Antibiotic Use in Primary Care

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The art of medicine consists in amusing the patient while nature cures the disease.

―Voltaire

Learning Objectives:
1. Discuss the potential benefits and harms of antibiotic use from both an individual and a community-based standpoint
2. Describe principles of responsible antibiotic prescribing
3. Practice methods to counsel family members about antibiotics.

Primary Reference:

CASE ONE:

Anna Byotic, an anxious mother well known to your practice, phones the on call physician at midnight and states that her 6-year-old son has had 2 days of worsening sore throat. He is having trouble sleeping because of the discomfort, which is what prompted her call. After determining that the child is in no acute danger, the on call doctor recommends coming into the office for the first morning appointment slot with you. When they arrive in your office Mrs. Byotic states “He must have strep throat or sinusitis! The last time this happened he got antibiotics that made all the difference.”

1. What is the incidence of inappropriate antibiotic prescribing? What features of a visit (demographic characteristics, parental traits, and exam findings) might increase the likelihood of inappropriate antibiotic prescribing?

One third of patients diagnosed with common cold receive an antibiotic prescription. This number increases up to 60% of patients presenting with bronchitis and other signs and/or symptoms of a respiratory viral illness. Unnecessary antibiotic use contributes to excess health care costs, promotes antibiotic resistance and causes many preventable adverse drug reactions. It is therefore important for providers to be self-reflective regarding what triggers them to pull out their prescription pads and how we are responsible for educating our patients and guiding their healthcare expectations.

Studies reveal a variety of visit characteristics predict inappropriate antibiotic prescribing. Perceived patient or parental satisfaction or pressure is a key driver. Physicians are more likely to prescribe antibiotics if they believe that the parent or patient expects this course of treatment. Parental anxiety about the child’s illness increases the likelihood of antibiotic prescribing for viral illnesses. Parents or patients offering a candidate bacterial diagnosis (“strep throat”, “pneumonia”, “ear infection”) during the encounter is associated with receipt of antibiotics. Parental questioning of a provider’s treatment plan is associated with higher incidence of inappropriate antibiotic prescribing. However, one study showed that meeting parental expectations for communication predicted satisfaction, not prescribing practices.

Minority patients and patients with low socioeconomic status receive different treatment in regards to antibiotic prescribing, though the direction of prescribing patterns has varied across studies (i.e., different studies have revealed both greater and fewer unwarranted antibiotic prescriptions for viral syndromes). Proposed reasons for these differences are manifold, and include language barriers, poor access to a medical home, cultural expectations, provider bias, or other environmental factors. As noted above, parental expectations can influence prescribing behavior, and in one study, parents of
Medicaid-insured children had more misconceptions about antibiotic use and were more likely to request unnecessary antibiotics.

In another study, physicians were more likely to prescribe antibiotics for viral infections when they reported presence of rhonchi or wheezing on exam. It is critical to make distinctions between viral-induced wheezing, transmitted upper airway sounds, and bacterial pneumonia.

In addition to these patient-related factors, it has been shown that the likelihood of prescribing antibiotics inappropriately for acute respiratory infections increases with each subsequent hour of a clinical session and with higher patient visit volumes, consistent with decision fatigue.

**CASE continued:**

You assure her that you will do a thorough evaluation and turn your attention to the child, Faren Gyits. He has no significant medical history, and denies any fever, rash, runny nose, cough, or change in appetite. He is afebrile and his vital signs are normal. He looks comfortable and in no distress although quiet. His exam is unremarkable except for an erythematous posterior oropharynx without any petechiae or exudates, and tender anterior cervical lymphadenopathy. Chest, abdominal, and skin exams are normal.

2. The first principle of judicious use of antibiotics is to determine the likelihood of bacterial infection; how would you do that in Faren’s case? What features of his history and physical make a bacterial cause more or less likely?

With the hope of reducing antibiotic overuse through sound clinical decision making, the AAP issued a Clinical Report in which three “Principles of Judicious Antibiotic Prescribing” are defined:

1. determine the likelihood of a bacterial infection;
2. weigh the benefits and risks of treatment to determine whether antibiotics should be utilized;
3. implement judicious prescribing strategies (i.e., use the most narrow-spectrum and effective antibiotic for the appropriate duration).

