Evidence Based Treatment of Pediatric Respiratory Tract Infections
August 23, 2019
Objectives

• To review the treatments recommended by most recent American Academy of Pediatrics and Infectious Diseases Society of America guidelines regarding the following disease states:
  o Acute Otitis Media
  o Community Acquired Pneumonia
  o Pharyngitis
  o Sinusitis
“As many as 10 million antibiotic prescriptions per year are directed toward respiratory conditions for which they are unlikely to provide benefit.”

The number of new antibiotics developed and approved has steadily decreased in the past three decades, leaving fewer options to treat resistant bacteria.

MICROORGANISMS WITH A THREAT LEVEL OF SERIOUS

Multidrug-resistant *Acinetobacter*
Drug-resistant *Campylobacter*
Fluconazole-resistant *Candida* (a fungus)
Extended spectrum β-lactamase producing *Enterobacteriaceae* (ESBLs)
Vancomycin-resistant *Enterococcus* (VRE)
Multidrug-resistant *Pseudomonas aeruginosa*
Drug-resistant non-typhoidal *Salmonella*
Drug-resitant *Salmonella Typhi*
Drug-resistant *Shigella*
Methicillin-resistant *Staphylococcus aureus* (MRSA)
Drug-resistant *Streptococcus pneumoniae*
Drug-resistant *tuberculosis*
Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: a systematic review and meta-analysis

Costelloe, C et al. BMJ 2010:340;c2096
The Diagnosis and Management of Acute Otitis Media

Allan S. Lieberthal, Aaron E. Carroll, Tasnee Chonmaitree, Theodore G. Ganiats, Alejandro Hoberman, Mary Anne Jackson, Mark D. Joffe, Donald T. Miller, Richard M. Rosenfeld, Xavier D. Sevilla, Richard H. Schwartz, Pauline A. Thomas and David E. Tunkel

*Pediatrics* 2013;131;e964; originally published online February 25, 2013; DOI: 10.1542/peds.2012-3488
Definitions

**AOM** – the rapid onset of signs and symptoms of inflammation in the middle ear

**OME** – inflammation of the middle ear with liquid collected in the middle ear; the signs and symptoms of acute infection are absent

<table>
<thead>
<tr>
<th>Signs</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tympanic membrane:</td>
<td>otalgia</td>
</tr>
<tr>
<td>bulging</td>
<td>fever</td>
</tr>
<tr>
<td>erythema</td>
<td>irritability</td>
</tr>
<tr>
<td>otorrhea</td>
<td>nasal stuffiness</td>
</tr>
<tr>
<td>nonmobile</td>
<td>changes in sleep behavior</td>
</tr>
</tbody>
</table>
Definitions

Uncomplicated AOM - AOM without otorrhea (discharge from the ear)

Severe AOM – AOM with the presence of moderate to severe otalgia or fever equal to or higher than 39°C (102.2°F).

Non-severe AOM – AOM with the presence of mild otalgia and a temperature below 39°C (102.2°F)

Recurrent AOM:

a. Three or more well documented and separate AOM episodes in the past 6 months.

   OR

b. Four or more episodes in the preceding 12 months with at least 1 episode in the past 6 months.
Criteria for AOM:
• Moderate to severe bulging of tympanic membrane (TM) OR new onset otorrhea
• Mild bulging of the TM AND recent (<48 hours) ear pain or intense erythema of TM
Causes

Bacteria
- *S. Pneumoniae* 35-40%
- *H. Influenzae* 30-35%
- *M. Catarrhalis* 15-20%
- GAS 3%

Bacterial Resistance
- Rates vary geographically
- Beta lactamase production
  - *Hemophilus. influenza* 35-45%
  - *Moraxella Catarrhalis* 100%

Viruses
- 40 – 70% of cases
- RSV, rhinovirus, coronavirus, parainfluenza virus
Treatment: otalgia

Oral analgesics: relieve pain associated with AOM within 24 hours and should be used whether antibiotics are used or not.
- Ibuprofen 5 – 10 mg/kg/dose every 6 hours as needed (max 40 mg/kg/day)
- Acetaminophen 10-15 mg/kg/dose every 4-6 hours as needed (max dose 75 mg/kg/day)

Antibiotic therapy: Does NOT provide symptomatic relief in the first 24 hours, and even after 3-7 days, there may be persistent pain, fever, or both in 30% of children.¹

Topical therapy: There is limited evidence that ear drops are effective at 30 minutes and unclear if results are due to natural course of illness, placebo effect of receiving treatment, soothing effect of any liquid in the ear, or the drops themselves.²

Treatment: Observation an option for SOME

- Deferment of antibiotics for 48-72 hours
- Controlled trials indicate that between 7 to 20 children must be treated for one child to benefit from antibiotic therapy
- AOM resolves spontaneously in most patients
- Decreases cost, resistance, and unwanted adverse effects
- WHO QUALIFIES FOR OBSERVATION?
## Treatment: Summary

