities.


Who needs a CXR?

Results:
- **Primary outcome**
  - No significant difference in time to recovery (p=0.3)
- **Secondary outcomes**
  - CXR - > antibiotics used
  - No CXR - > Dx of bronchiolitis
  - Subsequent use of health facilities was equal


Where is the Pneumonia? – Wrong Time
Where is the Pneumonia? – Wrong Time

Where is the Pneumonia? – Too Fast

Where is the Pneumonia? – Too Fast

Where is the Pneumonia? – Wrong place

The case of the migratory round pneumonia
**Where is the Pneumonia? – Wrong place**
The case of the migratory round pneumonia

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**Laboratory findings**

**WBC**

- Likelihood of bacterial infection increases as WBC surpasses 15,000/mm³
  - Shuttleworth, D Amer J Dis Child., 1971
- Occult pneumonias in fever and leukocytosis (20,000/mm³)
  - Pre-PCV7 - 15 - 19%
  - Post-PCV7 - 9%
  - Rustman MS et al, Pediat. Emer. Care, 2009

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**TEXAS CHILDREN’S HOSPITAL COMMUNITY-ACQUIRED PNEUMONIA (CAP) CLINICAL GUIDELINE**

- CXR is not routinely recommended.
- Consider CXR in the setting of moderate or severe pneumonia where the findings are likely to aid in diagnosis or management (suspected abscesses, complicated pneumonias, etc.)

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**Table 2. Laboratory findings for 100 children with community-acquired pneumonia of various etiologies.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Streptococcus pneumonia (n = 50)</th>
<th>Alignedibacter (n = 50)</th>
<th>Mixed E. pneumoniae and Alignedibacter (n = 50)</th>
<th>Undiagnosed (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC, count, mean (± SD)</td>
<td>11,980 ± 3,093</td>
<td>11,354 ± 3,634</td>
<td>11,041 ± 4,366</td>
<td>12,980 ± 5,434</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>80 ± 15</td>
<td>79 ± 16</td>
<td>79 ± 16</td>
<td>82 ± 16</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>20 ± 10</td>
<td>20 ± 11</td>
<td>20 ± 11</td>
<td>27 ± 17</td>
</tr>
<tr>
<td>Monocytes</td>
<td>7 ± 3</td>
<td>8 ± 3</td>
<td>7 ± 3</td>
<td>8 ± 3</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>1 ± 1</td>
<td>1 ± 1</td>
<td>1 ± 1</td>
<td>1 ± 2</td>
</tr>
<tr>
<td>Basophils</td>
<td>0.4 ± 0.7</td>
<td>0.1 ± 0.1</td>
<td>0.1 ± 0.1</td>
<td>0.3 ± 0.1</td>
</tr>
<tr>
<td>CRP level, mean (± SD)</td>
<td>198 ± 155</td>
<td>188 ± 119</td>
<td>188 ± 119</td>
<td>136 ± 105</td>
</tr>
<tr>
<td>ESR, mean (± SD)</td>
<td>57 ± 29</td>
<td>57 ± 27</td>
<td>57 ± 27</td>
<td>50 ± 29</td>
</tr>
</tbody>
</table>

**NOTE:** Data are mean ± SD; < 55, unless otherwise indicated. Unless indicated, difference: p < 0.05; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate

*“Diagnosis not confirmed by clinical and supportive data.”

**Esposito et al, CID 2002**
CRP
- Several conflicting studies
  - Viral vs. Bacterial CAP
  - Typical vs. Atypical CAP
- Flood et al, PDJJ, 2/2008
  - Meta-analysis of 8 studies
  - 1230 children
  - Pooled incidence of bacterial CAP – 41%
  - CRP concentrations exceeding 4-6 mg/dl has a PPV of 64%

Blood Cultures in CAP
- Outpatient CAP
    - 409 children with radiographic evidence of CAP
    - 2.7% positive
    - No changes in management due to results
- Inpatient CAP
  - Inpatient incidence
    - Juven et al – 1 of 125 (0.8%)
    - Michelow et al – not reported
    - Cevey-Macherei et al
      - Positive - 2 of 99 (2%)
      - False + - 3 of 99 (3%)
    - Tsolia et al – 1 of 75 (1.3%)

