North Carolina SPICE
Statewide Program for Infection Control & Epidemiology

NC CLASP OUTPATIENT STEWARDSHIP
YEAR 2, SESSION 5

Outpatient Antimicrobial Stewardship: Pharyngitis and Acute Otitis Media

January 24, 2024

CONFLICT OF INTEREST DISCLOSURES

- The views and opinions expressed in this series are those of the speakers and do not reflect the official policy or position of any agency of the US or NC government or UNC.
- Our speakers have the following financial relationships with the manufacturer(s) and/or provider(s) of commercial services discussed in this activity:
  - Dr. Willis has performed contracted research with: Pfizer (pediatric nirmatrelvir-ritonavir and maternal RSV vaccine), Novavax (pediatric COVID-19 vaccine), and Merck (monoclonal antibody for RSV prevention)
- The speakers do not intend to discuss an unapproved/investigative use of a commercial product/device in this series, and all COI have been mitigated.
- These slides contain materials from a variety of colleagues, as well as the CDC, WHO, AHRQ, etc.

INTRODUCTIONS

Please put your name, clinic, and location in the chat!

CME AND CE CREDIT

- CME & CE for participants
  - Attendance and active participation per learning session
  - Click the link in the chat during the session to document your attendance
  - Complete surveys as requested

OUTLINE: UPCOMING SESSIONS

Date	Topic
January 24th	Pharyngitis, acute otitis media
February 28th	UTI and STI
March 27th	Skin and soft-tissue infections
April 24th	Antibiotic Allergies
May Conference	TBD
June 26th	Additional strategies to prevent antibiotic overuse

TODAY'S OVERVIEW

- Acute bronchitis, pneumonia, and COPD exacerbation
  - Quick review
- Pharyngitis
- Acute otitis media (AOM)

THREE WAYS TO OVERUSE ANTIBIOTICS

1. Prescribing antibiotics when none are indicated

2. Using an antibiotic that is too broad for the infection (or otherwise suboptimal)

3. Using an excessive duration

QUICK REVIEW: ACUTE BRONCHITIS

- Infection of the large airways without pneumonia
- Cough (may last 3 weeks), may have low-grade fever, mild dyspnea, wheezing
- Cause: viruses
- Antibiotics not indicated
  - But commonly prescribed

QUICK REVIEW: COMMUNITY-ACQUIRED PNEUMONIA

- Diagnosis of CAP:
  - Symptoms: fever, cough, shortness of breath
  - Chest X-ray: consolidation (lobar or interstitial)
  - Complications: hypoxemia, pleural effusion, progression to sepsis

- Etiology: viral or bacterial

Pneumococcus	*H. flu, Moraxella*	Atypicals
Group A Strep		Oral anaerobes*
MSSA^		MRSA^
E. coli, K. pneumoniae		*Pseudomonas*

- Outpatient Treatment:
  - Young, healthy adults: amoxicillin x 5-7 days +/- azithromycin
  - Adults with comorbidities: amox/clav x 7 days + azithromycin
  - Children: amoxicillin (+/- azithromycin in school-age and adolescents)

QUICK REVIEW: COPD EXACERBATION

- Symptoms:
  - Increase in cough, dyspnea, and/or sputum production
  - Severe: respiratory failure
- Triggers:
  - Viral infections
  - Environmental irritants (particulate matter)
  - Bacterial infections uncommon
- Indications for antibiotics
  - Purulent sputum plus either increased sputum or increased dyspnea
- Recommended antibiotics: amox-clav, azithromycin, or doxycycline x 5 days

PHARYNGITIS

CAUSES OF SORE THROAT

- Viruses cause **majority** of pharyngitis cases
  - Adenovirus (often with associated conjunctivitis)
  - Enterovirus – herpangina, hand-foot-mouth
  - COVID-19
  - **EBV**
- <u>After viruses</u>, Group A Strep is most common cause

