Upper Respiratory Tract and Lower Respiratory Tract Infections

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Financial Disclosure

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In the past 12 months, I have not had a significant financial interest or other relationship with the manufacturer(s) of the product(s) or provider(s) of the service(s) that will be discussed in this presentation.
# Common Pediatric Respiratory Tract Infections

<table>
<thead>
<tr>
<th>Infection</th>
<th>Systemic Antibiotics Indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Always</td>
</tr>
<tr>
<td>Viral URI</td>
<td></td>
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<tr>
<td>Acute Purulent Rhinitis</td>
<td></td>
</tr>
<tr>
<td>Acute Otitis Media</td>
<td></td>
</tr>
<tr>
<td>Acute Bacterial Sinusitis</td>
<td>X</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td></td>
</tr>
<tr>
<td>Bronchiolitis</td>
<td></td>
</tr>
<tr>
<td>Acute Bronchitis</td>
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</tr>
</tbody>
</table>
Viral Illnesses

• Common colds, nonspecific URI, Acute Purulent Rhinitis, Acute Cough Illness and Acute Bronchitis in children are due to virus infections

• Antibiotics are never indicated
Acute Purulent Rhinitis (Common Cold)

- Nasal discharge for viral URI (cold):
  - 80% last 10 days
  - clear → white → yellow → green

- There is no evidence that antibiotics provide any benefit to children who have acute purulent rhinitis of \( \leq 10 \) days*

Otitis Media

Early AOM with bulging of the pars flaccida and obliteration of the lateral process of the malleus.

Late AOM with bulging of the entire TM and loss of all visible landmarks.
Acute Otitis Media (AOM)

Diagnosis

• Requires middle ear purulent fluid and signs of inflammation
  – Moderate or severe bulging of TM with erythema of TM
  – Otorrhea not due to otitis externa
• Erythema of TM without bulging is not adequate for diagnosis of AOM
• AOM cannot be diagnosed without visualizing the TM

Acute Otitis Media

Severity

Illness severity increases with:
- Severe otalgia
- Otalgia lasting >48 hours
- Temperature ≥39°C
- Bilateral >> unilateral
- Age ≤23 months

Hersh AL. *Pediatrics* 2013;132:1146-1154.
Spontaneous Bacteriologic Cure Rate in Acute Otitis Media

- *Streptococcus pneumoniae: 10%*
- *Haemophilus influenzae: 50%*
- *Moraxella catarrhalis: 70%*
- *Viruses: 100%*

Klein JO. *Clin Infect Dis* 10:823-833, 1994
Acute Otitis Media

Benefits of Antibiotic Treatment

- ≥50% of children with AOM recover without antibiotic therapy
- Symptoms improve quicker when antibiotics are given; but you need to treat 4 to 7 children to have one child get better faster. (For most children antibiotics do not result in more rapid improvement in symptoms)
- Antibiotics → fewer tympanic membrane perforations (but these are rare)
- Antibiotics have not been shown to prevent mastoiditis or other complications of AOM
- Antibiotics do not have a role in the management of otitis media with effusion

Hersh AL. *Pediatrics* 2013;132:1146-1154.
Acute Otitis Media
Observation/”Wait and See”

• Reduces antibiotic use/exposure

• Well accepted by parents when explained appropriately (when not explained well, parents want immediate antibiotics); this has improved in last few years

• Does not result in worse outcomes
Acute Otitis Media

Therapy

- Consider watchful waiting for:
  - Children >2 years of age
  - Children of any age with unilateral disease
  - Children of any age without fever and/or otalgia

- First line antibiotics
  - Amoxicillin
  - Amoxicillin clavulanate (limited to children with recent exposure to amoxicillin, i.e. <6 weeks or known local prevalence of high rates of resistance by *Haemophilus influenzae*)

- Duration: 7 days adequate
- Not recommended: erythromycin, azithromycin and oral 3rd generation cephalosporins
- No evidence that antibiotics prevents mastoiditis

Hersh AL. *Pediatrics* 2013;132:1146-1154.
Lieberthal AS *Pediatrics* 2013;131:e964.
Empiric Therapy of Acute Otitis Media

- **High risk of resistant S. pneumoniae**
  - **Amoxicillin 80-90 mg/kg/d ÷ BID**
  - **Amoxicillin 40 mg/kg/d ÷ BID**