Blood Cultures Inpatient CAP
- Adults
  - IDSA/ATS guidelines recommends BCx’ for inpatient CAP
  - Evidence against
      - Systematic review – 13 studies, > 2700 cultures
      - ATBx narrowed < 3%
      - ATBx broadened in less than 1%
      - False positive cultures matched or exceeded the rate for true positives.
      - Clinical decisions were almost never made based on blood culture results

Blood Cultures Inpatient CAP
- TCH Experience
  - Method: Three year retrospective cohort chart review
    - Inclusion
      - Age 2months – 18 years
      - Previously healthy admitted with diagnosis of pneumonia
      - Blood Cx obtained
    - Exclusion
      - Immunocompromised or chronic pulmonary illness with the exception of asthma

Blood Cultures Inpatient CAP
- TCH Experience: Results
  - 134 patients 129 known results:
    - 3 were positive (2.3%, 95% CI 0.5-6.7%)
    - 2 of these were pathogens (1.6%, 95% CI 0.2-5.5%)
  - Management decision:
    - Repeat blood culture in all 3 cases
    - Antibiotics broadened only in the case of the false positive culture
    - Antibiotics were not narrowed in any case

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Missing Cx Result</th>
<th>Positive Cxs</th>
<th>Percent (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobar</td>
<td>91</td>
<td>1</td>
<td>0 % (0-4%)</td>
</tr>
<tr>
<td>Multilobar</td>
<td>29</td>
<td>2</td>
<td>0 % (0-13%)</td>
</tr>
<tr>
<td>Complicated</td>
<td>14</td>
<td>2</td>
<td>17% (2-48%)</td>
</tr>
</tbody>
</table>

Other Laboratory/Micro tests
- Procalcitonin (PCT)
  - High values (1-2 ng/ml) helpful
  - Low values not predictive in some studies
    - Toikka P et al, PIDJ, 2000
    - Moulin F et al, Arch Dis Child, 2001
- Sputum - children
  - Induced sputum high yield 90%
  - Unable to differentiate LRTI from URI or colonization
    - Laho E et al, Thorax, 2009
Other Laboratory/Micro tests
- Other microbiological testing
  - Pneumococcal urinary antigen detection
  - Real time PCR
  - Serology
- Limitations
  - Costs
  - Clinical utility
  - Mixed infections

Diagnosis - Summary
- There is no gold standard test for the diagnosis of CAP - clinical diagnosis
- Clinical findings can be highly sensitive, but not very specific
- CXR remains the diagnostic test of choice despite its shortcomings in the available evidence
- Laboratory data including microbiological testing is rarely indicated for uncomplicated CAP

Outline
- Background
- Etiology
- Diagnosis
- Management

CAP Management
- Treatment
  - What?
  - Where?
  - How long?
- Follow-up

Treatment – What?
- Antibiotics
- Adjunctive therapies
- Supportive therapy – O₂, IVF
- Factors influencing treatment
  - Etiology
  - Acuity or Severity
  - Complicated vs. uncomplicated
  - Risk factors
    - Immune status
    - Age

Texas Children's Hospital
Community-Acquired Pneumonia (CAP) Clinical Guideline
- Laboratory evaluation is not routinely recommended
- Laboratory test such as WBC should be obtained only when adjunctive information is necessary to help decide whether or not to use antibiotics
- Blood cultures are not routinely recommended in the evaluation of uncomplicated CAP

TCH CAP-Clinical Guideline, 2/2009
**Antibiotic Decisions – What?**

- Beta-Lactams
  - Amoxicillin
  - Amox/Clav
  - Cephalosporins
- Clindamycin
- Macrolides
- Fluoroquinolones

**Antibiotics – What to use**

*Etiology*
- **S. pneumoniae**
  - Penicillin resistance increasing
  - TCH – 60 % resistant
- **Atypical bacteria**
  - Worse outcomes if not treated
  - Principi et al, CID, 2001, Esposito et al, CID, 2002
- **Other bacteria**
  - *H. influenzae*, *M. catarrhalis*

**Antibiotics – What to use**

*H. influenzae*, *M. catarrhalis*
- Beta-lactamase producers
- Evidence behind their role in CAP controversial
  - Indirect evidence
  - Usually in mixed infections
  - May be “innocent bystanders” Lahti E et al, Thorax, 2009