UNCOMMON CAUSES

- *Neisseria gonorrhoeae*
- Groups C and G streptococci
  - Not detected by routine GAS testing; do not cause acute rheumatic fever
- *Arcanobacterium haemolyticum*
- *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*

PHARYNGITIS COMPLICATIONS

- Peritonsillar abscess, retropharyngeal abscess (Group A Strep, oral anaerobes most common)
- Lemierre's syndrome (oral anaerobes, esp *Fusobacterium*)
- Epiglottitis

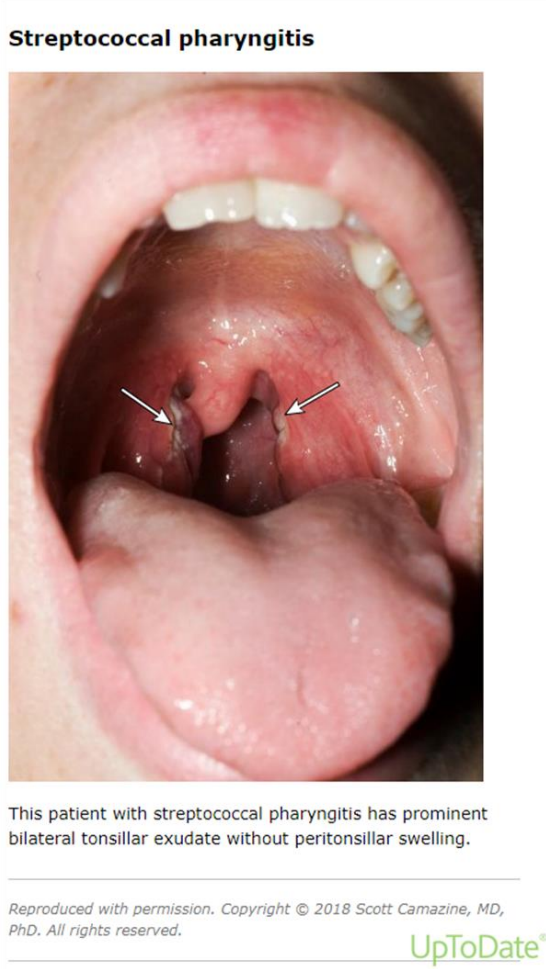
- Important to see the patients!

GROUP A STREP: EPIDEMIOLOGY

- 15-30% of all cases of pharyngitis in children 5-15 years
  - (At least 70% of pharyngitis cases are viral!)
- Most common in school-age children
  - Occasionally in younger children – usually in contact with school-age children
- 5-15% of cases of pharyngitis in adults
- Peaks in winter and early spring
  - Also common to see in fall after school starts

GAS PHARYNGITIS: PRESENTATION

- GAS pharyngitis is a clinical syndrome:
  - Sore throat and fever
  - Common: headache, abdominal pain, nausea, vomiting
  - Physical exam:
    - Pharyngeal and uvular erythema
    - Palatal petechiae common
    - Tonsillar enlargement and exudate common (also very common in EBV)
    - Anterior cervical lymphadenopathy
- Symptoms suggesting viral etiology:
  - Rhinorrhea, cough, conjunctivitis, hoarseness, discrete ulcerative lesions, or intraoral vesicles



WHOM TO TEST FOR STREP

- Modified Centor Criteria
  - McIsaac, *JAMA*, 2004

Criteria	Points
Temperature >38° C	1
Absence of Cough	1
Swollen, Tender Anterior Cervical Nodes	1
Tonsillar Swelling or Exudate	1
Age	
3-14 Years	1
15-44 Years	0
45 Years or Older	–1

- IDSA Guidelines (2012)
  - Avoid testing if viral features present
    - Cough, rhinorrhea, hoarseness, oral ulcers
  - Avoid testing children <3 years of age
    - Consider if risk factors, like symptoms plus an older sibling with strep
  - Follow-up posttreatment testing not recommended
  - Do not test asymptomatic household contacts

