

ANTIBIOTIC USE IN UPPER RESPIRATORY INFECTIONS

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DISCLOSURES

- None

OBJECTIVES

- Provide background on current antibiotic prescribing trends for upper respiratory infections in the United States
- Discuss the negative consequences of inappropriate antibiotic use and the three central tenants of antimicrobial stewardship
- Review common upper respiratory infections and the role of antibiotics in their treatments
- Explore strategies and interventions to reduce unnecessary antibiotics use

INTRODUCTION

- Upper respiratory infections account for millions of physician visits in the U.S. every year.
- Most URIs are caused by viruses and require no antibiotics yet studies show as many as 10 million antibiotic prescriptions per year are inappropriately directed toward upper respiratory infections.
- One cohort study from 2018 of almost 15,000 outpatients with acute URIs found that 41% of patients who were prescribed antibiotics did not have an indication for them.

INTRODUCTION

- Unnecessary antibiotic use results in adverse events, contributes to antibiotic resistance, and adds unnecessary costs.
 - What are some adverse events?

INTRODUCTION

- Unnecessary antibiotic use results in adverse events, contributes to antibiotic resistance, and adds unnecessary costs. Most adverse events are **mild** (diarrhea and rash) but can be **more severe** (Stevens-Johnson syndrome and *C. difficile* colitis) or even **life-threatening** (anaphylaxis and sudden cardiac death).
- It is essential that family physicians become familiar with an evidence-based approach to antibiotic use as it relates to URIs if they are to achieve the three central goals of antimicrobial stewardship to **improve patient outcomes, minimize unintended consequences, and prevent unnecessary health care costs.**

CASE #1

- 3 yo patient presents with onset nearly 1 week ago of fevers to 100.4 associated with fussiness, nasal congestion, runny nose and a sore throat. Dad is concerned because nasal congestion and sore throat have persisted.
 - **Do you need to know anything more? What are your treatment options?**

COMMON COLD

- Symptoms including low grade fever, myalgias, headache, nasal congestion, rhinorrhea, sneezing, sore throat, and cough often last up to ten days.
- Treatments with established effectiveness for those symptoms in adults are limited to over-the-counter analgesics and anti-histamine/decongestant combinations.
- **For children under four years of age, the AAP states that cough and cold medicines should be avoided for respiratory illness in their Choosing Wisely recommendations.**

COMMON COLD

No indication for antibiotics

CASE #2

- A 35yo M with no significant PMH presents to clinic c/o myalgias, fatigue, fevers, sore throat, headache and cough x 2 days. He smokes cigarettes socially. He is covid vaccinated x 3 doses (2 Moderna + booster shot 4 months ago) but has not received his flu vaccine this season. He has tried Tylenol x 1 dose at home for his sore throat with some relief.
 - **Is there anything else you want to know or diagnostic tests you would order?**
 - **What is the most likely diagnosis?**
 - **What is the treatment? -> Are antibiotics indicated?**

INFLUENZA

- Influenza caused an estimated 9 million - 41 million illnesses, 4.3 - 21 million medical visits, 140,000 - 710,000 hospitalizations, and 12,000 - 52,000 deaths annually between 2010 - 2020 in the U.S.
- **Symptoms:** Abrupt onset of fever and cough, chills, congestion, rhinorrhea, sore throat, headache, myalgias, fatigue
- **Diagnosis:**
 - Rapid antigen tests or rapid molecular assays, PCRs and cxs may be available
- **Prevention:** Yearly **vaccines** (≥ 6 months of age who have no contraindications)
- **The influenza vaccine also helps prevent antibiotic resistance** by reducing the number of acute febrile illnesses caused by influenza that may be inappropriately treated with antibiotics and by decreasing the number of secondary bacterial infections which may require antibiotic treatment.