<table>
<thead>
<tr>
<th>Acute Otitis Media</th>
<th>Children 6-23 months</th>
<th>Children ≥ 24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Severe</strong>&lt;br&gt;(moderate or severe otalgia OR otalgia for at least 48 hours OR temperature 39°C [102.2°F] or higher)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td>Antibiotics</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Bilateral</td>
<td>Antibiotics</td>
<td>Antibiotics</td>
</tr>
<tr>
<td><strong>Mild</strong>&lt;br&gt;(mild otalgia for less than 48 hours, temperature less than 39°C [102.2°F])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral</td>
<td>Antibiotics or observation</td>
<td>Antibiotics or observation</td>
</tr>
<tr>
<td>Bilateral</td>
<td>Antibiotics</td>
<td>Antibiotics or observation</td>
</tr>
<tr>
<td>Recommended First Line treatment</td>
<td>Alternative treatment (if penicillin allergic)</td>
<td>Recommended First Line treatment</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>-----------------------------------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Amoxicillin (80-90 mg/kg per day in 2 divided doses) OR Amoxicillin clavulanate (90 mg/kg per day of amoxicillin, with 6.4 mg/kg per day of clavulanate) (amox:clavulanate ratio, 14:1) in 2 divided doses</td>
<td>Cefdinir (3rd gen) (14 mg/kg/day in one or two doses) Cefuroxime (2nd gen) (30 mg/kg per day in 2 divided doses) Cefpodoxime (3rd gen) (10 mg/kg per day in 2 divided doses) Ceftriaxone (3rd gen) (50 mg IM or IV per day for 1 or 3 days)</td>
<td>Amoxicillin clavulanate (90 mg/kg per day of amoxicillin, with 6.4 mg/kg per day of clavulanate in 2 divided doses) OR Ceftriaxone (50 mg IM or IV for 3 days)</td>
</tr>
<tr>
<td>Initial Immediate or Delayed treatment abx</td>
<td>Abx treatment after 48-72 of failure of initial abx</td>
<td></td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>-----------------------------------------------</td>
<td></td>
</tr>
<tr>
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<td>Amoxicillin clavulanate (90 mg/kg per day of amoxicillin with 6.4 mg/kg per day of clavulanate in 2 divided doses)</td>
<td></td>
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<tr>
<td>OR</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Amoxicillin clavulanate (90 mg/kg per day of amoxicillin, with 6.4 mg/kg per day of clavulanate) (amox:clavulanate ratio, 14:1) in 2 divided doses</td>
<td>Ceftriaxone, 3 d Clindamycin (30-40 mg/kg /day in 3 divided doses), with 3rd generation cephalosporin</td>
<td></td>
</tr>
<tr>
<td><strong>Alternative treatment (if penicillin allergic)</strong></td>
<td><strong>Alternative treatment</strong></td>
<td></td>
</tr>
<tr>
<td>Cefdinir (3rd gen) (14 mg/kg/day in one or two doses)</td>
<td>Clindamycin (30-40 mg/kg /day PLUS 3rd generation cephalosporin)</td>
<td></td>
</tr>
<tr>
<td>Cefuroxime (2nd gen) (30 mg/kg per day in 2 divided doses)</td>
<td>Failure of second antibiotic</td>
<td></td>
</tr>
<tr>
<td>Cefpodoxime (3rd gen) (10 mg/kg per day in 2 divided doses)</td>
<td>Clindamycin (30-40 mg/kg/day PLUS 3rd generation cephalosporin)</td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone (3rd gen) (50 mg IM or IV per day for 1 or 3 days)</td>
<td>Tympanocentesis</td>
<td></td>
</tr>
<tr>
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<td></td>
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<td></td>
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<tr>
<td>OR</td>
<td>OR</td>
<td></td>
</tr>
<tr>
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<td></td>
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<td></td>
</tr>
<tr>
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<td>Tympanocentesis</td>
<td></td>
</tr>
</tbody>
</table>

Consult specialist
Beta lactamases

Penicillin

Lactam ring

β-lactamase (penicillinase) breaks this bond

Inactive penicillin
Clavulanic acid

β-lactamase inhibitor (clavulanic acid) + β-lactamase → Acyl enzyme complex
Pharmacodynamics of beta lactams

• Amoxicillin half life 1-2 hours in children
• Dosing infants and children: 80-90 mg /kg/day every 12 hours
• Compliance important to prevent resistance
# Amoxicillin clavulanate preparations

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Amoxicillin</th>
<th>Clavulanate</th>
<th>Clav to Amox ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>125/5 ml suspension</td>
<td>125 mg</td>
<td>31.25 mg</td>
<td>1:4</td>
</tr>
<tr>
<td>200/5 ml suspension</td>
<td>200 mg</td>
<td>28.5 mg</td>
<td>1:7</td>
</tr>
<tr>
<td>250/5 ml suspension</td>
<td>250 mg</td>
<td>62.5 mg</td>
<td>1:4</td>
</tr>
<tr>
<td>400/5 ml suspension</td>
<td>400 mg</td>
<td>57 mg</td>
<td>1:7</td>
</tr>
<tr>
<td>600/5 ml suspension</td>
<td>600 mg</td>
<td>42.9 mg</td>
<td>1:14</td>
</tr>
<tr>
<td>250 mg tablet</td>
<td>250 mg</td>
<td>125 mg</td>
<td>1:2</td>
</tr>
<tr>
<td>500 mg tablet</td>
<td>500 mg</td>
<td>125 mg</td>
<td>1:4</td>
</tr>
<tr>
<td>875 mg tablet</td>
<td>875 mg</td>
<td>125 mg</td>
<td>1:7</td>
</tr>
<tr>
<td>200 mg chewable tablet</td>
<td>200 mg</td>
<td>28.5 mg</td>
<td>1:7</td>
</tr>
<tr>
<td>400 mg chewable tablet</td>
<td>400 mg</td>
<td>57 mg</td>
<td>1:7</td>
</tr>
<tr>
<td>1000 mg XR tablet</td>
<td>1000 mg</td>
<td>62.5</td>
<td>1:16</td>
</tr>
</tbody>
</table>
Penicillin allergy

• Cross reactivity to cephalosporins among penicillin allergic patients has been reported to be approximately 10%.

• The chemical structure of the cephalosporin determines the risk of cross reactivity between specific agents.