Score	Risk of Streptococcal Infection[8,9]	Suggested Management
≤0	1%-2.5%	No Further Testing or Antibiotic
1	5%-10%	
2	11%-17%	Culture All; Antibiotics Only for Positive Culture Results
3	28%-35%	
≥4	51%-53%	Treat Empirically With Antibiotics and/or Culture

GROUP A STREP COLONIZATION

- Martin JM et al., *Pediatrics* 2014
  - Swabbed schoolchildren (K-8) twice-monthly for four years
  - On average, 15.5% of asymptomatic participants were culture-positive at any time
  - 75% of positive cultures were in asymptomatic kids
  - In any school year, 30% of kids were asymptomatic carriers at some point
  - True recurrent infections rare

- **Kids with pharyngitis and a positive GAS test often have a viral infection**

Bacterial pharyngitis

Pneumococcus	*H. flu, Moraxella*	Atypicals
Group A Strep		Oral anaerobes*
MSSA		MRSA
E. coli, K. pneumoniae		*Pseudomonas*

*Oral anaerobes are rare causes of peritonsillar and pharyngeal abscess.

~100% (Always active)
90-99% (Almost always active)
50-89% (Resistance more frequent)
<50% (Usually or always inactive)

Amoxicillin

Pneumococcus	*H. flu, Moraxella*	Atypicals
Group A Strep		Oral anaerobes
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Penicillin

Pneumococcus	*H. flu, Moraxella*	Atypicals
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Azithromycin

Pneumococcus	*H. flu, Moraxella*	Atypicals
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Clindamycin

Pneumococcus	*H. flu, Moraxella*	Atypicals
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Cephalexin

Pneumococcus	*H. flu, Moraxella*	Atypicals
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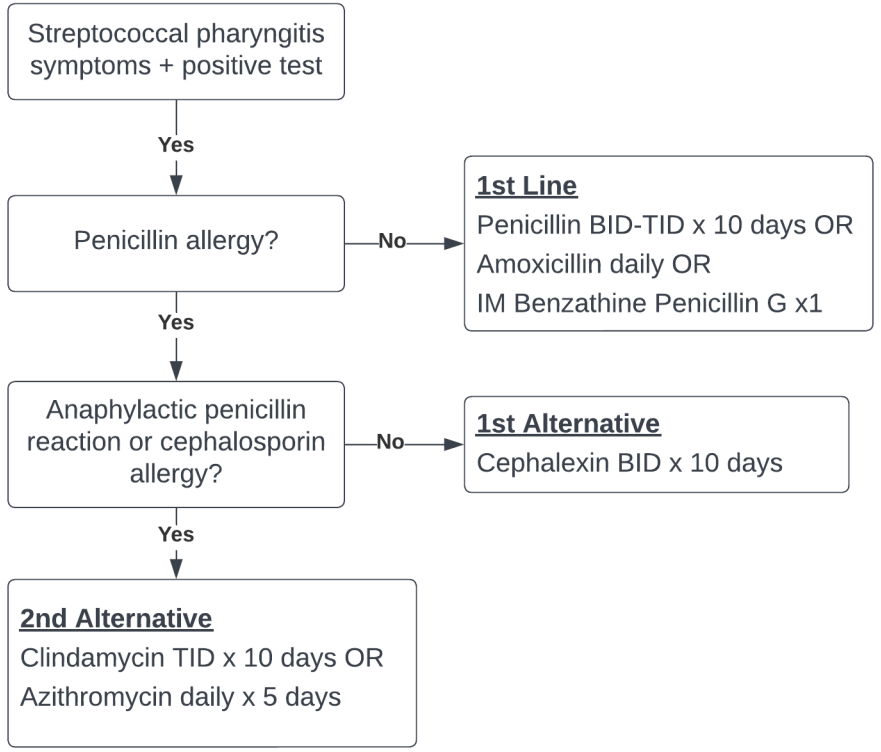
STREPTOCOCCAL PHARYNGITIS TREATMENT