- **Clinical improvement?**
  - **No**
  - **Amoxicillin/clavulanate or cefuroxime axetil**
    - **Clinical improvement?**
      - **No**
        - **IM Ceftriaxone X3d, or Clindamycin; consider tympanocentesis**
          - **Clinical improvement?**
            - **No**
              - **Tympanocentesis**
        - **Yes**
          - **Complete RX and Check for clearance of effusion in 1 month**
    - **Yes**
      - **Complete RX and Check for clearance of effusion in 1 month**
Otitis Media with Effusion

- Isn’t the same as acute otitis media
- Evidence does not support the routine use of antibiotics for children with otitis media with effusion

*Cochrane Database Syst. Rev. 2013;June4:6.CD000247*
Tympanostomy Tube Guidelines
(American Academy of Otolaryngology-Head and Neck Surgery Foundation [AAO-HNSF])

**Indications**

- Bilateral otitis media with effusion (OME) for greater than 3 months **AND** hearing impairment.
- Bilateral or unilateral OME for $\geq 3$ months **AND** one of the following associated symptoms: vestibular symptoms, school or behavior problems (new/associated with OME), ear discomfort or lowered quality of life.
- Bilateral or unilateral OME for $\geq 3$ months in “at-risk” children: permanent hearing loss, speech, language or developmental delay, autism-spectrum disorder, Trisomy 21, craniofacial disorders and/or cleft palate.

*Otolaryngol Head Neck Surg* 2013;149:8-16.
Tympanostomy Tube Guidelines
(American Academy of Otolaryngology-Head and Neck Surgery Foundation [AAO-HNSF])

**Not Indicated**

- Recurrent acute otitis media without persistent middle ear effusion $\geq 3$ months.

Acute Tympanostomy Tube Otorrhea

230 children with acute tympanostomy tube otorrhea were randomized into 3 groups:

1. Hydrocortisone – bacitracin – colistin ear drops
2. Amoxicilllin clavulanate
3. No initial treatment/observation

*NEJM* 2014;370:723-733.
# Acute Tympanostomy – Tube Otorrhea

## Study Results

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Otorrhea at 2 weeks</th>
<th>Median Duration of Otorrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone – Bacitracin-Colistin ear drops</td>
<td>5%</td>
<td>4 days</td>
</tr>
<tr>
<td>Amoxicillin Clavulanate</td>
<td>44%</td>
<td>5 days</td>
</tr>
<tr>
<td>Observation</td>
<td>55%</td>
<td>12 days</td>
</tr>
</tbody>
</table>

*NEJM 2014;370:723-733.*
Persistence of Otorrhea Following Randomization
Acute Bacterial Sinusitis

Diagnosis

- Diagnosis is based on:
  - Persistence of nasal discharge/congestion with or without daytime cough beyond 10 days
  - Worsening of symptoms after initial improvement of URI, e.g. new onset fever ≥39°C, new onset daytime cough or increase in nasal drainage after improvement

- Color or characteristics of nasal discharge cannot differentiate viral URI from sinusitis. Viral URI: drainage – clear → gray → yellow → green (can last up to 15 days in 10%)

- NO role for routine imaging

Acute Bacterial Sinusitis

Benefits of Antibiotics

• Antibiotics → improved resolution of symptoms but only in those for whom strict criteria are used to make diagnosis of acute bacterial sinusitis

• Antibiotics have not been shown to prevent complications of sinusitis such as orbital cellulitis or intracranial abscess

Hersh AL. *Pediatrics* 2013;132:1146-1154.
Wald ER. *Pediatrics* 2013;132:e262.
Acute Bacterial Sinusitis
Therapy

• First line therapy
  – Amoxicillin (preferred)
  – Amoxicillin clavulanate

• No evidence that antibiotics prevent complications of sinusitis

• Antibiotics can improve symptoms of bacterial sinusitis at days 3 and 14 following onset of treatment

Hersh AL. *Pediatrics* 2013;132:1146-1154.
Wald ER. *Pediatrics* 2013;132:e262.
Streptococcal Pharyngitis

Diagnosis

• Requires evidence of pharyngitis and a positive test for group A *streptococcus*

• Test for group A *streptococcus* if 2 of the following are present
  - Fever
  - Tonsillar exudate
  - Tonsillar swelling
  - Tender and swollen anterior cervical lymph nodes
  - Absence of cough
  - Age >3 years and <15 years of age