• The degree of cross reactivity is higher between penicillins and first generation cephalosporins but is negligible with second and third generation cephalosporins.
## Antibiotic susceptibilities

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Strep pneumo susceptibility</th>
<th>H Influenza susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefdinir</td>
<td>70-80%</td>
<td>98%</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>70-80%</td>
<td>98%</td>
</tr>
<tr>
<td>Amoxicillin¹</td>
<td>84-92%</td>
<td>58%</td>
</tr>
<tr>
<td>Amoxicillin clavulanate²</td>
<td>&gt; 90%</td>
<td>100%</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Usually susceptible but will not likely be effective for multi-drug resistant serotypes</td>
<td>0%</td>
</tr>
</tbody>
</table>

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Penicillin – cephalosporin cross reactivity

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Studies</th>
<th>No. of patients</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1st generation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All 1st-generation cephalosporins</td>
<td>2</td>
<td>115</td>
<td>OR, 95% CI</td>
<td>4.13 (0.70–24.51)</td>
</tr>
<tr>
<td><strong>2nd generation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All 2nd-generation cephalosporins</td>
<td>2</td>
<td>685</td>
<td>OR, 95% CI</td>
<td>1.13 (0.33–5.40)</td>
</tr>
<tr>
<td><strong>3rd generation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All 3rd-generation cephalosporins</td>
<td>1</td>
<td>685</td>
<td>OR, 95% CI</td>
<td>0.75 (0.15–3.66)</td>
</tr>
<tr>
<td>All generation of cephalosporins</td>
<td>7</td>
<td>1831</td>
<td>OR, 95% CI</td>
<td>1.44 (0.65–3.19)</td>
</tr>
<tr>
<td>2nd- and 3rd-generation cephalosporins</td>
<td>3</td>
<td>1370</td>
<td>OR, 95% CI</td>
<td>1.02 (0.36–2.88)</td>
</tr>
</tbody>
</table>
# Duration of treatment

<table>
<thead>
<tr>
<th>Age</th>
<th>Duration</th>
<th>Illness type</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 years</td>
<td>10 days</td>
<td>All</td>
</tr>
<tr>
<td>2-5 years</td>
<td>7 days</td>
<td>Mild to moderate</td>
</tr>
<tr>
<td>≥ 6 years</td>
<td>5-7 days</td>
<td>Mild to moderate</td>
</tr>
</tbody>
</table>

# Follow-up

<table>
<thead>
<tr>
<th>Time after successful treatment of</th>
<th>Presence of MEE</th>
<th>If asymptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two weeks</td>
<td>60-70%</td>
<td>NO ANTIBIOTICS</td>
</tr>
<tr>
<td>One month</td>
<td>40%</td>
<td>NO ANTIBIOTICS</td>
</tr>
<tr>
<td>Three months</td>
<td>10-25%</td>
<td>NO ANTIBIOTICS</td>
</tr>
</tbody>
</table>
Probiotics for the prevention and treatment of antibiotic associated diarrhea (AAD)

• Meta-analysis including 23 studies involving 3,938 children (2 weeks to 17 years of age) studied from 1 – 12 weeks following antibiotic therapy.

• Received probiotics or placebo co-administered with antibiotics to prevent AAD

• Incidence of AAD in probiotic group 8% (163/1992) compared to 19% (364/1992) in the control group

• No significant difference in adverse effects compared to placebo

• Probiotics *Lactobacillus rhamnosus* or *Saccharomyces boulardii* at 5 to 40 billion CFU/day

• Serious side effects have been noted in severely debilitated or immunocompromised children with underlying risk factors including central venous catheters and disorders associated with bacterial or fungal translocation.

Antibiotic Prophylaxis?

- Long term low dose antibiotic use has been used to treat children with recurrent AOM to prevent subsequent episodes.
- An estimated 5 children would need to be treated for 1 year to prevent 1 episode of AOM.
- This decrease occurred only while the prophylactic antibiotic was given.
- Antibiotic prophylaxis is not appropriate for MEE or for children with infrequent episodes of AOM.
- Risk of antibiotic resistance, adverse effects of diarrhea and allergic reactions benefit ratio must be weighed.

Prevention of recurrent otitis media

• Insertion of tympanostomy tubes
• Modification of risk factors - eliminate smoking
• Vaccination
  o Pneumococcal conjugate vaccine (Prevnar)
  o Influenza vaccine
  o H. influenza vaccine (Hib)
Streptocci pneumoniae

- Aerobic, gram + cocci that grow in pairs
- Alpha hemolytic
- Encapsulated
- 90 different serotypes
- Difference in polysaccharide capsule
  - Target for the vaccine
  - Normal flora of the upper respiratory tract
- Most common cause of community acquired pneumonia
  - Responsible for about 25% of all cases
- Frequent cause of sinusitis and otitis media
Prevention

Two pneumococcal polysaccharide vaccines are currently available in the US:
– PPSV23 (Pneumovax 23)
  Covers 23 serotypes of *S. pneumoniae*;
  1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14,
  15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F
  Indicated for adults age 50 or greater, however may be used in kids and adults older than 2 YEARS OF AGE at higher risk for pneumococcal disease (i.e. diabetics, CHF, CVD, chronic Pulmonary disease and anatomic asplenia)

– PCV13 (Prevnar 13)
  Covers 13 serotypes of *S pneumoniae*
  1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F
  Has an indication for kids aged from 6 weeks to 17 years in addition to that of PPSV23 indication

Both vaccines also indicated in immunocompromised patients
Figure 1. Annual and semiannual incidences per 1000 of pneumococcal (Pneu omococcal) otitis media (OM) episodes in children aged <2 years in southern Israel, July 2004–June 2013. Arrows indicate (1) 7-valent pneumococcal conjugate vaccine (PCV7) in private market; (2) PCV7 introduced to the Israeli National Immunization Plan (NIIP); (3) 13-valent pneumococcal conjugate vaccine (PCV13) introduced to the Israeli NIIP; (4) >70% of children aged 7–11 months received ≥2 doses of PCV13. Abbreviation: PCV, pneumococcal conjugate vaccine.