IDSA Guidelines, 2012

- First-line: Penicillin IM x 1 OR oral penicillin OR oral amoxicillin
- Non-anaphylactic “allergy” to penicillin: cephalexin
- Unable to take cephalosporins:
  - Clindamycin OR azithromycin
  - There is some resistance to both, but <10%
- Not recommended: amox-clav, broad cephalosporins, fluoroquinolones



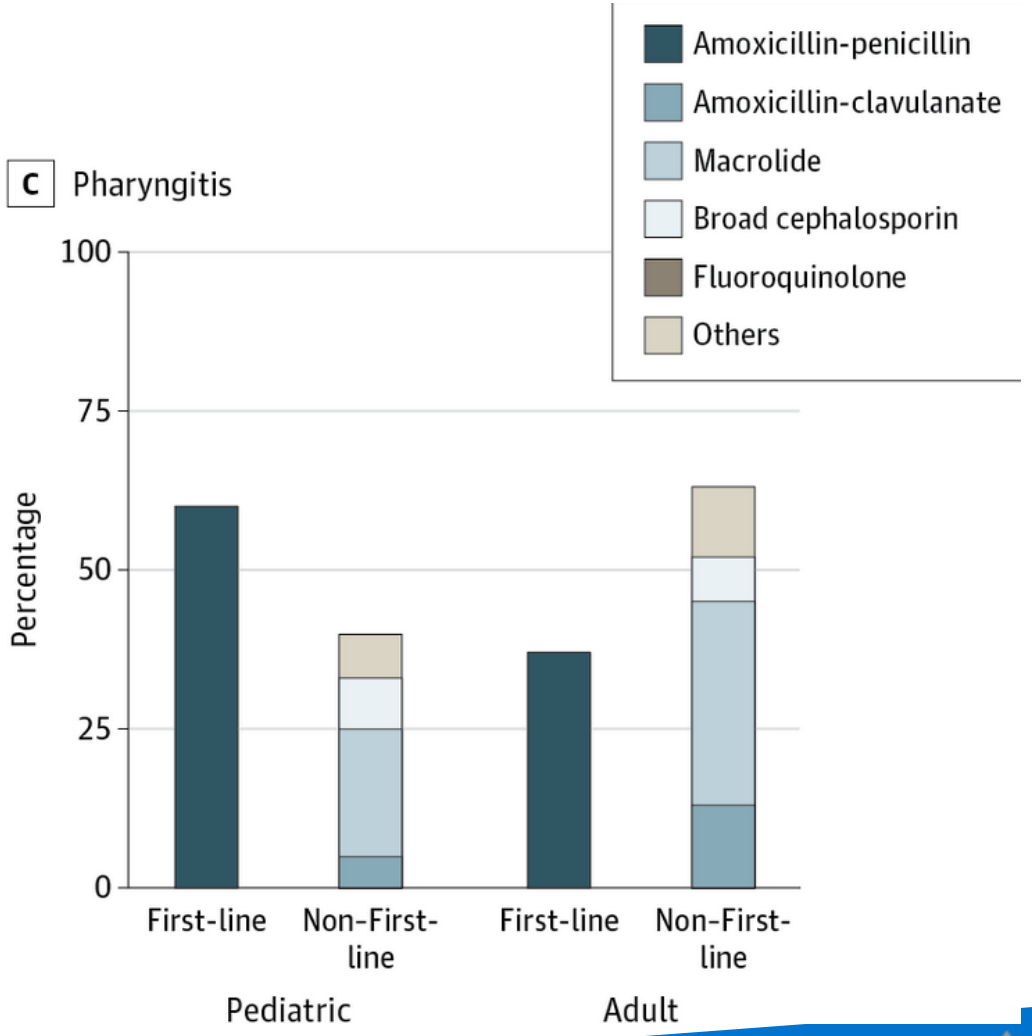
PHARYNGITIS: STEWARDSHIP ISSUES

- Antibiotics without positive test
- Overuse of testing – treatment of false-positives
- Broad-spectrum antibiotic use

