

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

Infection	Systemic Antibiotics Indicated		
	<u>Always</u>	<u>Sometimes</u>	<u>Never</u>
Viral URI			X
Acute Purulent Rhinitis			X
Acute Otitis Media		X	
Acute Bacterial Sinusitis	X		
Pharyngitis		X	
Pneumonia		X	
Bronchiolitis			X
Acute Bronchitis			X

Viral Illnesses

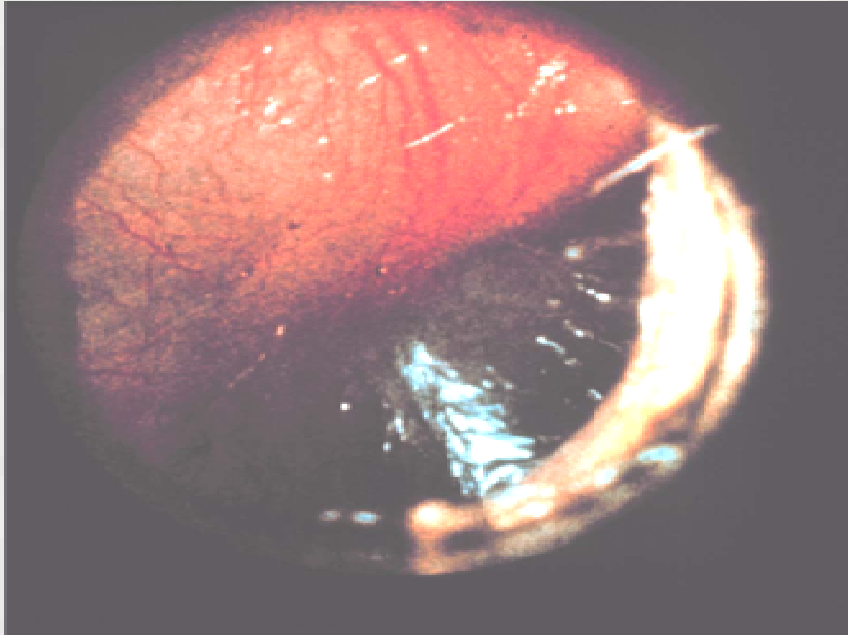
- **Common colds, nonspecific URI, Acute Purulent Rhinitis, Acute Cough Illness and Acute Bronchitis in children are due to virus infections**
- **Antibiotics are never indicated**

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 ≤ 10 days***

*Cochrane Database Syst. Rev. 2013;June4:6.CD000247

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 $\geq 39^{\circ}\text{C}$
- Bilateral >> unilateral
- Age ≤ 23 months

Spontaneous Bacteriologic Cure Rate in Acute Otitis Media

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

Acute Otitis Media

Benefits of Antibiotic Treatment

- $\geq 50\%$ 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 \rightarrow 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