INFLUENZA

- Treatment:
 - Supportive care
 - Antivirals (oseltamivir, zanamivir, peramivir, baloxavir) in select populations
 - **No indication for antibiotics**

CASE #3

- A 55yo F with h/o HTN, DM type 2, obesity and asthma presents c/o 1 day of fever to 101, chills, myalgias, and sore throat. Pt is fully vaccinated against covid-19 (received 2nd booster shot 1 week prior.) She works as a CMA in a primary care clinic but is not aware of any known covid exposures recently.
 - **Is there anything else you want to know or diagnostic tests you would order?**
 - **What is the most likely diagnosis?**
 - **What is the treatment? -> Are antibiotics indicated?**

COVID-19

- Serious complications can result from COVID-19 and include pneumonia, acute respiratory distress syndrome, arrhythmias, multiorgan failure, septic shock and death.
- **Symptoms:** Fever, chills, cough, shortness of breath, sore throat, loss of sense of taste or smell, headache, rhinorrhea, congestion, malaise, myalgias, gastrointestinal symptoms
- **Diagnosis:** Rapid antigen test, PCR
- **Prevention:** **Vaccines** against SARS-CoV-2 have proven to decrease the incidence of contracting SARS-CoV-2 as well as prevent hospitalization and death in those who develop symptomatic infections.

COVID-19

- **Treatment:**
 - Supportive care
 - High-risk patients with mild to moderate illness: consider monoclonal antibodies or antivirals (i.e., Paxlovid)
 - Hospitalized patients with severe illness: glucocorticoids, remdesivir, janus kinase inhibitors and/or interleukin 6 inhibitors
 - **No indication for antibiotics**
 - Use of azithromycin with hydroxychloroquine in patients with COVID-19 has been associated with an increased risk of QT prolongation without clear benefit in mortality.

CASE #4

- 32 yo singer presents with onset nearly 1 week ago of fevers to 100.4 associated with nasal congestion, sore throat and a hoarse voice. The hoarse voice has persisted and the patient has a concert in 2 days. He is requesting antibiotics.
- **How do you respond?**

LARYNGITIS

- Clinically presents as a hoarse voice typically associated with other symptoms of URI.
- A recent Cochrane review of laryngitis concluded that antibiotics are not typically effective for treatment and **any benefits including slight improvement in voice** likely do not outweigh costs.

CASE #5

- 42 yo gentleman with PMH of allergic rhinitis presenting with onset of fevers up to 102 degrees F associated with thick green nasal discharge and facial headaches on the day prior to presentation.

What is the likely diagnosis?

How would you treat?

RHINOSINUSITIS

- Common presenting symptoms include fever, purulent nasal discharge, facial pain, and headache.
- ARS is overwhelmingly viral in etiology with viruses responsible for 90-98% of the cases.
- Comparatively, acute bacterial rhinosinusitis (ABRS) develops in 0.5-2% of all URIs with only a percentage of these cases warranting antibiotics.
- A Cochrane review of treatments for ARS in 2018 concluded that considering antibiotic resistance and the very low incidence of serious complications, there is no place for antibiotics in the treatment of uncomplicated ARS.

RHINOSINUSITIS

- Based on the 2012 IDSA guidelines, antibiotics should be started for those patients manifesting **any one** of the constellations of symptoms below:
 - **Any one know the 4 constellations of symptoms?**

RHINOSINUSITIS

- Based on the 2012 IDSA guidelines, antibiotics should be started for those patients manifesting **any one** of the constellations of symptoms below:
 - Persistent symptoms or sign compatible with ARS lasting >10 days without clinical improvement.
 - Onset with severe symptoms or signs including high fever (>39 degrees C/102 degrees F) and purulent nasal discharge.
 - Facial pain lasting at least 3-4 consecutive days at the beginning of the illness.
 - Worsening symptoms or signs for three to four days characterized by the onset of fever, headache or increase in nasal discharge following a typical viral URI that lasted five to six days and was initially improving (double sickening)

CASE #5

- 42 yo gentleman with PMH of allergic rhinitis presenting with onset of fevers up to 102 degrees F associated with thick green nasal discharge and facial headaches on the day prior to presentation.

What is the likely diagnosis?

How would you treat? What is the microbiology?

CASE #5

How would you treat?

-The predominant causes of ABRS are *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis* . Based on this microbiology, first line treatment for ABRS is amoxicillin/clavulanate with a treatment duration of 5-7 days in adults and 10-14 days in children.