Hersh AL. *Pediatrics* 2013;132:1146-1154.
Streptococcal Pharyngitis

Diagnosis

Group A *streptococcus* is less likely to be responsible for pharyngitis if any of the following are present:

- Nasal discharge/congestion
- Cough
- Conjunctivitis
- Hoarseness
- Oropharyngeal lesions such as ulcers or vesicles

Hersh AL. *Pediatrics* 2013;132:1146-1154.
Streptococcal Pharyngitis

Benefits of Antibiotics

In children with pharyngitis and a positive test for group A *streptococcus*, antibiotics:

- Shortens the duration of sore throat and headache (improvement seen in ≤3 days)
- Reduces secondary transmission
- Prevention of rheumatic fever
- Prevention of suppurative complications, such as peritonsillar abscess, AOM and sinusitis

Hersh AL. *Pediatrics* 2013;132:1146-1154.
Streptococcal Pharyngitis Therapy

- DO NOT treat empirically

- Antibiotics – 10 days
  - Amoxicillin (once daily dosing – 50 mg/kg/day)
  - Penicillin
Definition of Pediatric Community-Acquired Pneumonia (CAP)

- CAP is the presence of signs and symptoms of pneumonia in a previously healthy child due to an infection acquired outside of the hospital

- Signs and symptoms
  - Best positive predictive value
    - Nasal flaring (<12 months)
    - Oxygen saturation < 94% (sea level)
    - Tachypnea/retractions
  - Best Negative Predictive Value
    - Absence of tachypnea or other respiratory signs
## Common Etiologies of Pediatric Community-Acquired Pneumonia

<table>
<thead>
<tr>
<th>Age</th>
<th>Organism</th>
</tr>
</thead>
</table>
| <5 years | Viruses (RSV, PIV, Influenza, HMPV, Adenovirus, Rhinovirus)  
             Streptococcus pneumoniae  
             Streptococcus pyogenes  
             Staphylococcus aureus |
| >5 years | Streptococcus pneumoniae  
             Mycoplasma pneumoniae  
             Chlamydophila pneumoniae |
Etiology of Community-Acquired Pneumonia (CAP) in 154 Hospitalized Children

Current Issues in the Diagnosis and Management of Community-Acquired Pneumonia

• A specific etiology is not identified in many cases, making targeted therapy difficult

• Appropriate triage can be problematic as clinical features are neither specific nor consistent

• No reliable tools can be used to classify patients by severity and predict who will develop complications
Executive Summary: The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age: Clinical Practice Guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America

John S. Bradley,1,3 Carrie L. Byington,2,8 Samir S. Shah,3,9 Brian Alverston,4 Edward R. Carter,5 Christopher Harrison,6 Sheldon L. Kaplan,7 Sharon E. Mace,8 George H. McCracken Jr,9 Matthew R. Moore,10 Shawn D. St Peter,11 Jana A. Stockwell,12 and Jack T. Swanson13

Clin Infect Dis 2011;53:613-630
Community-Acquired Pneumonia: Who Should Be Hospitalized?

- Sustained hypoxemia <90%**
- Respiratory distress
- Complicated pneumonia
- Age <3-6 months with suspected bacterial pneumonia (e.g. inadequately immunized)
- Suspected MRSA or other virulent pathogen
- Concern regarding social situation/compliance with outpatient therapy
- Dehydration, vomiting, or inability to take oral medications

**Some experts would consider hospitalization for SpO2 <93%
Community-Acquired Pneumonia: Ancillary Diagnostic Testing

- Complete blood count:
  - Not routinely recommended in outpatients
  - May be helpful in those with more serious disease
- Acute phase reactants (e.g. ESR, CRP):
  - Cannot alone distinguish between viral and bacterial CAP (Though more likely bacterial if CRP >3.5-6 mg/dL)
  - Not routinely recommended for outpatients
  - May be helpful in more serious disease (e.g. hospitalized patients or those with complications)
Diagnostic Testing: Blood Cultures

• Blood cultures should not be performed in non-toxic, immunized children who will be managed as outpatients
  – Positive in < 2% prior to introduction of HiB
  – Positive < 1% after introduction of HiB and PCV-7
Blood Cultures