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

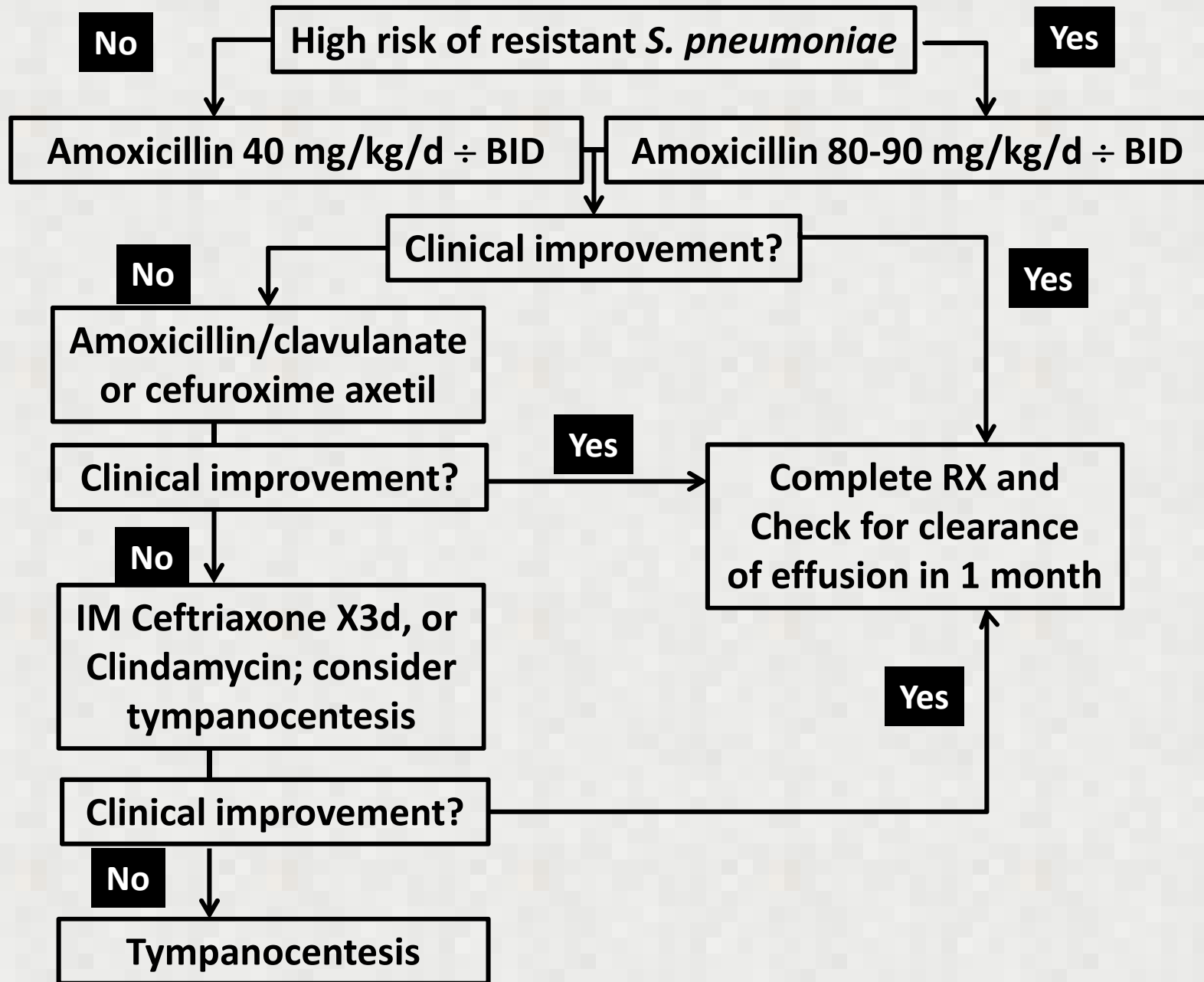
Therapy

- 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



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 ≥ 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 ≥ 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 ≥ 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. Amoxicillin clavulanate
3. No initial treatment/observation

