LEARNING OBJECTIVES:

At the end of the class session, the student will be able to:

1. describe the etiology, epidemiology, and incidence of otitis media and pharyngitis
2. list signs and symptoms of each disorder which serve as guides to diagnosis and therapeutic monitoring
3. propose pharmacotherapeutic treatment plans for the various forms of otitis media as well as streptococcal pharyngitis
4. discuss the controversies of treatment of otitis media including use of antibiotics, decongestants and antihistamines and chemoprophylaxis for recurrent episodes
5. discuss the controversy regarding drug-of-choice for streptococcal pharyngitis

The Impact of Otitis Media

- The most common bacterial infection in children
- The most common reason for pediatric office visits
- The most common reason for outpatient antibiotic treatment
  - About 30 million physician visits/year among children <12 months of age
  - Annual cost of treatment in USA ~ $3.5 billion
Terminology of Otitis Media

- Otitis media (OM)
  - Inflammation of the middle ear
- Acute otitis media (AOM)
  - Rapid onset of signs & symptoms of OM
- Otitis media with effusion (OME)
  - Accumulation of fluid in middle ear
- Chronic purulent otitis media
  - Chronic inflammation with purulent otorrhea

Pathophysiology of AOM

- Dysfunction of the Eustachian tube
  - Leads to negative middle ear pressure
  - Associated with URIs in children and adults

Anatomy of the Ear
Etiology of Otitis Media

Virtues
- Can cause otitis media and probably predispose to bacterial infection
- Typical isolates:
  - RSV
  - Parainfluenza virus
  - Influenza virus
- Other likely pathogenic viruses:
  - Rhinovirus
  - enteroviruses

Bacterial Etiology of Otitis Media (>1 year of age)

- More likely to encounter:
  - β-lactamase positive
  - H. influenzae
  - M. catarrhalis
  - Drug/penicillin-resistant S. pneumoniae
Etiology of Otitis Media

Chronic Purulent Otitis

- *Staphylococcus aureus*
- *Staphylococcus epidermidis*
- *Pseudomonas aeruginosa*

Factors Relating to Incidence

- Age at first episode
- Environmental
- Season
- Gender
- Race
- Malformations
- Nutrition
- Immunity
- Socioeconomic status

Risk Factors in General

- Family member with AOM
- Day care outside of home*
- Parental smoking*
- Use of pacifier

*most important

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Risk Factors for AOM in First 6 Months of Life

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Rel. Risk</th>
<th>95% C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day Care</td>
<td>1.7</td>
<td>1.5, 2.5</td>
</tr>
<tr>
<td>Resp. Infection</td>
<td>7.5</td>
<td>5.4, 10.3</td>
</tr>
<tr>
<td>Family Hx AOM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mother</td>
<td>1.5</td>
<td>1.1, 2.0</td>
</tr>
<tr>
<td>father</td>
<td>1.6</td>
<td>1.3, 1.9</td>
</tr>
<tr>
<td>sibling</td>
<td>1.7</td>
<td>1.4, 2.2</td>
</tr>
</tbody>
</table>


Epidemiology

<table>
<thead>
<tr>
<th>Age Group</th>
<th>% with Otitis annually</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3 months</td>
<td>35</td>
</tr>
<tr>
<td>4</td>
<td>21</td>
</tr>
<tr>
<td>10-14</td>
<td>3</td>
</tr>
</tbody>
</table>

Signs and Symptoms*

- Bulging, red tympanic membrane
- Loss of boney landmarks
- Ear pulling
- Pain
- Diarrhea
- Partial deafness
- Fever

*these symptoms mild or absent in OME
Normal Tympanic Membrane

Acute Otitis Media

Acute Otitis Media
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Treatment

Pharmacodynamics In Otitis Media
(WHITE = S. pneumoniae, RED = H. flu)