-If allergic to PCN:

Adults: Doxycycline or Cefixime

Children: Cefpodoxime or Cefdinir

CASE #6

- A 2yo F ex-FT with no significant PMH is brought into clinic by mother for 4 days of fever, cough and runny nose. Her po intake is slightly decreased but she is making a normal number of wet diapers. She seems a little tired when she is febrile but defervesces with acetaminophen/ibuprofen and is otherwise behaving normal. Mom notes that patient started tugging on her left ear this morning but denies any drainage from the ear. She is UTD on vaccines. She attends daycare.
 - **Is there anything else you want to know or diagnostic tests you would order?**
 - **What is the most likely diagnosis?**
 - **What is the treatment? -> Are antibiotics indicated?**

ACUTE OTITIS MEDIA

- Acute otitis media (AOM) is defined as **the rapid onset of signs and symptoms of inflammation in the middle ear.**
- It is the most common diagnosis leading to antibiotic prescriptions for children in the U.S.
- Pathogens: *S. pneumonia*, nontypeable *Haemophilus influenzae*, *Moraxella catarrhalis*.
- ABX treatment of AOM leads to modest improvement in symptoms compared to placebo or delayed antibiotics, but between 4-10% of children treated with antibiotics for AOM will experience adverse effects, primarily diarrhea and rash.
- Correct diagnosis of AOM in infants and young children is difficult because symptoms can be mild and proper visualization of the patients' tympanic membranes can be limited by patient cooperation, cerumen in the ear canal, and the self-limiting nature of the disease.

ACUTE OTITIS MEDIA

- **Signs/symptoms:** Middle ear effusion and signs of middle ear inflammation (fever; tugging, rubbing, or holding the ear; irritability, or excessive crying)
- **Diagnosis:** *Per the 2013 AAP/AAFP guidelines*
 - moderate to severe bulging of the TM,
 - new onset of otorrhea not due to acute otitis externa, or
 - mild bulging of the TM with either less than 48 hours onset of ear pain or intense erythema of the TM

ACUTE OTITIS MEDIA

- **Treatment:**
 - Analgesics
 - Watchful waiting (f/u in 2-3 days vs Rx provided at initial visit to be filled if child does not improve or clinically worsens in 2-3 days)
 - children ≥ 2 years with mild signs and symptoms of illness
 - children 6 to 23 months with mild, unilateral AOM
 - Consider ABX in children with
 - severe illness (severe otalgia, otalgia lasting >48 hours or temperature $\geq 39^{\circ}\text{C}$)
 - bilateral infections
 - children ≤ 23 months

ACUTE OTITIS MEDIA

- Appropriate Antibiotics (Children)
 - **First line:** Amoxicillin 80-90 mg/kg/d po divided q12h x 5-10 days*
 - **PCN allergy:**
 - Cefdinir 14 mg/kg/day po divided in 1-2 doses x 5-10 days*
 - Cefpodoxime (10 mg/kg/day divided in 2 doses) x 5-10 days*
 - **Second line** (*children who have taken amoxicillin within the past 30 days, with concurrent purulent conjunctivitis, with a history of recurrent AOM unresponsive to amoxicillin, or with no improvement after 48-72 hours of initial treatment with amoxicillin*):
 - Amoxicillin/clavulanate (90 mg/kg per day of amoxicillin, with 6.4 mg/kg per day of clavulanate, in 2 divided doses) x 5-10 days*

**Children <2 years or ≥2 years with severe symptoms should receive a 10-day course of oral antibiotics. Children 2 to 5 years with mild to moderate symptoms can be treated for 7 days, children ≥6 years with mild to moderate symptoms can be treated for 5-7 days.*

ACUTE OTITIS MEDIA

- Appropriate Antibiotics (Adults)
- **First Line:** Augmentin 875 mg po BID OR 500 mg po q8h x 5-10 days**
- **PCN allergy:**
 - Cefdinir 300 mg po BID or 600 mg po daily x 5-10 days**
 - Cefpodoxime 200 mg po bid x 5-10 days**
 - Doxycycline 100 mg bid x 5-10 days**
 - Azithromycin 500 mg po on day 1 then 250 mg po daily days 2 through 5

***Adults with mild to moderate infection can be treated for 5-7 days, those with severe illness should be treated for 10 days.*

CASE #7

- A 12yo M presents with his grandmother for 2 days of fever and sore throat. He is fully vaccinated including 2 covid vaccines. He denies myalgias, rhinorrhea, or cough. His exam is notable for a T of 101.4, tonsillar exudates, and tender anterior cervical lymphadenopathy.
 - **Is there anything else you want to know or diagnostic tests you would order?**
 - **What is the most likely diagnosis?**
 - **What is the treatment? -> Are antibiotics indicated?**