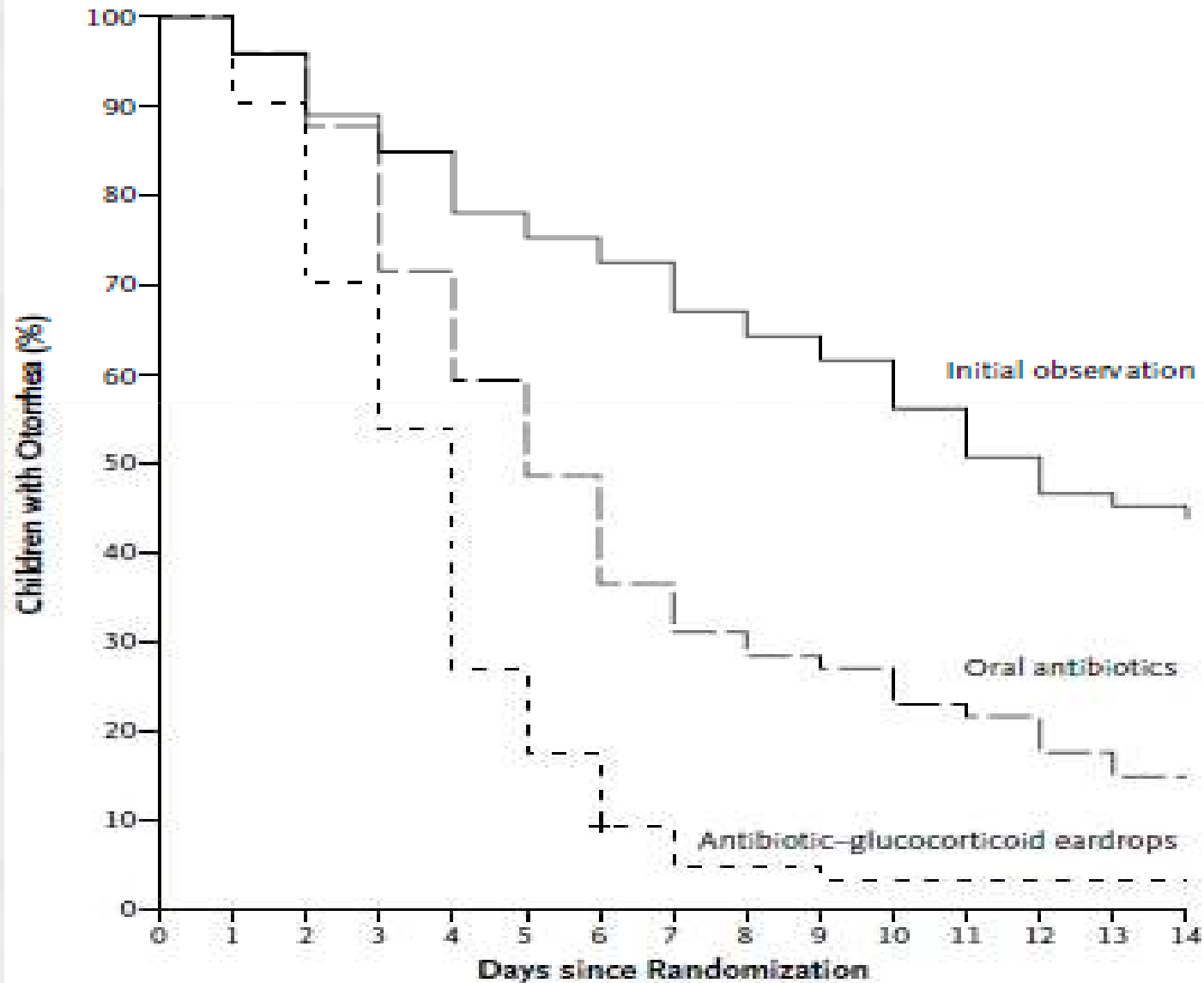
Acute Tympanostomy – Tube Otorrhea

Study Results

Treatment	Otorrhea at 2 weeks	Median Duration of Otorrhea
Hydrocortisone – Bacitracin-Colistin ear drops	5%	4 days
Amoxicillin Clavulanate	44%	5 days
Observation	55%	12 days

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 $\geq 39^{\circ}$ 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**

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

Wald ER. *Pediatrics* 2013;132:e262.

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

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**

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**

Streptococcal Pharyngitis

Therapy

- **DO NOT treat empirically**
- **Antibiotics – 10 days**
 - **Amoxicillin (once daily dosing – 50 mg/kg/day)**
 - **Penicillin**