ANTIBIOTIC SELECTION

Hersh et al., *JAMA Internal Medicine*, 2016

- First-line antibiotics: just amoxicillin or penicillin
- ~60% of children and ~40% of adults receive guideline-recommended antibiotics
- Other choices:
  - Amox-clav: not recommended
  - Macrolides: third-line
  - Broad cephalosporins: not recommended



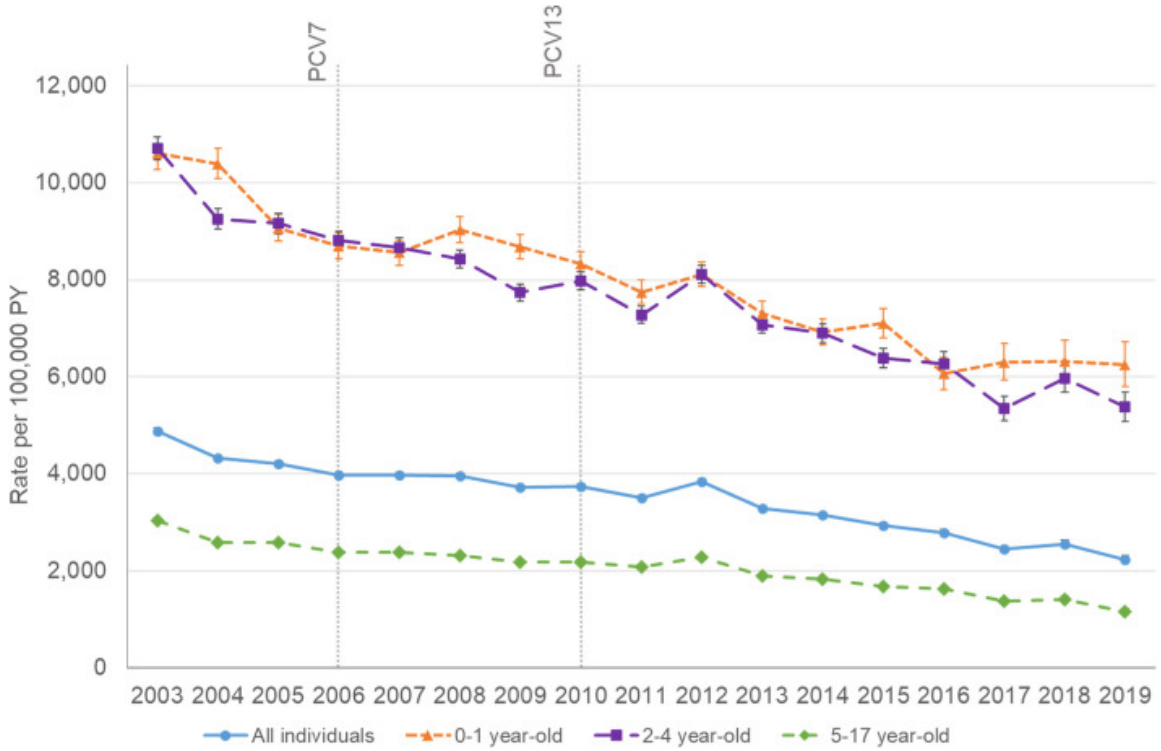
STREP THROAT: ANTIBIOTIC STEWARDSHIP OPPORTUNITIES

- Do NOT treat without a positive test
  - No presumptive treatment
  - Negative test → extremely unlikely to benefit from antibiotics
- Avoid over-testing
  - Ensure adequate pre-test probability
    - Centor criteria, screen for viral symptoms (cough, runny nose)
  - Avoid nurse-initiated throat swabs
  - Consider phone triage for pharyngitis
    - CC of sore throat and patient has cough/rhinorrhea, they can probably stay home
- Use amoxicillin or penicillin unless allergic

ACUTE OTITIS MEDIA

AOM: EPIDEMIOLOGY

- Most common indication for antibiotics in children:
  - <5 years of age: ~6 cases/100 children each year
- Incidence cut by more than 50% by pneumococcal vaccination
- Often triggered by viral URTI
  - Seasonal