PHARYNGITIS

- Majority of cases are viral!
- Group A beta-hemolytic streptococcal (GAS) pharyngitis = the most common bacterial cause of acute pharyngitis, accounting for 5-15% of sore throat visits in adults and 20-30% in children.
- GAS pharyngitis is more common in children ages 5-15 years old than in adults.
- **Signs/Symptoms:** Sore throat, pain with swallowing, fever, absence of cough. Headache, nausea and abdominal pain may be symptoms for children.

PHARYNGITIS

- **Diagnosis:** difficult to distinguish viral vs bacterial clinically
 - Validated scoring tools (Centor Criteria, Mclsaac Score)
 - Rapid Antigen Detection Tests (high specificity, low sensitivity)
 - Throat cultures
 - Point-of-care molecular testing (high sensitivity, fast turnaround, but possible false positives)
- Testing for GAS pharyngitis is discouraged in children and adults who also have signs or symptoms suggestive of a viral etiology such as diarrhea, rhinorrhea, and/or cough and in children <3 years (low incidence of streptococcal pharyngitis and acute rheumatic fever in this age group.)

CENTOR CRITERIA

Clinical Finding	Points
Absence of cough	+1
Tender anterior cervical lymphadenopathy	+1
Fever (≥ 100.4 F)	+1
Tonsillar exudates/swelling	+1
Modified Centor Criteria (in addition to above)	
Age	
3 to 14 years	+1
15 to 45 years	0
Older than 45 years	-1

Patients with a score of ≤ 1 do not require further testing or treatment, although contact with a person who has documented streptococcal infection should be considered in patients with a score of 1, and testing should be performed in these cases; rapid antigen detection testing should be considered for those with a score of 2 or 3 and, if results are positive, should receive antibiotics; and those with a score of 4 or 5 should receive antibiotics.

PHARYNGITIS

- Treatment:
 - Supportive care
 - **GAS pharyngitis: ABX** help prevent the rare complications of acute rheumatic fever and peritonsillar abscess, hastens clinical resolution, and decreases contagion.

PHARYNGITIS

- Appropriate Antibiotics
- **First Line:** Penicillin/Amoxicillin
 - Children ≥ 3 yo: PCNV 250 mg po bid-tid x 10 days
 - Adolescents and Adults: PCNV 250 mg po qid or 500 mg po bid x 10 days
 - Amoxicillin 50mg/kg po daily (max 1000 mg) OR 25 mg/kg po (max 500 mg) bid x 10 days
 - Benzathine Penicillin G (<27 kg) 600,000 U IM x 1 vs (≥ 27 kg) 1,200,000 U IM x 1
- **Penicillin allergy:**
 - Cephalexin 20 mg/kg/dose po (max 500 mg) bid x 10 days
 - Clindamycin 7 mg/kg/dose po (max 300 mg) tid x 10 days
 - Azithromycin 12 mg/kg/dose po (max 500 mg) daily x 5 days

CASE #8

- A 25yo F presents to the ED with 3 days of worsening throat pain, difficulty swallowing, fever and hoarseness. She has a temp of 100.8, is mildly tachycardic but otherwise vitals are stable. She is most comfortable sitting up. On exam she is in mild distress, her OP is erythematous but otherwise unremarkable, and you notice mild inspiratory stridor.
 - **Is there anything else you want to know or diagnostic tests you would order?**
 - **What is the most likely diagnosis?**
 - **What is the treatment? -> Are antibiotics indicated?**

EPIGLOTTITIS

- Epiglottitis is a rare but life-threatening condition that results from inflammatory edema of the epiglottis and its surrounding supraglottic tissues which is often due to infection.
- Pathogens: *Streptococcus pneumoniae*, GAS and *Staphylococcus aureus*, Hib
- Adults > children
- Signs/symptoms:
 - Children: rapid development of high fever, inspiratory stridor, restlessness, drooling, a muffled “hot potato” voice, and a preference to sit forward in the “sniffing” position.
 - Adults: slower onset of sore throat, odynophagia, dysphagia, fever, dyspnea, hoarseness, muffled voice, drooling, cough, and stridor
- **Diagnosis:** Direct visualization with laryngoscopy or an x-ray demonstrating an enlarged epiglottis (“thumb print” sign)
- **Treatment:** Supplemental humidified oxygen, corticosteroids, and **IV broad-spectrum ABX** (third-generation cephalosporin [ceftriaxone or cefotaxime] or ampicillin/sulbactam, +/- vanc, consider additional ABX vs antifungals)

What determines a true PCN allergy?