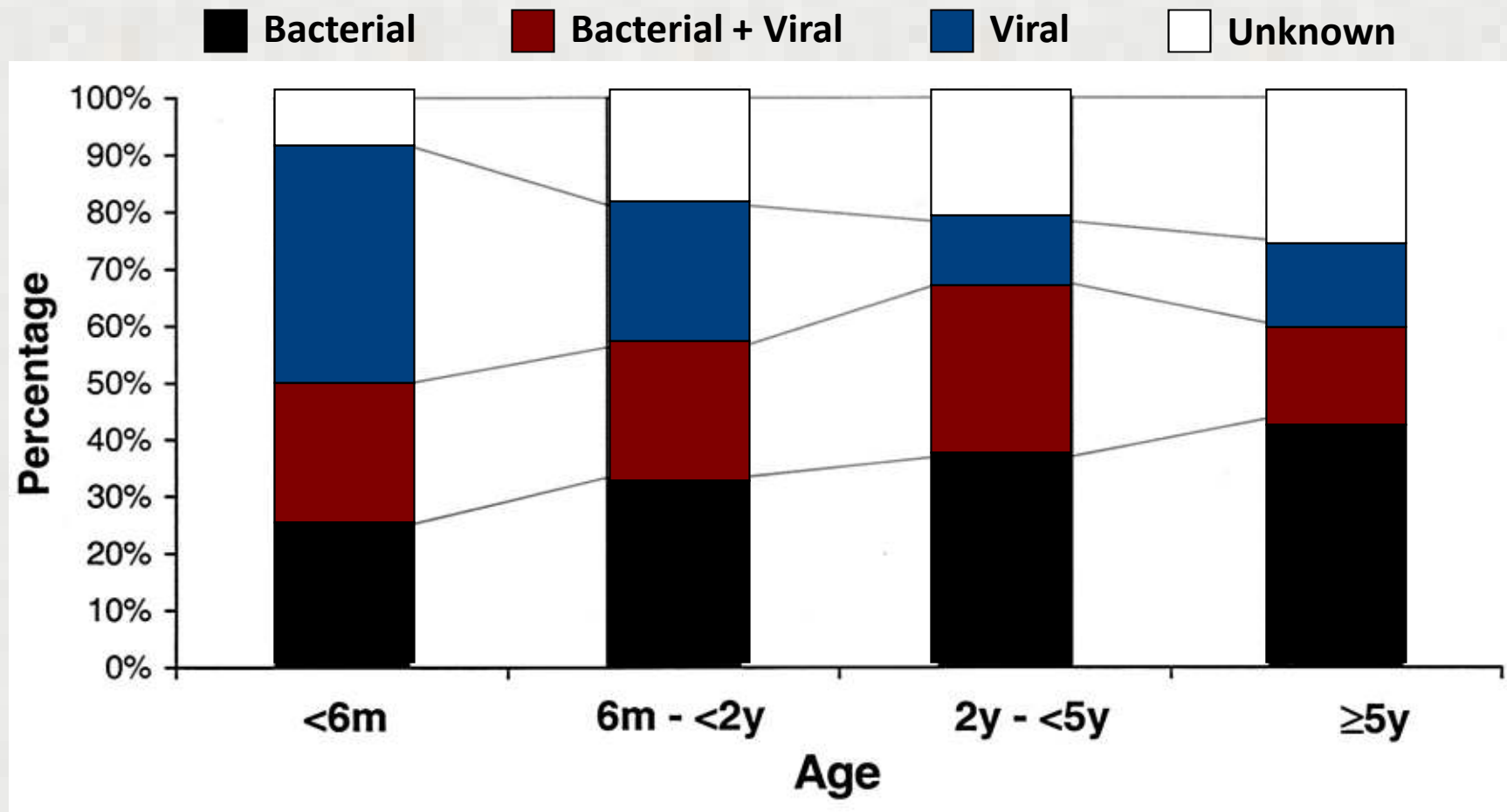
Definition of Pediatric Community-Acquired Pneumonia (CAP)

- 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

Age	Organism
<5 years	Viruses (RSV, PIV, Influenza, HMPV, Adenovirus, Rhinovirus) <i>Streptococcus pneumoniae</i> <i>Streptococcus pyogenes</i> <i>Staphylococcus aureus</i>
>5 years	<i>Streptococcus pneumoniae</i> <i>Mycoplasma pneumoniae</i> <i>Chlamydia pneumoniae</i>

Etiology of Community-Acquired Pneumonia (CAP) in 154 Hospitalized Children



Michelow, et al. *Pediatrics* 2004;113:701-707

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,a} Carrie L. Byington,^{2,a} Samir S. Shah,^{3,a} Brian Alverson,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