Pharmacodynamic Goals of Treatment

- β-lactams: MEF conc > MIC for ≥40% of dosing interval
- Macrolides: MEF conc > MIC for <50% (≥40%) of dosing interval
- Azalides & FQ: AUC/MIC ≥ 25
- MEF conc / MIC; an indirect marker of T>MIC

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<table>
<thead>
<tr>
<th>Agent (dose/mg/kg/d)</th>
<th>S. Pneumoniae</th>
<th>H. influenzae</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pen-S</td>
<td>Pen-R</td>
</tr>
<tr>
<td>Amoxicillin (45)</td>
<td>85</td>
<td>60</td>
</tr>
<tr>
<td>Amoxicillin (90)</td>
<td>85</td>
<td>60</td>
</tr>
<tr>
<td>Amoxic/Clav (90)</td>
<td>85</td>
<td>60</td>
</tr>
<tr>
<td>Ceftaxime (30)</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Cefuroxime (30)</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>Cefprozil (30)</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>Cefixime (8)</td>
<td>80</td>
<td>0</td>
</tr>
<tr>
<td>Azithromycin (10/5)</td>
<td>50</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>


Issues to consider* in choosing antibiotic therapy for AOM

- Efficacy
- Toxicity/safety
- Compliance (regimen/dosage forms)
- Palatability
- Cost

*In order of importance

Comparative Taste Ratings for Antibiotic Suspensions

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loracarbef*</td>
<td>3.25</td>
</tr>
<tr>
<td>Cefdinir</td>
<td>3.00</td>
</tr>
<tr>
<td>Cefixime*</td>
<td>2.77</td>
</tr>
<tr>
<td>Azithromycin*</td>
<td>2.50</td>
</tr>
<tr>
<td>TMP-SMX*</td>
<td>1.92</td>
</tr>
<tr>
<td>Clarithromycin*</td>
<td>1.82</td>
</tr>
<tr>
<td>Amox/Clav</td>
<td>1.61</td>
</tr>
<tr>
<td>Cefpodoxime*</td>
<td>1.59</td>
</tr>
<tr>
<td>Cefuroxime*</td>
<td>1.39</td>
</tr>
</tbody>
</table>

*Resistance issues with one or more common pathogens
**Comparative Costs of Antibiotic Suspensions**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Average Cost($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>25</td>
</tr>
<tr>
<td>Cefpodoxime</td>
<td>34</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>35</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>41</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>42</td>
</tr>
<tr>
<td>Cefixime</td>
<td>42</td>
</tr>
<tr>
<td>Loracarbef</td>
<td>44</td>
</tr>
<tr>
<td>Cefdinir</td>
<td>46</td>
</tr>
<tr>
<td>Amox/clav</td>
<td>75</td>
</tr>
</tbody>
</table>


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**Diagnosis & Treatment of AOM Current Guidelines**

- This guideline:
  - Provides a definition of AOM
  - Addresses pain management
  - Addresses immediate tx vs observation
  - Addresses appropriate antibiotic tx
  - Addresses preventative measures

Diagnosis & Treatment of AOM Current Guidelines

• Pain should be treated
  – Proven interventions:
    • Acetaminophen/ibuprofen
    • Topical agents containing benzocaine
    • Narcotic analgesics
    • Tympanostomy / myringotomy
  – Unproven
    • Home remedies (e.g., heat/cold; oil)
    • Homeopathic / naturopathic remedies


Diagnosis & Treatment of AOM Current Guidelines

• Initial observation (vs. abx tx)
  – For children ≥ 2 yo
  – Mild disease/symptoms
  – Popular in Europe
    • Avoids unnecessary antibiotic use
    • Avoids costs of antibiotic therapy


The “wait & see” approach

• Immediate vs. delayed (72 hr) prescribing of abx
• Immediate abx prescription provided mainly symptomatic relief after first 24 hr
  – Shorter illness (1.1 d), fewer nights disturbed (0.72) and less APAP use (0.52 “spoons” per day)
  – No differences in pain scores or missed school
• In children with mild systemic symptoms, wait & see seemed feasible and was acceptable to parents.