PEN-FAST Penicillin Allergy Clinical Decision Rule

PEN Penicillin Allergy Criteria	If yes, proceed with assessment
F Five years or less since reaction	2 points
A Anaphylaxis or angioedema OR S Severe Cutaneous Adverse Reaction	2 points
T Treatment required for allergy episode	1 point

Interpretation	
Points	
0	Very low risk of positive penicillin allergy test (<1% or <1 in 100 patients reporting penicillin allergy)
1-2	Low risk of positive penicillin allergy test (5% or 1 in 20 patients)
3	Moderate risk of positive penicillin allergy test (20% or 1 in 5 patients)
4-5	High risk of positive penicillin allergy test (50% or 1 in 2 patients)

Forms of severe delayed reactions include potential Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, and acute generalized exanthematous pustulosis. Patients with a severe delayed rash with mucosal involvement should be considered to have a severe cutaneous reaction.

INTERVENTIONS TO REDUCE UNNECESSARY ANTIBIOTIC USE

- Antibiotic resistance is among the greatest public health threats today with the CDC estimating over 2 million antibiotic resistant infections resulting in at least 23,000 deaths per year in the U.S.
- Antibiotic stewardship is a national effort to improve antibiotic prescribing by clinicians and use by patients so that antibiotics are only prescribed and used when needed. It also works to ensure that the right drug, dose and duration are selected.
- In the CDC's review of antibiotic stewardship in 2013, it identified high priority conditions to target for improving antibiotic prescribing including nonspecific URI, viral pharyngitis, uncomplicated ABRS, and AOM.

INTERVENTIONS TO REDUCE UNNECESSARY ANTIBIOTIC USE

- A review of AHRQ's 2016 summary of the effectiveness and adverse consequences of strategies to reduce antibiotic use in adults and children with uncomplicated URIs found that **rapid antibody detection tests in adults** reduced inappropriate antibiotic prescribing without adverse consequences. In contrast, **delayed prescribing** reduced antibiotic use but also decreased patient satisfaction and increased symptom length.

INTERVENTIONS TO REDUCE UNNECESSARY ANTIBIOTIC USE

- A similar review performed two years later looked at 133 studies and found the best evidence for three interventions for URIs that improved or reduced antibiotic prescribing without causing significant adverse consequences.
 - **Clinic-based parent education**
 - **Public patient education campaigns combined with clinician education**
 - **Electronic decision support systems**

INTERVENTIONS TO REDUCE UNNECESSARY ANTIBIOTIC USE

- Looking at children specifically, a cross-sectional study of 1,285 visits for acute URIs between December 2007 and April 2009 demonstrated that a **combination of positive treatment recommendations (suggestions to reduce patient's symptoms) with negative treatment recommendations (explanations of the inappropriateness of antibiotics)** was associated with decreased antibiotic prescribing and higher visit satisfaction ratings.

CONCLUSIONS

- Most URIs are caused by viruses and do not require antibiotics.
- Unnecessary antibiotic use results in adverse events, contributes to antibiotic resistance, and adds unnecessary costs.
- URIs can be categorized as those that never require antibiotics (the common cold, influenza, covid-19, laryngitis), those that sometimes require antibiotics (rhinosinusitis, AOM, pharyngitis) and those that almost always require antibiotics (epiglottitis).
- Antimicrobial stewardship aims to improve patient outcomes, minimize unintended consequences, and prevent unnecessary health care costs by ensuring antibiotics are prescribed correctly and only when necessary.
- Proven interventions to decrease unnecessary antibiotics use include the implementation of rapid antibody detection tests in adults, delayed prescribing of antibiotics, clinic-based parent education, public patient education campaigns combined with clinician education, electronic decision support systems, and a combination of positive and negative treatment recommendations

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