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

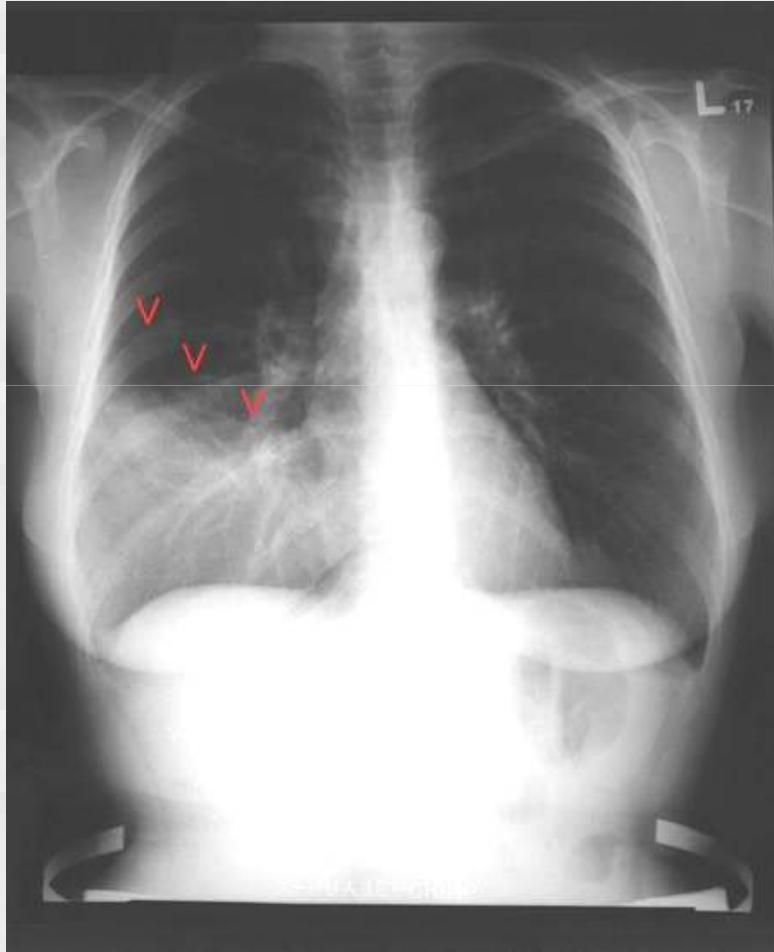
Community-Acquired Pneumonia: Imaging

- **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**

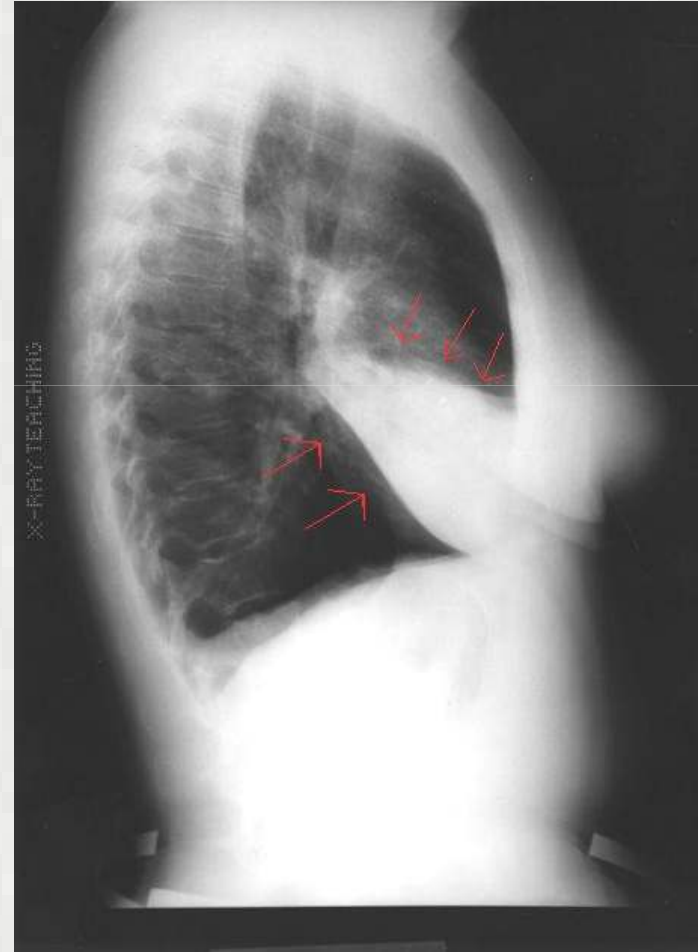
Diagnostic Testing: Radiography

- **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. pneumoniae*
 - 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

	Empiric Therapy for Presumed Bacterial Pneumonia	Empiric Therapy for Presumed Atypical Pneumonia
Less than 5 years of age (Preschool)**	Amoxicillin, oral (90 mg/kg/day <u>div tid</u>)	Azithromycin oral (10 mg/kg on day 1, followed by 5 mg/kg/day once daily days 2-5)
	Alternatives: Amoxicillin/clavulanate	Alternatives: Clarithromycin oral (15 mg/kg/day <u>div bid</u> x 7-14 d); erythromycin oral (40 mg/kg/day <u>div qid</u>)
5 years of age and older	Amoxicillin, oral (90 mg/kg/day <u>div tid</u> to a max of 3 gm/day) 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.	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)
	Alternatives: Amoxicillin/clavulanate	Alternatives: Clarithromycin oral (15 mg/kg/day <u>div bid</u> to a max of 1 gm daily); erythromycin; doxycycline for children older than 7 years

**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

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

**Antibiotics are not routinely required for preschool-aged children with pneumonia, without suspicion of bacterial co-infection

Anti-Infective Treatment

- **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.