• Blood cultures should be performed in children requiring admission for CAP or those who have evidence of empyema
  – Positive in 2%-11% of CAP
  – Positive in 14%-27% CAP complicated by empyema
Community-Acquired Pneumonia: Testing for Bacterial Pathogens

• **Blood culture:**
  - Not routinely recommended for outpatients
    - Positive in <2% of children
    - More false positives than true positives
  - Obtain in children requiring hospitalization for presumed bacterial CAP
    - Positive in up to 11% of hospitalized children

• **Sputum culture:**
  - Hospitalized children who can produce sputum (older children and adolescents)

• **Pleural fluid analysis:**
  - Culture positive in <50% of cases
  - PCR available for *S. pneumoniae, S. pyogenes*, and *M. pneumoniae*
Community-Acquired Pneumonia: Testing for Viral & Atypical Pathogens

• Viral testing:
  - Rapid viral testing should be used when indicated and available, especially during winter months

• Atypical pathogens:
  - Should test for *M. pneumoniae* if suspicious signs/symptoms
  - Testing for *C. pneumoniae* is not recommended
Community-Acquired Pneumonia: Imaging

- CXR not routinely recommended for outpatients
- CXR should be obtained in all hospitalized patients
- Follow-up imaging if not routinely necessary to document resolution
- Indications for repeat CXR after 4-6 weeks
  - Recurrent pneumonia in same lobe
  - Suspicion of anatomic anomaly, chest mass, or foreign body aspiration
Diagnostic Testing: Radiography

- Chest Radiographs should be obtained for
  - All children who will be admitted
  - For children with hypoxia or significant respiratory distress
  - CAP is prolonged or unresponsive to antimicrobials
  - A pleural effusion or empyema is suspected
Pneumococcal Pneumonia:
Right Middle Lobe Consolidation

PA View

Lateral View
Pneumococcal Pneumonia: Right Lower Lobe Consolidation
Anti-Infective Treatment

- Which antibiotic should be offered to a child with CAP in the outpatient setting?
  - Children who are preschool aged (< 5), previously healthy, and immunized should receive amoxicillin to provide coverage for *S. pneumonias*
  - For PCN allergic clindamycin is preferred
  - Alternatives: Amoxicillin/clavulanate (especially if no HiB vaccine) or second or third generation cephalosporin
## Community-Acquired Pneumonia: Outpatient Therapy

<table>
<thead>
<tr>
<th>Age Category</th>
<th>Empiric Therapy for Presumed Bacterial Pneumonia</th>
<th>Empiric Therapy for Presumed Atypical Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Less than 5 years of age (Preschool)</strong>**</td>
<td>Amoxicillin, oral (90 mg/kg/day div tid)</td>
<td>Azithromycin oral (10 mg/kg on day 1, followed by 5 mg/kg/day once daily days 2-5)</td>
</tr>
<tr>
<td></td>
<td>Alternatives: Amoxicillin/clavulanate</td>
<td>Alternatives: Clarithromycin oral (15 mg/kg/day div bid x 7-14 d); erythromycin oral (40 mg/kg/day div qid)</td>
</tr>
<tr>
<td><strong>5 years of age and older</strong></td>
<td>Amoxicillin, oral (90 mg/kg/day div tid to a max of 3 gm/day)</td>
<td>Azithromycin oral (10 mg/kg on day 1, followed by 5 mg/kg/day once daily days 2-5 to a max of 500 mg on day 1, followed by 250 mg on days 2-5)</td>
</tr>
<tr>
<td></td>
<td>For children with clinical, laboratory, and radiographic evidence consistent with either pneumococcal or atypical CAP, a macrolide can be added to a beta-lactam antibiotic for empiric therapy.</td>
<td>Alternatives: Clarithromycin oral (15 mg/kg/day div bid to a max of 1 gm daily); erythromycin; doxycycline for children older than 7 years</td>
</tr>
</tbody>
</table>

**Antibiotics are not routinely required for preschool-aged children with pneumonia, without suspicion of bacterial coinfection.**
Anti-Infective Treatment

• Which antibiotic should be offered to a child with CAP in the inpatient setting?
  – Ampicillin or penicillin G should be administered to the immunized infant or child when local epidemiologic data document lack of substantial high-level penicillin resistance for *S. pneumoniae*. 
# Community-Acquired Pneumonia: Inpatient Therapy – Any Age