The first step is to determine the likelihood of a bacterial infection. It is important to use diagnostic criteria and clinical guidelines when available and to confirm with diagnostic testing when appropriate. In the case of pharyngitis, various clinical scoring tools have been studied. While none of these rubrics are perfect, familiarity with clinical predictors of a disease can help the clinician develop an informed pre-test probability. Since only 20-30% of pediatric sore throat visits are due to Group A Streptococcal (GAS) pharyngitis, these scores can aid the decision of whether or not laboratory testing would be useful.

The modified Centor score is an example of one such tool for use in children over 2 years of age presenting with a sore throat. It is validated to help determine the likelihood of GAS infection based on the clinical presentation. The score provides a pre-test probability which can inform whether testing for GAS is appropriate with rapid antigen detection testing or culture, or if no testing is warranted based on a very high likelihood of viral etiology. There is a 15-20% GAS colonization rate in asymptomatic patients, and therefore a higher risk of false positive results in patients who have a low pre-test probability.

The modified Centor score states that if 2 or more of the following are present in children with pharyngitis, a diagnosis of GAS and therefore further diagnostic testing should be considered: 1) absence of cough; 2) presence of tonsillar exudates; 3) history of fever; 4) swollen and tender anterior cervical lymph nodes; and 5) age 3-15. Likewise if the patient has 0 or 1 of these criteria, the likelihood of GAS pharyngitis is low (<10%), and laboratory testing can be avoided in most cases.

While not part of the scoring rubric, the Infectious Diseases Society of America (IDSA) points to other features that make GAS pharyngitis less likely such as overt viral features like rhinorrhea, oral ulcers, and/or hoarseness, which should also deter the clinician from any GAS testing. It should be noted that the full Centor recommendation of empiric treatment when a high score is reached is NOT recommended in either pediatric or adult cases by the IDSA due to a pre-test probability of GAS pharyngitis of about 50% even when ≥4 features are present. The modified Centor score, like other...
clinical prediction rules for GAS pharyngitis, is most useful in identifying those children who are very unlikely to have bacterial illness.

In Faren’s case, he gets a total of 3 points for the absence of cough, tender anterior cervical lymphadenopathy, and his age. Additionally, he does not have any obvious clinical symptoms that are consistent with viral etiologies. It is appropriate to proceed with rapid antigen detection testing, if available, or throat culture for GAS.

Moderators may wish to highlight that specific recommendations exist to assist with the diagnosis of other common bacterial illnesses in children (e.g., pneumonia, sinusitis, otitis media, urinary tract infection). Dedicated chapters for many of these conditions can be found elsewhere in the curriculum.

CASE continued:

You decide to perform a rapid antigen detection test for Group A Streptococcus (RADT) and with Faren’s cooperation and bravery, you are able to get an excellent sample from both tonsils, pillars, and the posterior oropharynx. The RADT comes back negative within minutes.

3. What is the most appropriate next step? What if the test had come back positive?

In children, more so than adults, RADT has a significant false negative rate with a sensitivity of about 85%, so a confirmatory culture should be done if the RADT is negative. No antibiotics should be given unless there is a positive RADT or GAS throat culture. Rare exceptions to this rule include pharyngitis in a close household contact with culture-documented GAS pharyngitis.

RADT has a high specificity, so if it is positive, there is a high likelihood of bacterial pharyngitis and no need to perform throat culture.

CASE continued:

You send a throat swab for culture and send Faren home with advice for symptom management. Two days later, the throat culture comes back positive.

4. Apply the second principle of judicious antibiotic use by weighing the benefits and harms of antibiotics in this case to determine if antibiotics are indicated.

Potential benefits of treating with antibiotics are decreased duration of symptoms and prevention of rare but serious complications. For GAS pharyngitis, studies have shown that antibiotic treatment decreases sore throat and headache by 1 day and reduces contagiousness to close contacts within 24 hours of initiation- suggesting a broader impact on lost school and work days. Rare but serious complications include peritonsilar abscess (number needed to treat is 4000) and acute rheumatic fever (2-14 cases per 100,000 in the US). In developing countries, there is a higher incidence of rheumatic disease both because of increased prevalence of rheumatogenic strains of GAS and less access to testing and treatment.