Figure 3. Annual incidences per 1000 of all-cause otitis media (OM) episodes in children aged <2 years in southern Israel, July 2004–June 2013. Arrows indicate (1) 7-valent pneumococcal conjugate vaccine (PCV7) in private market; (2) PCV7 introduced to the Israeli National Immunization Plan (NIIP); (3) 13-valent pneumococcal conjugate vaccine (PCV13) introduced to the Israeli NIIP; (4) >70% of children aged 7–11 months received ≥2 doses of PCV13. Abbreviation: PCV, pneumococcal conjugate vaccine.
Case 1

A.R. is an 11 month old girl (weight 10 kg) who presents with a 3 day history of fever (38.5°C), increased fussiness, decreased appetite, and increased lethargy. She has also been pulling on her right ear. An examination of both ears reveals that each ear has a bulging, erythematous, nonmobile tympanic membrane. Her medical history is noncontributory. She has no history of antibiotic use and no drug allergies. She has two older siblings and attends day care 3 days per week. Which treatment option is best to recommend for A. R.?

A. Augmentin ES 400 mg orally twice daily.
B. Amoxicillin 450 mg orally twice daily.
C. Ceftriaxone 750 mg IM X 1 dose
D. Observation plus pain management X 48 hours
Best treatment option

A. Augmentin ES 400 mg orally twice daily
   ✓ Amoxicillin 450 mg orally twice daily
C. Ceftriaxone 750 mg intramuscularly X 1 dose
D. Observation plus pain management X 48 hours
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,1,2 Carrie L. Byington,2,3 Samir S. Shah,3,4 Brian Alverson,4 Edward R. Carter,5 Christopher Harrison,6 Sheldon L. Kaplan,7 Sharon E. Mace,4 George H. McCracken Jr,9 Matthew R. Moore,10 Shawn D. St Peter,11 Jana A. Stockwell,12 and Jack T. Swanson13

1Department of Pediatrics, University of California San Diego School of Medicine and Rady Children's Hospital San Diego, San Diego, California; 2Department of Pediatrics, University of Utah School of Medicine, Salt Lake City, Utah; 3Departments of Pediatrics, and Biostatistics and Epidemiology, University of Pennsylvania School of Medicine, and Division of Infectious Diseases, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania; 4Department of Pediatrics, Rhode Island Hospital, Providence, Rhode Island; 5Pulmonary Division, Seattle Children's Hospital, Seattle Washington; 6Department of Pediatrics, Children's Mercy Hospital, Kansas City, Missouri; 7Department of Pediatrics, Baylor College of Medicine, Houston, Texas; 8Department of Emergency Medicine, Cleveland Clinic, Cleveland, Ohio; 9Department of Pediatrics, University of Texas Southwestern, Dallas, Texas; 10Centers for Disease Control and Prevention, Atlanta, Georgia; 11Department of Pediatrics, University of Missouri—Kansas City School of Medicine, Kansas City, Missouri; 12Department of Pediatrics, Emory University School of Medicine, Atlanta, Georgia; and 13Department of Pediatrics, McLennan Clinic, Ames, Iowa

Evidence-based guidelines for management of infants and children with community-acquired pneumonia (CAP) were prepared by an expert panel comprising clinicians and investigators representing community pediatrics, public health, and the pediatric specialties of critical care, emergency medicine, hospital medicine, infectious diseases, pulmonology, and surgery. These guidelines are intended for use by primary care and subspecialty providers responsible for the management of otherwise healthy infants and children with CAP in both outpatient and inpatient settings. Site-of-care management, diagnosis, antimicrobial and adjunctive surgical therapy, and prevention are discussed. Areas that warrant future investigations are also highlighted.
CAP Guideline

Inclusion Criteria
• Healthy children > 56 days through 18 years

Exclusion Criteria
• Cystic Fibrosis
• Immunodeficiency
• Tracheostomy
• Patients at risk for aspiration pneumonia
• Hospital or institutional acquired pneumonia
# CAP diagnostic testing in the *outpatient* setting

<table>
<thead>
<tr>
<th>Test</th>
<th>Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood cultures</td>
<td>NO if patient nontoxic, fully immunized YES if fail to demonstrate clinical improvement, progressive symptoms or clinical deterioration after initial antibiotics</td>
</tr>
<tr>
<td>Sputum gram stain and culture</td>
<td>NO</td>
</tr>
<tr>
<td>Urinary antigen detection for pneumococcal PNA</td>
<td>NO</td>
</tr>
<tr>
<td>Sensitive and specific testing for viral pathogens</td>
<td>YES</td>
</tr>
<tr>
<td>Atypical bacteria</td>
<td>YES – IF with signs and symptoms of <em>Mycoplasma</em> pneumonia</td>
</tr>
<tr>
<td>CBC</td>
<td>NO</td>
</tr>
<tr>
<td>Acute phase reactants (ESR, CRP, procalcitonin)</td>
<td>NO</td>
</tr>
<tr>
<td>Pulse oximetry</td>
<td>YES</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>NO</td>
</tr>
</tbody>
</table>
CAP Pathogens

- *Streptococcus pneumoniae*
- *Haemophilus influenza* (due to H flu type b conjugate vaccine for past 25 years this has virtually been eliminated in children; most seen in chronic lung disease)
- Group A Strep (Pyogenes)
- *Staphylococcus aureus*
- *Mycoplasma pneumoniae*
Table 7. Empiric Therapy for Pediatric Community-Acquired Pneumonia (CAP)