Diagnosis & Treatment of AOM
Current Guidelines

- Antibiotic Therapy
  - Amoxicillin 80 - 90 mg/kg/d
  - Amoxicillin/CA 90/6.4 mg/kg/d
    - For more severe illness and/or better H. influenzae and M. catarrhalis coverage
  - In penicillin-allergic patients
    - Type I: a macrolide
    - Non-Type I: an oral, 2nd generation cephalosporin


Treatment of AOM
Amoxicillin Failure

- Definition: persistence of symptoms after 2-3 days of treatment; does not include non-specific symptoms or effusion after 10 days of treatment
- Amoxicillin/clavulanate
- An oral, 2nd generation cephalosporin
- Ceftriaxone (IM x 3 d)


Diagnosis & Treatment of AOM
Current Guidelines

- Avoidance of risk factors
- Immunization
  - Viral
    - Respiratory Syncytial Virus
    - Influenza Virus
  - Bacterial
    - S. pneumoniae

Adjunct Therapies

- Antihistamines and decongestants
  - Often prescribed
    - Majority of experimental data does not support their use

Response to Treatment

- Improvement in 48-72 hours
- Re-examination in 10-14 days
- Middle Ear Effusion
  - Up to 70% of children
  - May persist for up to 3 months
  - Treatments
    - Course of antibiotic therapy
    - Topical or systemic decongestant, oral antihistamine, or combo
    - Systemic steroids

Treatment of Otitis Media

Recurrent Episodes

- Defined as 3 or more in preceding 6 mos
- Options
  - Antibiotic prophylaxis
    - Sulfisoxazole, amoxicillin, SMX/TMP, erythromycin
  - Antibiotic treatment of each episode
  - Myringotomy with tympanostomy tubes
Treatment of Otitis Media
Recurrent Episodes - Antibiotic Prophylaxis

• This is effective in reducing # episodes/yr
• Works best when
  – sulfisoxazole is used
  – Treatment is continued for < 6 mos
  – Used in populations with highest rate of recurrence (< 2 yo, child care, Native Amer.)


Treatment of Otitis Media
Chronic OME

• Effusion lasting more than 3 months
• Options
  – Antibiotic treatment
  – Short course steroids
  – Tympanostomy tubes

Vaccine Efficacy

• Heptavalent conjugate vaccine or placebo administered to 37,868 infants
• PCV:
  – reduced otitis visits by 7.8%
  – reduced antibiotic prescriptions by 5.7%
  – reduced tube placement by 24%
• Non-controlled, observational study of PCV:
  – Reduced proportion of S. pneumoniae from 48 to 31%
  – Less are penicillin resistant
  – Increased proportion of H. influenzae from 41 to 56%
  – More are ß-lactamase producing

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OTITIS MEDIA
Areas of Change & Controversy

• Should AOM be treated with antibiotics?
• What is the appropriate length of therapy?
• What is the role of antihistamine/decongestants?

Other things to consider.....

• It has been estimated that:
  – 59% of children not treated with abx will have resolution of pain and fever in 24 hr
  – 87% will have resolution of pain and fever within 2-3 days
  – 88% will have resolution of pain and fever within 4-7 days
  – Few episodes of mastoiditis or other suppurative complications occur in children with AOM not treated with antibiotics

Evidence Report/Technology Assessment: no. 15, 6/00. AHQR

Other things to consider.....

• Meta-analysis suggests that the following outcomes of AOM do not appear to be affected by antibiotic use:
  – Pain resolution at 24 hrs.
  – Pain and fever resolution at 4-7 days
  – TM perforation, vomiting/diarrhea/rash
  – 1 month tympanometry
  – Recurrent AOM

Evidence Report/Technology Assessment: no. 15, 6/00. AHQR
OTITIS MEDIA
Areas of Change & Controversy
• Should AOM be treated with antibiotics?
• What is the appropriate length of therapy?
• What is the role of antihistamine/decongestants?