Mohanty S et al., BMC Public Health, 2023

AOM: MICROBIOLOGY

- Very similar to sinusitis
- Viruses: RSV, enterovirus, rhinovirus, coronaviruses, influenza, etc.
- Bacteria:
  - Pneumococcus – falling due to vaccines
    - Causes the most severe disease
  - *H. influenzae*
  - *Moraxella catarrhalis*
  - Rare: Group A Strep, *Staph aureus*, *Mycoplasma pneumoniae*

AOM TREATMENT

~100% (Always active)
90-99% (Almost always active)
50-89% (Resistance more frequent)
<50% (Usually or always inactive)

Acute otitis media, acute bacterial sinusitis

Pneumococcus	*H. flu, Moraxella*	Atypicals
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Amoxicillin

Pneumococcus	*H. flu, Moraxella*	Atypicals
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Cefdinir

Pneumococcus	*H. flu, Moraxella*	Atypicals
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Amoxicillin-clavulanate

Pneumococcus	*H. flu, Moraxella*	Atypicals
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Azithromycin

Pneumococcus	*H. flu, Moraxella*	Atypicals
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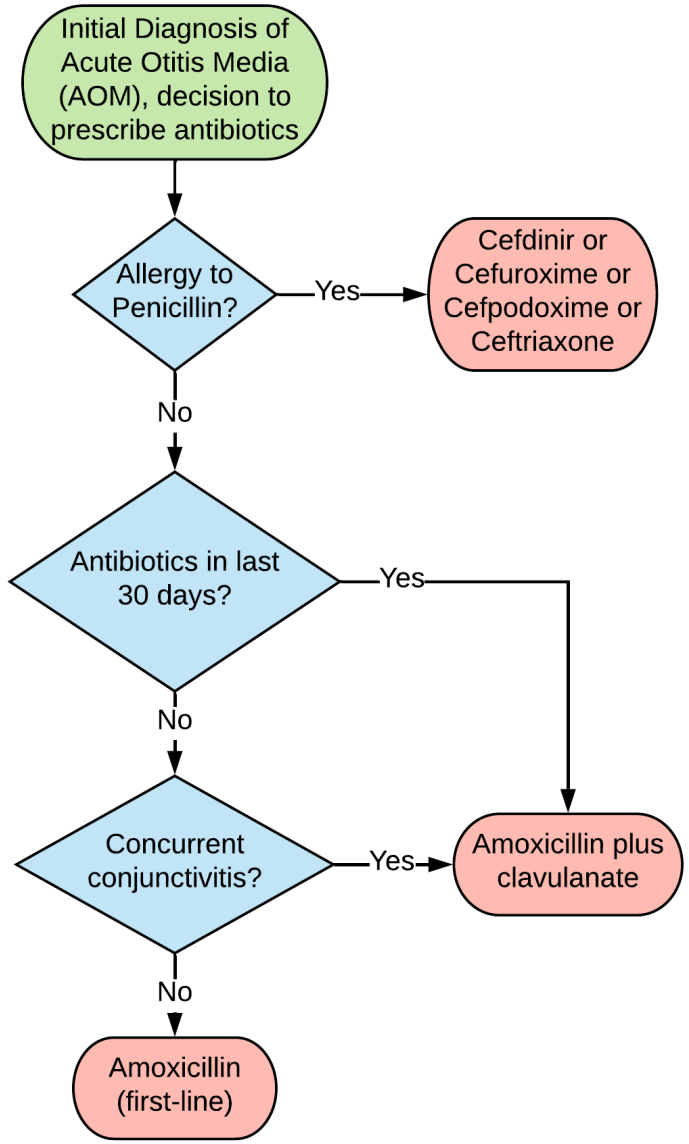
ACUTE OTITIS MEDIA TREATMENT