<table>
<thead>
<tr>
<th>Site of care</th>
<th>Presumed bacterial pneumonia</th>
<th>Presumed atypical pneumonia</th>
<th>Presumed influenza pneumonia¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 years old (preschool)</td>
<td>Amoxicillin, oral (90 mg/kg/day in 2 dosesᵇ)</td>
<td>Azithromycin oral (10 mg/kg on day 1, followed by 5 mg/kg/day once daily on days 2–5);</td>
<td>Oseltamivir</td>
</tr>
<tr>
<td></td>
<td>Alternative: oral amoxicillin clavulanate (amoxicillin component, 90 mg/kg/day in 2 dosesᵇ)</td>
<td>Alternatives: oral clarithromycin (15 mg/kg/day in 2 doses for 7–14 days) or oral erythromycin (40 mg/kg/day in 4 doses)</td>
<td></td>
</tr>
<tr>
<td>≥5 years old</td>
<td>Oral amoxicillin (90 mg/kg/day in 2 dosesᵇ to a maximum of 4 g/dayᶜ); for children with presumed bacterial CAP who do not have clinical, laboratory, or radiographic evidence that distinguishes bacterial CAP from atypical CAP, a macrolide can be added to a β-lactam antibiotic for empiric therapy; alternative: oral amoxicillin clavulanate (amoxicillin component, 90 mg/kg/day in 2 dosesᵇ to a maximum dose of 4000 mg/day, eg, one 2000-mg tablet twice dailyᵇ)</td>
<td>Oral azithromycin (10 mg/kg on day 1, followed by 5 mg/kg/day once daily on days 2–5 to a maximum of 500 mg on day 1, followed by 250 mg on days 2–5); alternatives: oral clarithromycin (15 mg/kg/day in 2 doses to a maximum of 1 g/day); erythromycin, doxycycline for children ≥7 years old</td>
<td>Oseltamivir or zanamivir (for children 7 years and older); alternatives: peramivir, oseltamivir and zanamivir (all intravenous) are under clinical investigation in children; intravenous zanamivir available for compassionate use</td>
</tr>
</tbody>
</table>

ᵇ Dosage recommendations are based on local susceptibility data.
Proportion of guideline-concordant antibiotics prescribed for children by type of infection at FH-MCHS August 2009–July 2010

Saleh, et al Clin Res Infect Dis 2015 10;2(1)
How can resistance be minimized?

- Limit exposure
- Limit spectrum of activity of antimicrobials
- Use proper dosage of antimicrobial to achieve a minimal effective concentration at the site of infection
- Treat for the shortest effective duration
Treatment courses of 10 days have been best studied. Although shorter courses may be just as effective, particularly for more mild disease managed on an outpatient basis.

Infections caused by MRSA may require longer treatment than those caused by *S. Pneumoniae*.

### Table 6. Influenza Antiviral Therapy

<table>
<thead>
<tr>
<th>Drug [186187]</th>
<th>Formulation</th>
<th>Dosing recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Treatment</td>
</tr>
<tr>
<td>Ose-ltamivir</td>
<td>75-mg capsule; 60 mg/5 mL Suspension</td>
<td>≥24 months old: 150 mg/day in 2 doses for 5 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥24 months old: 4 mg/kg/day in 2 doses, for a 5-day treatment course</td>
</tr>
</tbody>
</table>
Prevention of pediatric CAP

• Immunize with vaccines for bacterial pathogens including
  o *Strep pneumomiae*
  o *Haemophilus influenza* type b
  o *Bordetella pertussis*

• All infants ≥ 6 months of age and all children and adolescents should be immunized annually with vaccines for influenza

• Parents and caretakers of infants < 6 months of age, including pregnant adolescents, should be immunized with vaccines for influenza and pertussis to protect the infant from exposure
Effect of pneumococcal conjugate vaccine on penicillin resistance

Figure 2. Annual Incidence of Invasive Disease Caused by Penicillin-Nonsusceptible Pneumococci in Persons Two Years of Age or Older, 1996 to 2004.
Case 2

A previously healthy 13-month-old girl is brought to the office with a 2-day history of fever and increasing cough. Her mother states that the child has continued to breastfeed and has a normal number of wet diapers. Her immunizations are up to date. She is alert and mildly ill appearing. Her temperature is 102.1°F (38.9°C), heart rate is 142 beats/min, respiratory rate is 50 breaths/min, and oxygen saturation is 95% on room air. At physical examination, there is no grunting or chest retractions. There are crackles heard over the right lung base. The remainder of the examination findings are normal. She has no known allergies. Which of the following is the most likely pathogen?

A. Bordetella pertussis.
B. Haemophilus influenzae type B.
C. Histoplasma capsulatum.
D. Mycoplasma pneumoniae.
E. Streptococcus pneumoniae.
For the same 13-month-old girl in the previous question, which of the following is the most appropriate next step in treatment?

A. Admit her to the hospital for intravenous (IV) ceftriaxone and vancomycin.
B. Admit her to the hospital for IV ceftriaxone and levofloxacin.
C. Outpatient amoxicillin.
D. Outpatient azithromycin.
E. Outpatient cefdinir.
Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012 Update by the Infectious Diseases Society of America

Stanford T. Shulman,1 Alan L. Bisno,2 Herbert W. Clegg,3 Michael A. Gerber,4 Edward L. Kaplan,5 Grace Lee,6 Judith M. Martin,7 and Chris Van Beneden8