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

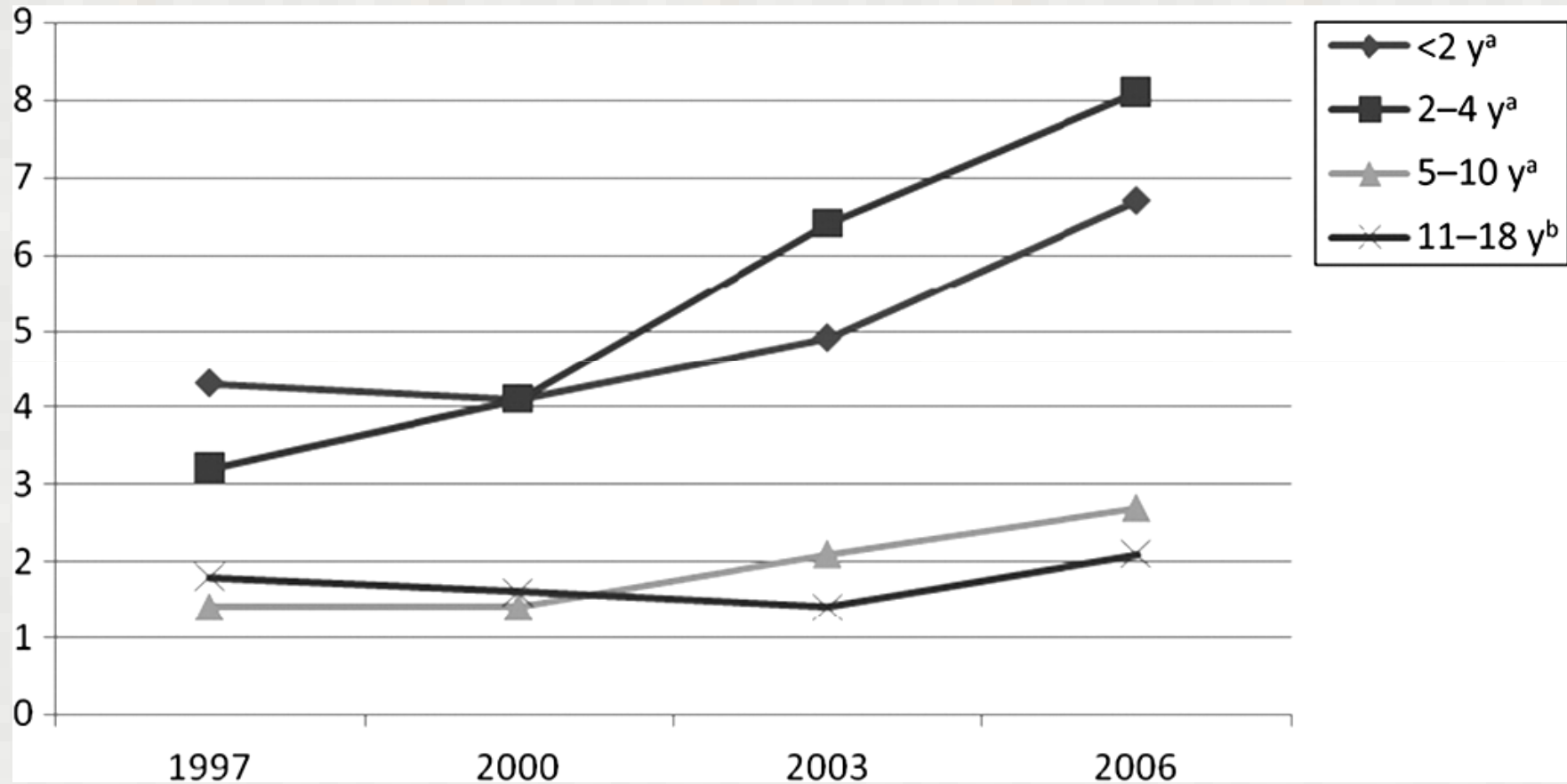
- Prolonged fever or fever that resolved and has now returned
- Chest pain
- Abdominal pain
- Use of ibuprofen
- Use of azithromycin or IM ceftriaxone without improvement
- Recent history of varicella or influenza