- AAP Guidelines, 2013
- Diagnosis of AOM:
  - Moderate or severe bulging of the TM *or*
  - Mild bulging of the TM with new onset of ear pain or intense erythema of the TM
- Whom to Treat:
  - Severe AOM: moderate or severe otalgia, otalgia for at least 48 hours, or temp >= 39 (102.2F)
  - Non-severe *bilateral* AOM in young children (<2 years of age)
- OK to treat or observe (can use a safety-net prescription):
  - Non-severe unilateral AOM in young children
  - Non-severe AOM in older children

ACUTE OTITIS MEDIA TREATMENT

- AAP Guidelines, 2013
- Amoxicillin is first-line unless:
  - Treated with amoxicillin in prior 30 days
  - *or* purulent conjunctivitis (usually *H. influenzae*)
  - Penicillin-allergic
- Duration:
  - <2 years or severe symptoms: 10 days
  - 2-5 years: 7 days
  - 6 years and up: 5-7 days
- Remember: oral cephalosporins are *much less* effective than high-dose amoxicillin against pneumococcus!
- Rarely recommended: azithromycin, TMP-SMX, clindamycin



AOM IN ADULTS

- Relatively uncommon – probably ~2-5 cases per 1,000 person-years
- Similar microbiology as in children
- No published guidelines for treatment
- Antibiotic choices:
  - First-line: amoxicillin or amox-clav
  - Alternative (penicillin allergy): cephalosporins
  - Cephalosporin allergy: doxycycline or azithromycin
- Duration: generally 5-7 days