Short Course Therapy
• Traditional therapy is for 7-10 days
• Azithromycin (20mg/kg) X 5 days
• Azithromycin (10mg/kg) X 3 days
  (Dunne et al. J Antimicrob Chemother 2003;52:469)
• Azithromycin (30mg/kg) X 1
EXAMPLE CASE

LP is a 15 month old white male seen in the pediatrician’s office for complaints of crying, irritability, and ear-pulling over the last 18 hours. On physical exam, the physician discovers general nasal congestion, red, bulging tympanic membranes bilaterally and a rectal temperature of 102°F. This is the third time in the last four months that this child has been seen for acute otitis media. The first two episodes were treated with cefaclor suspension and with complete clinical resolution in both instances. The child has no known allergies although the father is allergic to penicillin and sulfonamides.

1. Describe a short- and long-term treatment for the treatment of this patient’s recurrent otitis media.
2. Discuss what factors you considered in the patient’s past medical history is arriving at these recommendations.
3. Propose an alternative plan for both short- and long-term treatments should your original recommendation prove ineffective or unacceptable to the prescriber or parents.
Etiology of Pharyngitis

- Viruses are principle cause in children < 3 years of age
- Peak ages for β-hemolytic streptococcus
  - 4 - 10 years of age
- Peak incidence
  - Fall/winter/spring

Epidemiology of Pharyngitis

- Viruses are principle cause in children < 3 years of age
- Peak ages for β-hemolytic streptococcus
  - 4 - 10 years of age
- Peak incidence
  - Fall/winter/spring

Exudative Pharyngitis
# OTITIS MEDIA & PHARYNGITIS

## PHMPR-734

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### Symptoms of Pharyngitis

- **General**
  - Tender cervical lymph nodes
  - Exudate
  - Hoarseness

- **Streptococcal**
  - Abrupt onset
  - Headache
  - Redness
  - Dysphagia
  - Fever
  - Sore throat
  - Abdominal pain
  - Exudate
  - Rash

### Diagnosis of Pharyngitis

- Throat culture
- Rapid antigen detection
- Clinical symptomatology

### Complications of Pharyngitis

- **Non-suppurative**
  - Acute rheumatic fever
  - Acute glomerulonephritis
  - (secondary to host response)

- **Suppurative**
  - Peritonsillar abscess
  - Cervical lymphadenitis
  - Cellulitis
Desired Outcomes in Treatment of Acute Pharyngitis

- Prevention of acute rheumatic fever
- Prevention of suppurative complications
- Improvement in clinical symptoms
- Rapid decrease in infectivity
- Minimize complications of therapy

Principles of Appropriate Antibiotic Use for Acute Pharyngitis

- Group A β-hemolytic Strep accounts for only 10% of adult cases (up to 30% for children)
- Antibiotics benefit only those with GABHS
- Screen for presence of Centor criteria
  - Fever
  - Tonsillar exudates
  - No cough
  - Tender anterior cervical lymphadenopathy
- Throat cultures not recommended

Treatment Strategies Based on Centor Criteria

<table>
<thead>
<tr>
<th>Positive Criteria</th>
<th>Treatment Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No treatment</td>
</tr>
<tr>
<td>2</td>
<td>Rapid antigen test, treat if positive</td>
</tr>
<tr>
<td>3</td>
<td>Rapid antigen test, treat if positive</td>
</tr>
<tr>
<td>4</td>
<td>Treat</td>
</tr>
</tbody>
</table>

Ann Intern Med 2001; 134: 509-517
Treatment of Pharyngitis

- Penicillin V 250mg 3-4 x daily x 10 days
- Other alternatives
  - Amoxicillin
  - Amoxicillin/CA x 5 days
  - Benzathine penicillin
  - Macrolides
    - Azithromycin x 5 days
    - Clarithromycin x 5 days
  - Oral cephalosporins
    - 4-5 days


Table: Recommendations for antimicrobial therapy for group A streptococcal pharyngitis.