Complications of Community-Acquired Pneumonia

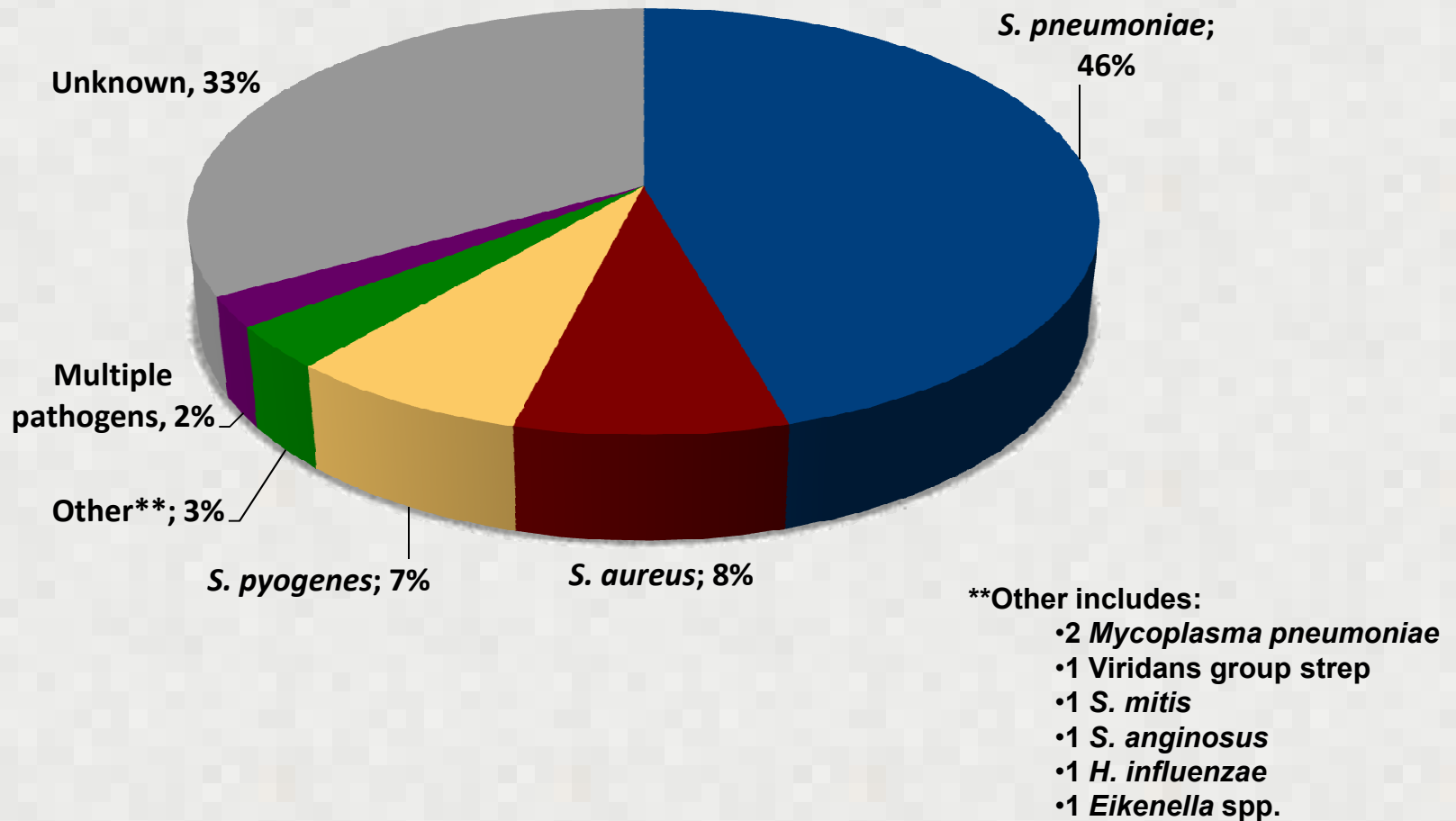
- Parapneumonic effusion
- Empyema
- Necrotizing pneumonia
 - *S. pneumoniae*, *S. aureus*, GAS
- Lung abscess
 - Anaerobes, *Streptococcus* species, *S. aureus*
- Bronchopleural fistula
- Empyema necessitans



Empyema-associated Hospitalization Rates Per 100,000 Children in 1997, 2000, 2003, and 2006



Bacterial Pathogens in Complicated Community-Acquired Pneumonia: NCH 2006-2010



Pneumococcal pneumonia with massive effusion pushing the mediastinal structures into the left area of the chest.