1Department of Pediatrics, Division of Infectious Diseases, Ann & Robert H. Lurie Children’s Hospital, Northwestern University Feinberg School of Medicine, Chicago, Illinois; 2Department of Medicine, University of Miami Miller School of Medicine, Miami Veterans Affairs Healthcare System, Miami, Florida; 3Department of Pediatrics, Hemby Children’s Hospital and Eastover Pediatrics, Charlotte, North Carolina; 4Department of Pediatrics, Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio; 5Department of Pediatrics, University of Minnesota Medical School, Minneapolis, Minnesota; 6Division of Infectious Diseases, Boston Children’s Hospital, Boston, Massachusetts; 7Department of Pediatrics, University of Pittsburgh, Pittsburgh, Pennsylvania; and 8Respiratory Diseases Branch, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia
Gram Positive Cocci in Chains / Pairs

GPC in chains (GPCch)
- streptococci enterococci
  - α-hemolytic
    - viridans group pneumococci
  - β-hemolytic
    - γ-hemolytic [nonhemolytic (NHS)]
      - group A (S. pyogenes)
      - group B (S. agalactiae)
      - groups C, F, G
  - peptostreptococci (anaerobic)
    - Enterococci group D (S. bovis)
Streptococcus pyogenes

- Two major virulence factors:
  - Hyaluronic acid capsule
    - Resists phagocytosis
    - Adherence factor
  - M protein
    - Antigenic determinant
    - Multiple different types
    - Cross-reactivity of anti-M protein antibodies with heart muscle is the basis for rheumatic fever
# Pharyngitis features

## Group A Streptococcal
- Sudden onset of sore throat
- Age 5-15 years
- Fever
- Headache
- Nausea, vomiting, abdominal pain
- Tonsillopharyngeal inflammation
- Patchy tonsillopharyngeal exudates
- Palatial petechiae
- Anterior cervical adenitis (tender nodes)
- Winter and early spring presentation
- History of exposure to strep pharyngitis
- Scarlatiniform rash

## Viral
- Conjunctivitis
- Coryza
- Cough
- Diarrhea
- Hoarseness
- Discrete ulcerative stomatitis
- Viral exanthema
Diagnosis

• Rapid antigen detection test (RADT) and /or throat culture (children and adolescents, not adults)
• If RADT negative, obtain throat culture (swab obtained form surface of tonsils or posterior pharyngeal wall). (recommendation strong, high)
• If RADT positive, no backup throat culture needed. (recommendation strong, high)
• Anti-streptococcal antibody titers are not recommended in routine diagnosis of acute pharyngitis as they reflect past but not current events. (recommendation strong, high)
Who should undergo testing for Group A Streptococcal Pharyngitis

• NOT suggested for those with features which strongly suggest viral etiology. (Recommendation strong, high)

• NOT indicated for children < 3 years of age because rheumatic fever is RARE in children < 3 years of age. (Recommendation strong, moderate)

• SELECTED children < 3 years old who have other risk factors, such as an older sibling with GAS infection, may be considered for testing. (Recommendation strong, moderate)

Shulman, et al CID 2012:55; e86-e102
Antibiotic regimens recommended for Group A Strep pharyngitis

<table>
<thead>
<tr>
<th>Drug, route</th>
<th>Dose</th>
<th>Duration or quantity</th>
<th>Recommendations Strength, Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin V, oral</td>
<td>Children: 250 mg twice daily or 3 times daily; adolescents and adults: 250 mg 4 times daily or 500 mg twice daily</td>
<td>10 days</td>
<td>Strong, High</td>
</tr>
<tr>
<td>Amoxicillin, oral</td>
<td>50 mg/kg once daily (max = 1000 mg); alternate: 25 mg/kg (max = 500 mg) twice daily</td>
<td>10 days</td>
<td>Strong, high</td>
</tr>
<tr>
<td>Benzathine penicillin G, intramuscular</td>
<td>&lt;27 kg: 600 U; &gt; 27 kg:1,200,000 U</td>
<td>1 dose</td>
<td>Strong, high</td>
</tr>
</tbody>
</table>
# Antibiotic regimens recommended for Group A Strep pharyngitis

<table>
<thead>
<tr>
<th>Drug, route</th>
<th>Dose</th>
<th>Duration or quantity</th>
<th>Recommendations Strength, Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalexin¹, oral</td>
<td>20 mg/kg/dose twice daily (max = 500 mg/dose)</td>
<td>10 days</td>
<td>Strong, high</td>
</tr>
<tr>
<td>Cefadroxil², oral</td>
<td>30 mg/kg once daily (max = 1 gram)</td>
<td>10 days</td>
<td>Strong, high</td>
</tr>
<tr>
<td>Clindamycin, oral</td>
<td>7 mg/kg/dose 3 times daily (max = 300 mg/dose)</td>
<td>10 days</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Azithromycin³, oral</td>
<td>12 mg/kg once daily (max = 500 mg)</td>
<td>5 days</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Clarithromycin⁴, oral</td>
<td>7.5 mg/kg/dose twice daily (max = 250 mg/dose)</td>
<td>10 days</td>
<td>Strong, moderate</td>
</tr>
</tbody>
</table>

* Recommend patient to allergist for penicillin allergy testing
Adjunctive therapy

- Acetaminophen or NSAIDs may be used for moderate to severe symptoms and fever
- Avoid aspirin (recommendation strong, moderate)
- Avoid corticosteroids
RADT and Cultures

• Neither throat culture or RADT accurately differentiate acutely infected persons from asymptomatic streptococcal carriers with inter-current viral pharyngitis.

• Nevertheless, negative RADT and cultures allow providers to withhold antibiotics from the great majority of patients with sore throats.