Sy MG, et al, Pediatr. Pulm., July 2010
- Comprehensive review of children and *M. Catarrhalis*
- All studies sputum, nas/o/phonaryngeal Cx or serology
- 8 well documented case reports in all of literature
- Extremely uncommon cause

**Streptococcus pneumoniae**

Is penicillin resistance clinically relevant?
- Resistance is due to alterations in penicillin binding proteins
- Increasing dose overcomes resistance
  - Pigla et al, Ped. Inf. Dis. 2003

**S. pneumo discordant therapy**

Clinical outcomes in adults

- Multinational prospective study of adults hospitalized with pneumococcal bacteremia
- 844 patients
- Discordant therapy with penicillin or third generation cephalosporins did not affect time to recovery or mortality
- Discordant therapy with cefuroxime
  - 30% higher mortality (p=0.02)

**Drug resistance and clinical outcomes - children**

  - Multicenter retrospective study of invasive infections caused by *S. pneumoniae*
  - 2100 children
  - No difference in outcome due to antibiotic resistance
  - MIC up to 2.0 microg/ml (interm. resistance)
TEXAS CHILDREN'S HOSPITAL COMMUNITY-ACQUIRED PNEUMONIA (CAP) CLINICAL GUIDELINE

**Outpatient**
- Children < 2 years of age
  - High dose amoxicillin (80-90 mg/kg/dose div. Q 8-12 hours)
- Children > 2 to 5 years
  - High dose amoxicillin +/- azithromycin (10 mg/kg once day one, 5 mg/kg days 2-5)
  - Could start with one antibiotic and add the second one if no clinical improvement in 24-48 hour follow-up
- Children > 5 years
  - High dose amoxicillin + azithromycin

TCH CAP-Clinical Guideline, 2/2009

**Management – adjunctive therapy**

**Chest physiotherapy in CAP**
- No effect on clinical resolution
- No decrease in LOS
- Increased duration of cough and auscultatory findings
  - Paluda C et al, Thorax. 2008 Sep
- Increased duration of fever
  - Britton S et al, BMJ. 1985

**Surgical therapy**

**Complicated pneumonias**
- Video assisted thoracoscopic surgery (VATS) versus chest tube only
  - VATS reduces LOS, charges, time of chest tube, complication rate and need for re-intervention
    - Kurt et al, Pediatrics 2004
    - Aronsen et al, PEDI 2005
  - VATS vs. fibrinolytics – prospective studies
    - Same clinical outcome
    - Chest tube + fibrinolytics reduces costs

**Antibiotics - How Long?**
- Depends on severity
- Non-severe/uncomplicated
  - 10 days pneumococcus
  - 5 days atypical CAP - Azithromycin
- TCH-CAP Guidelines
  - 3-5 day course of high dose amoxicillin
    - Argued J, BMJ. 2004
    - Hoir. Lancet, 2002
- Severe/complicated
  - Should be individualized
  - Most antibiotics 14 – 21 days
Treatment - Where?
- Equal efficacy PO vs. IV even in WHO severe pneumonias

TCH-CAP CLINICAL GUIDELINE
- Admission Criteria
  • Unable to tolerate oral fluids and medications
  • Moderate or severe respiratory distress
  • Failed outpatient antibiotic treatment
  • Altered mental status
  • Oxygen saturation consistently < 90 %
  • Unsafe to send home/poor follow-up

Management
Follow up
- 48 hours — TCH-CAP Guidelines
  • Follow up labs – not needed
  • Follow up CXR
    - Not needed if fully recovered

Conclusions
- CAP is a significant cause of morbidity and mortality in children nationally and world wide
- The etiology is extensive but S. pneumoniae continues to be the major bacterial player followed closely by atypical pathogens
- Diagnosis remains primarily a clinical endeavor
- Imaging studies such as CXR and laboratory testing are of unproven benefit and not routinely indicated in the evaluation of uncomplicated CAP

Future Considerations
- Effects of vaccination with PCV
  • Less systemic/invasive complications
  • Increasing local complications - Empyema
    - Lee et al, Pediatrics, 2010
    - Grijalva et al, Clin. Inf. Disease, 2010
    - Li ST et al, Pediatrics, 2010
- Emergence of multidrug resistant strains
  S. pneumoniae (serotype 19A)
- Development of national guidelines

Thank you