AOM: ANTIMICROBIAL STEWARDSHIP

Stringent diagnostic criteria

- Overdiagnosis probably common

Guideline-recommended treatment and duration

- Overuse of broad-spectrum antibiotics, excessive durations

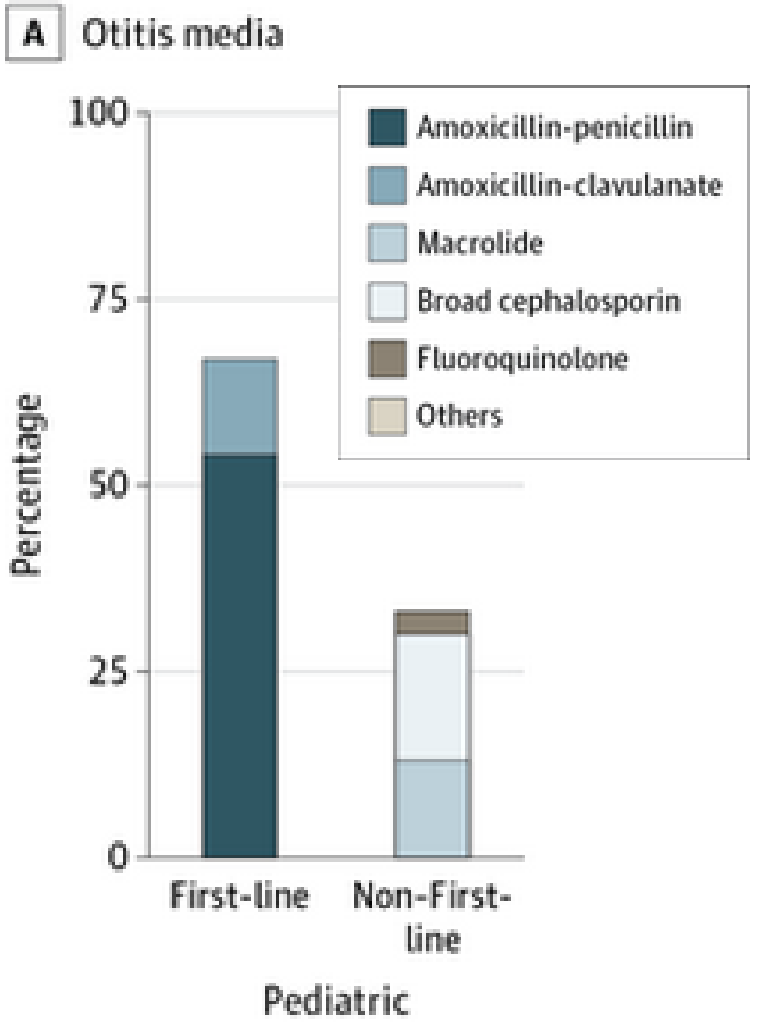
Defer treatment when not needed

- Older children with non-severe disease

ANTIBIOTIC SELECTION

Hersh et al., *JAMA Internal Medicine*, 2016

- Compared to sinusitis and pharyngitis: first-line antibiotics actually most likely for AOM
- Still: 30% of children with AOM received non-first-line antibiotics – mostly macrolides and cephalosporins
  - Broader-spectrum and likely less efficacious than first-line therapy
- How to measure:
  - Proportion of AOM diagnoses with prescription for amoxicillin or amox-clav
  - Proportion of AOM diagnoses with cephalosporin or azithromycin



AMOXICILLIN: IT WORKS!

Frost HM, et al., *Jour Pediatrics*, 2022

- Reviewed over 1 million cases in large nationwide databases in 2019
- Both treatment failure and recurrence were *least* common in amoxicillin recipients
- Short durations (5-7) days: slightly more treatment failure, slightly less recurrence

Table IV. Odds of primary and secondary outcomes for outpatient AOM visits by antibiotic type*, MarketScan Commercial Database, 2018

	Treatment failure			Recurrence		
Antibiotics	**OR (95% CI)**	**aOR (95% CI)**	***P***	**OR (95% CI)**	**aOR (95% CI)**	***P***
Amoxicillin	Ref	–	–	Ref	–	–
Amoxicillin-clavulanate	11.80 (11.27, 12.35)	11.36 (10.82, 11.93)	<.0001	5.15 (4.99, 5.31)	4.96 (4.80, 5.13)	<.0001
Cefdinir	9.85 (9.43, 10.29)	9.66 (9.22, 10.12)	<.0001	4.69 (4.56, 4.83)	4.59 (4.45, 4.74)	<.0001
Azithromycin	11.01 (10.49, 11.56)	11.79 (11.19, 12.43)	<.0001	4.11 (3.96, 4.26)	4.36 (4.19, 4.54)	<.0001

*Adjusted for age (ref—6 mo to <2 y), sex (ref—male), visit region (ref—West), setting.

REDUCING ANTIBIOTIC EXPOSURE

1. Ensure appropriate durations for children older than 2
   - 10-day durations commonly seen; 5-7 days recommended by guidelines

Increasing Guideline-Concordant Durations of Antibiotic Therapy for Acute Otitis Media

Holly M. Frost, MD, FAAP[1,2,3], Yingbo Lou, MS[4], Amy Keith, MPH[2], Andrew Byars, BS[5], and Timothy C. Jenkins, MD[6,7]

2. Consider deferring antibiotics in older children with non-severe symptoms (no severe ear pain, no fever of 39.0 or above)
   - Options:
     1. Close follow-up within 48-72 hours (phone or telehealth reasonable)
     2. Safety-net antibiotic prescriptions: family can fill only if needed

BREAKOUT SESSION

- Does your practice setting see a lot of patients for pharyngitis or ear infections?
- What's the approach to swabbing for Strep throat?
- Do you see opportunities for antibiotic stewardship for these common conditions?

THE NORTH CAROLINA CLINICAL ANTIBIOTIC STEWARDSHIP PARTNERS (NC CLASP)

- All the information from today's session will be on our website https://spice.unc.edu/ncclasp/

RESOURCES

- IDSA Clinical Practice Guidelines: Group A Streptococcal Pharyngitis
- AAP Guidelines: Acute Otitis Media
- New York State Antibiotic Prescribing Guide
  - Compendium of diagnostic and treatment guidelines for common outpatient conditions
- CDC Treatment Recommendations
  - Summarizes professional society guidelines, management of penicillin allergy