• Nationally, up to 70% of patients with sore throats seen in primary care settings receive prescriptions for antimicrobials while only 20-30% are likely to have GAS pharyngitis.
## Treatment Regimens for Chronic Carriers of Group A Streptococci

<table>
<thead>
<tr>
<th>Route, Drug</th>
<th>Dose or Dosage</th>
<th>Duration or Quantity</th>
<th>Recommendation, Strength, Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Clindamycin</td>
<td>20-30 mg/kg/d in 3 doses (max = 300 mg/dose)</td>
<td>10 days</td>
<td>Strong, High</td>
</tr>
<tr>
<td>Penicillin and rifampin</td>
<td>Penicillin V: 50 mg/kg/d in 4 doses X 10 days (max = 2000 mg/day); rifampin: 20 mg/kg/day in 1 dose X last 4 days of treatment (max = 600 mg/day)</td>
<td>10 days</td>
<td>Strong, Moderate</td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>40 mg amoxicillin/kg/day in 3 doses (max = 2000 mg amoxicillin /day)</td>
<td>10 days</td>
<td>Strong, moderate</td>
</tr>
<tr>
<td>Intramuscular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzathine penicillin G IM</td>
<td>Benzathine penicillin G: 600,000 U for &lt; 27 kg and 1,200,000 U for ≥ kg; rifampin: 20 mg/kg/day in 2 doses (max = 600 mg/day)</td>
<td>Benzathine penicillin G: 1 dose; rifampin: 4 days</td>
<td>Strong, high</td>
</tr>
</tbody>
</table>
Case 3

• LL is a 12 year old female presenting to her pediatrician, complaining of sore throat and cough. She has had some hoarseness in her voice over the past few days and subjective sweats but no documented fever. She has a history of seasonal allergies in the fall, and takes loratidine only during that season. Upon review of systems, she complains of isolated throat pain, without any rhinorrhea, sinus pressure, or headache. Her mother has been taking her temperature at home, and they have fluctuated from 97.8°F- 99.2°F. Rapid strep antigen: negative; throat culture pending.

• How would you proceed?
Case 3

A. Ibuprofen 15 mg/kg q 6 h prn
B. Amoxicillin 90 mg/kg divided q 8 h
C. Clindamycin 40 mg/kg/day divided every 8 hours
D. Benzathine penicillin 1,200,000 X 1 dose IM
Clinical Infectious Diseases Advance Access published March 20, 2012

IDSA GUIDELINES

IDSA Clinical Practice Guideline for Acute Bacterial Rhinosinusitis in Children and Adults

Anthony W. Chow,1 Michael S. Benninger,2 Itzhak Brook,3 Jan L. Brozek,4,5 Ellie J. C. Goldstein,6,7 Lauri A. Hicks,8 George A. Pankey,9 Mitchel Seleznick,10 Gregory Volturo,11 Ellen R. Wald,12 and Thomas M. File Jr13,14

1Division of Infectious Diseases, Department of Medicine, University of British Columbia, Vancouver, Canada; 2Otolaryngology, The Head and Neck Institute, Cleveland Clinic, Ohio; 3Department of Pediatrics, Georgetown University School of Medicine, Washington, D.C.; 4Department of Clinical Epidemiology and Biostatistics and 5Department of Medicine, McMaster University, Hamilton, Ontario, Canada; 6Department of Medicine, David Geffen School of Medicine at the University of California, Los Angeles, 7R. M. Alden Research Laboratory, Santa Monica, California; 8National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; 9Department of Infectious Disease Research, Ochsner Clinic Foundation, New Orleans, Louisiana; 10Division of General Internal Medicine, University of South Florida College of Medicine, Tampa; 11Department of Emergency Medicine, University of Massachusetts, Worcester; 12Department of Pediatrics, University of Wisconsin School of Medicine and Public Health, Madison; 13Department of Infectious Diseases, Northeast Ohio Medical University, Rootstown; and 14Summa Health System, Akron, Ohio
Conventional Criteria for diagnosis of Sinusitis: 2 major or 1 major and ≥ 2 minor symptoms

**Major symptoms**
- Purulent anterior nasal discharge
- Purulent or discolored posterior nasal discharge
- Nasal congestion or obstruction
- Facial congestion or fullness
- Facial pain or pressure
- Hyposmia or anosmia
- Fever (for acute sinusitis only)

**Minor symptoms**
- Headache
- Ear pain, pressure, or fullness
- Halitosis
- Dental pain
- Cough
- Fever (for subacute or chronic sinusitis)
- Fatigue
Uncomplicated viral URI

Diagnosis when child with acute URI presents with:

• PERSISTENT illness, ie nasal discharge (of any quality) OR daytime cough OR both lasting more than 10 days without improvement

  OR

• WORSENING course, ie worsening or new onset of discharge, daytime cough, or fever after initial improvement

  OR

• SEVERE onset, concurrent fever (temperature ≥ 39°C/102.2°F) and purulent nasal discharge for at least 3 consecutive days
Diagnosis

• Do NOT obtain imaging studies (plain films, contrast enhanced computed tomography, MRI, or ultrasonography) to distinguish acute bacterial sinusitis from viral URI
Initial management of acute bacteria sinusitis

- Antibiotic therapy for acute bacterial sinusitis in children with severe onset or worsening course (signs, symptoms, or both)

- Persistent illness – (nasal discharge of any quality or cough or both for at least 10 days): may either
  - prescribe antibiotic therapy OR
  - offer additional outpatient observation for 3 days to children with persistent illness
Treatment

• Prescribe amoxicillin with or without clavulanate as first-line treatment when a decision has been made to initiate antibiotic treatment of acute bacterial sinusitis.
<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Severe Acute Bacterial Sinusitis&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Worsening Acute Bacterial Sinusitis&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Persistent Acute Bacterial Sinusitis&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncomplicated acute bacterial sinusitis without coexisting illness</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy or additional observation for 3 days&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Acute bacterial sinusitis with orbital or intracranial complications</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy</td>
</tr>
<tr>
<td>Acute bacterial sinusitis with coexisting acute otitis media, pneumonia, adenitis, or streptococcal pharyngitis</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy</td>
<td>Antibiotic therapy</td>
</tr>
</tbody>
</table>

<sup>a</sup> Defined as temperature \( \geq 39^\circ \text{C} \) and purulent (thick, colored, and opaque) nasal discharge present concurrently for at least 3 consecutive days.