<table>
<thead>
<tr>
<th>Empiric Therapy for Presumed Bacterial Pneumonia</th>
<th>Empiric Therapy for Presumed Atypical Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin; penicillin G</td>
<td>Azithromycin (in addition to beta-lactam, if diagnosis in doubt)</td>
</tr>
<tr>
<td>Alternatives: Ceftriaxone; cefotaxime</td>
<td>Alternatives: Clarithromycin; erythromycin; doxycycline for children older than 7 years. Levofloxacin for children who have reached growth maturity, or those who cannot tolerate macrolides</td>
</tr>
<tr>
<td>Addition of vancomycin or clindamycin for suspected CA-MRSA or critically-ill</td>
<td></td>
</tr>
<tr>
<td>Not fully immunized for <em>Hib and S. pneumoniae</em>; local penicillin resistance in invasive strains of pneumococcus is significant</td>
<td>Azithromycin (in addition to beta-lactam, if diagnosis in doubt)</td>
</tr>
<tr>
<td>Ceftriaxone; cefotaxime</td>
<td>Alternatives: Clarithromycin; erythromycin; doxycycline for children older than 7 years. Levofloxacin for children who have reached growth maturity, or those who cannot tolerate macrolides</td>
</tr>
<tr>
<td>Addition of vancomycin or clindamycin for suspected CA-MRSA or critically ill</td>
<td></td>
</tr>
<tr>
<td>Alternatives: cefuroxime</td>
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</tr>
</tbody>
</table>

**Antibiotics are not routinely required for preschool-aged children with pneumonia, without suspicion of bacterial co-infection**
Empiric therapy with a third-generation parenteral cephalosporin (ceftriaxone or cefotaxime) should be prescribed for hospitalized infants and children who are not fully immunized, in regions where local epidemiology of invasive pneumococcal strains documents high-level penicillin resistance, or for infants and children with life-threatening infection, including those with empyema.
Treatment of Childhood CAP
Empiric Antibiotics: Narrow vs Broad Spectrum

• Narrow Spectrum Antibiotics
  – Similar outcomes
  – Shorter hospital stay (43 vs. 52.3 hrs)
  – No statistical difference in duration of fever nor duration of supplemental oxygen.

*Pediatrics 2014; 133: e23-e29*
CAP: Treatment Duration

• Treatment courses of 10 days have been studied the most and are effective for most cases of pneumonia
  – There are trials ongoing evaluating shorter courses

• Complicated pneumonia with empyema or necrosis or pneumonia caused by drug resistant pathogens such as MRSA will require longer treatment courses
  – In general treatment is ~ 4 weeks for empyema with combination of IV agents followed by oral agent(s)
When to Suspect an Empyema

• Prolonged fever or fever that resolved and has now returned
• Chest pain
• Abdominal pain
• Use of ibuprofen
• Use of azithromycin or IM ceftriaxone without improvement
• Recent history of varicella or influenza
Complications of Community-Acquired Pneumonia

- Parapneumonic effusion
- Empyema
- Necrotizing pneumonia
  - *S. pneumoniae*, *S. aureus*, GAS
- Lung abscess
  - Anaerobes, *Streptococcus* species, *S. aureus*
- Bronchopleural fistula
- Empyema necessitans

Li ST, Tancredi DJ. *Pediatrics* 2010;125:26-33
Bacterial Pathogens in Complicated Community-Acquired Pneumonia: NCH 2006-2010

- S. pneumoniae; 46%
- Unknown, 33%
- S. aureus; 8%
- S. pyogenes; 7%
- Multiple pathogens, 2%
- Other**; 3%

**Other includes:
- 2 Mycoplasma pneumoniae
- 1 Viridans group strep
- 1 S. mitis
- 1 S. anginosus
- 1 H. influenzae
- 1 Eikenella spp.
Pneumococcal pneumonia with massive effusion pushing the mediastinal structures into the left area of the chest.
S. pneumoniae necrotizing pneumonia

7/17/01
Necrotizing Pneumonia with Pyopneumothorax

Necrotizing pneumonia

Pyopneumothorax
Treatment of Complicated CAP

- Pleural fluid drainage is recommended for all moderate or large effusions
- Choice of drainage technique depends on local expertise
  - Chest thoracostomy and fibrinolytics
  - Video-assisted thoracoscopic surgery (VATS)