<table>
<thead>
<tr>
<th>Route of admin, agent</th>
<th>Dosage &amp; Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Penicillin V</td>
<td>Children: 250mg b.i.d. or t.i.d. for 10 days</td>
</tr>
<tr>
<td></td>
<td>Adolescents and adults: 250mg t.i.d. or q.i.d. for 10 days</td>
</tr>
<tr>
<td></td>
<td>Adolescents and adults: 500mg b.i.d. for 10 days</td>
</tr>
<tr>
<td>IM Benzathine penicillin G</td>
<td>1.2 X 10^6 U for 1 dose</td>
</tr>
<tr>
<td></td>
<td>6.0 X 10^5 U for 1 dose for patients &lt;27kg</td>
</tr>
<tr>
<td>Mix of benzathine &amp; procaine pen G</td>
<td>Varies with formulation (for 1 dose)</td>
</tr>
<tr>
<td>Oral, pen allergy</td>
<td>Erythromycin</td>
</tr>
<tr>
<td></td>
<td>1st gen. cepha</td>
</tr>
</tbody>
</table>

Bisno et al. CID 2002;35:133-25. (IDSA guidelines)

Table: Recommendations for tx of symptomatic patients with multiple, recurrent, episodes of pharyngitis proven by culture or rapid strep test.

<table>
<thead>
<tr>
<th>Route &amp; Agent</th>
<th>Dosage</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Clindamycin</td>
<td>Children: 20-30mg/kg/d Adults: 600mg/day</td>
<td>10 days</td>
</tr>
<tr>
<td>Amox-clav</td>
<td>Children: 40mg/kg/d Adults: 500mg bid</td>
<td>10 days</td>
</tr>
<tr>
<td>Parenteral with or without oral</td>
<td>10 days</td>
<td></td>
</tr>
<tr>
<td>Benzathine pen G</td>
<td>1.2 X 10^6 U for patients &lt;27kg 6.0 X 10^5 U</td>
<td>1 dose</td>
</tr>
<tr>
<td>Benzathine pen G Plus rifampin</td>
<td>As above for pen; rifampin: 200mg/kg/d Pen: 1 dose Ril: 4 days</td>
<td></td>
</tr>
</tbody>
</table>

Bisno et al. CID 2002;35:133-25. (IDSA guidelines)
Controversies in the treatment of Pharyngitis

- Penicillin vs cephalosporin
  - Eradication of carrier state
  - Re-acquisition from family members
  - Lab error?
  - Compliance
- Recent outbreaks of rheumatic fever
- Meta-analysis indicates likelihood of bacteriologic and clinical failure twice as likely with penicillin*

*Casey & Pichichero. CID 2004;38:1526-34.

Meta-analysis of Short Course Treatment

- 22 trials (involving bacteriologic confirmation of GAS) involving 7470 patients
- Cephalosporins, macrolides*, and penicillin
- Outcome was bacteriologic eradication
- Superior bacteriologic cure with short course cepha vs 10 d penicillin but not with short course penicillin or macrolide

*not including azithromycin

EXAMPLE CASE
MW is a six year old black male who presents to the emergency room at Charleston Memorial Hospital with complaints of sore throat, headache, stomach ache and fever. Physical examination reveals an erythematous pharynx, tender, swollen cervical lymph nodes and a temperature of 101.5°F. A rapid streptococcal antigen detection test performed in the ER is negative.

1. Discuss options for and against treatment in this case.

2. Assuming that antibiotic treatment will be given, propose a treatment plan and discuss what factors, evident in this case, were considered in making your recommendations. Include a therapeutic monitoring plan.

3. Propose an alternative pharmacotherapeutic plan should your first recommendation be ineffective or unacceptable.