<sup>b</sup> Defined as nasal discharge or daytime cough with sudden worsening of symptoms (manifested by new-onset fever \( \geq 38^\circ \text{C} / 100.4^\circ \text{F} \) or substantial increase in nasal discharge or cough) after having experienced transient improvement of symptoms.

<sup>c</sup> Defined as nasal discharge (of any quality), daytime cough (which may be worse at night), or both, persisting for \( > 10 \) days without improvement.

<sup>d</sup> Opportunity for shared decision-making with the child’s family; if observation is offered, a mechanism must be in place to ensure follow-up and begin antibiotics if the child worsens at any time or fails to improve within 3 days of observation.
Treatment Reassessment

• Provider should change antibiotic therapy OR initiate antibiotic therapy:
  o If there is either a caregiver report of worsening (progression of initial signs/symptoms) OR
  o Failure to improve (lack of reduction in all presenting signs/symptoms) within 72 hours of initial management
## Worsening or lack of improvement in 72 hours

<table>
<thead>
<tr>
<th>Initial Management</th>
<th>Worse in 72 hours</th>
<th>Lack of improvement in 72 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>Initiate amoxicillin with or without clavulanate</td>
<td>Additional observation or initiate antibiotic based on shared decision-making</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>High dose amoxicillin clavulanate</td>
<td>Additional observation or high-dose amoxicillin-clavulanate OR clindamycin and cefixime OR linezolid and cefixime OR levofloxacin</td>
</tr>
<tr>
<td>High dose amoxicillin clavulanate</td>
<td>Clindamycin and cefixime OR linezolid and cefixime OR Levofloxacin</td>
<td>Continued high-dose amoxicillin clavulanate OR clindamycin and cefixime OR linezolid and cefixime OR levofloxacin</td>
</tr>
</tbody>
</table>
Adjuvant Therapy

Intranasal glucocorticoids
- Significant improvement in adults
- No good RCT's in children

Nasal saline irrigation
- 1 study showed improvement in nasal airflow
- c/w patient treated with antibiotics and decongestants only

Decongestant, Mucolytic, Antihistamine
- Data insufficient
- Antihistamines should not be used as primary tx for ABS
Adjuvants

- Intranasal steroids
  - Studies showed good results however had methodological problems with mixed populations of allergic and non-allergic subjects

- Saline irrigations
  - Most studies were too small or contained bias

- Nasal decongestants
  - Should not be used

- Mucolytics
  - Should not be used

- Antihistamines
  - Should not be used
Recurrent acute bacterial sinusitis (RABS)

- Defined by episodes of bacterial infection of the paranasal sinuses lasting fewer than 30 days and separated by intervals of at least 10 days during which the patient is asymptomatic.

- Evaluate for:
  - underlying allergies,
  - functional immunologic defects,
  - chiefly immunoglobulin A and G deficiency,
  - cystic fibrosis;
  - gastro-esophageal reflux disease,
  - dysmotile cilia syndrome,
  - anatomical defects.
Case 4

• A 7 year old previously healthy female presents to her primary care physician with a 12 day history of persistent thick nasal discharge, nasal congestion, cough, and intermittent low grade fever. She also seems to have one temperature spike daily to about 38.2 degrees (100.8 degrees F). She is not taking any medications. She denies any vomiting, headache, earache, or rashes.

• Her past medical history is negative for hospitalizations, asthma, allergic rhinitis, or cystic fibrosis. Mom states that she is allergic to penicillin.

• Exam: Temp 37.2, Pulse 90, Resp 15, BP 88/50. She is an alert, interactive female breathing comfortably. She has no eye abnormalities. Her tympanic membranes are clear. She has nasal congestion with thick yellow purulent mucus in the posterior nasal pharynx. Her nasal turbinates are red and swollen. She has mild tenderness to palpation of her maxillary sinuses. Her breath is malodorous. Her lungs are clear.
Case 4, cont.

Which antibiotic would you prescribe:

a. None. Her illness does not require antibiotics for treatment
b. Levofloxacin
c. Cefixime
d. Amoxicillin clavulanate
Quality improvement within your practice (AAP) change concepts

- Accurately diagnose common pediatric infections, including upper respiratory infection (URI), acute otitis media, acute bacterial sinusitis, and group A streptococcal pharyngitis to ensure appropriate and effective treatment.
- Make treatment decisions for these infections based on accurate diagnoses.
- Avoid misuse of antibiotics by not treating patients when antibiotics have no benefit.
- Prescribe narrow-spectrum antibiotics versus broad-spectrum antibiotics when viable to limit antibiotic resistance and unnecessary healthcare costs, while maintaining high-quality care.
- Provide guidance and education to patients and families about the benefits of judicious use of antibiotics for mitigating antibiotic resistance and adverse events for patients.
- Respond effectively to patients and families when unnecessary antibiotics are requested.
- Assess the diagnostic and prescribing patterns of your practice.

https://shop.aap.org/eqipp-judicious-use-of-antibiotics/
Summary: Prevent Antimicrobial Resistance

- Limit exposure to antibiotics whenever possible
- Limit spectrum of activity of antimicrobials to that specifically required to treat the identified pathogen
- Use proper dosage of antimicrobial to be able to achieve a minimal effective concentration at the site of infection
- Treat for the shortest duration to minimize exposure of pathogen and normal flora to antimicrobials
Questions?

Thanks!