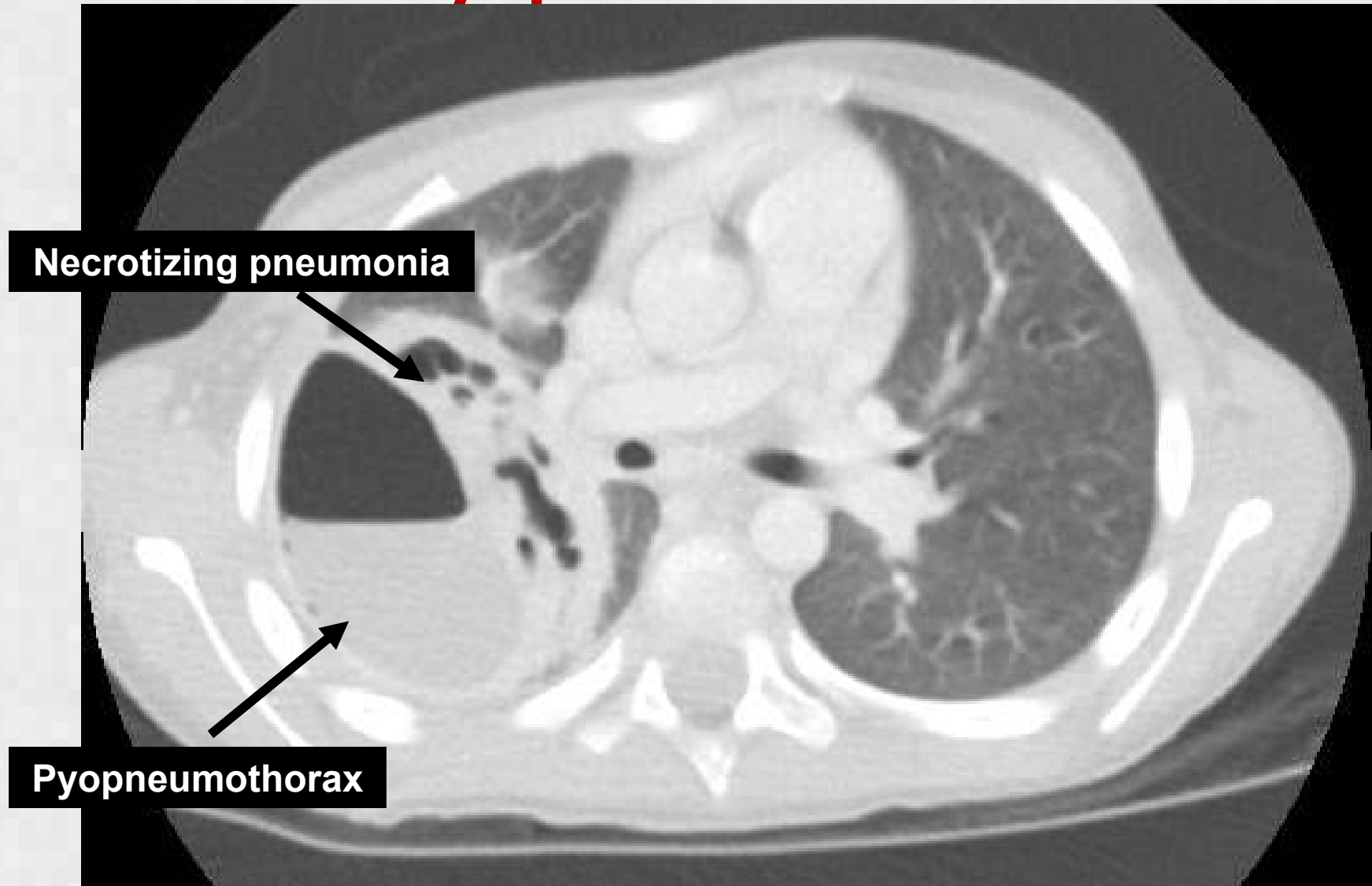


S. pneumoniae necrotizing pneumonia



7/17/01

Necrotizing Pneumonia with Pyopneumothorax



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)**