Potential harms of antibiotics to the individual patient include upset stomach, allergic reaction (ranging from mild to life-threatening), antibiotic associated diarrhea, \textit{Clostridium difficile} colitis and Candidal infection. Beyond these acute complications, there is ongoing research underway about the possible impact of antibiotics on the human microbiome and how it may change metabolism and risk for many disease states. There is some animal data suggesting that antibiotic use may be correlated with inflammatory bowel disease, asthma, and obesity. Large retrospective cohort studies suggest some small increase in weight in children given antibiotics before age 2 compared to those who are not given antibiotics.

Harms to the local and global community include increased resistance of microbes to available agents by applying selective pressure to microbes as they are exposed to antibiotics. In the past few decades there has been a pandemic of methicillin resistant \textit{Staphylococcus aureus} (MRSA) both in healthcare
settings and in communities, resistant *Streptococcus pneumoniae*, many resistant Gram negative rods including extended spectrum beta lactamase and carbapenemase producing enterobacteriaceae (e.g., *Escherichia coli*, Klebsiella and Enterobacter species), and “extensively drug resistant tuberculosis” (XDR) which hugely affects the global community. More recently, *Candida auris* has emerged as a highly drug resistant yeast which has become endemic in some countries (e.g., India, Pakistan, and Venezuela) and has led to healthcare associated outbreaks in New York City, Chicago, and New Jersey. Infections with these resistant organisms are more costly to treat, increase health care utilization, and add significant morbidity and mortality. CDC reports that more than two million Americans suffer from antimicrobial resistant infections annually and 23,000 of these infections result in death. Economic effects are estimated at 20 billion dollars annually, plus 35 billion dollars in lost productivity and 8 million excess hospital days.

What compounds this problem is a limited investment in antibiotic research and development by the pharmaceutical industry, which is largely driven by the limited return-on-investment for producing drugs that require only short therapeutic courses and are utilized sparingly in order to protect efficacy.

Current recommendations from the IDSA and AAP recommend treating for GAS pharyngitis if there is a positive RADT or a positive throat culture in the right clinical setting. No antibiotics should be given prior to a positive test result due to the predominance of viral pharyngitis and the low specificity of the modified Centor score in children.

5. **What antibiotic would you prescribe? Apply the third principle of judicious antibiotic use to frame your answer. How would your decision differ if Faren had a penicillin allergy?**

Once you have determined that antibiotics are indicated, the third principle of judicious antibiotic use is to implement judicious prescribing strategies. That means using the most narrow and effective antibiotic possible with appropriate dosing and duration, including the option of “wait and see” if applicable to the clinical situation. In this case, penicillin or standard-dose amoxicillin should be used for a 10-day course. If the patient has an anaphylactic allergy to penicillin or amoxicillin, clarithromycin or clindamycin for a 10-day course or azithromycin for a 5-day course can be used. If there is a penicillin allergy without history of anaphylaxis, a first generation cephalosporin can still be prescribed.

Macrolides and cephalosporins should not be used unless the patient has an allergy to penicillin, as these agents do not have superior activity against GAS and are no better at preventing rheumatic fever. Additionally, data does not demonstrate increased adherence with these regimens, and unnecessary use of these wider-spectrum agents can promote bacterial resistance.

6. **What techniques might increase your success in mitigating a parent’s insistence on antibiotics when they are not clinically indicated?**

Providers can take a variety of steps to circumvent the predictors of inappropriate antibiotic prescribing. Addressing and understanding a patient’s specific concerns early in the visit can be helpful to unite parent-patient expectations with the provider’s assessment. It may be useful to reiterate that both you and the parent-patient have the same goal of getting the child feeling better in a safe and effective way. A discussion about the clinical features (related to history and physical exam) consistent and inconsistent with the candidate diagnoses can help to tailor the visit towards the patient’s specific concerns, rather than simply focusing on arriving at a diagnosis. The use of patient-centered strategies to avoid minimizing the significance of symptoms, delegitimizing a parents’ decision to seek medical care, and to directly address parental anxiety can also serve to build rapport. **Moderator’s may wish to review the “5-step patient-centered interviewing” method included as a resource in the module on “Agenda Setting in the Outpatient Visit” (see Resources section below)**.

Strategies such as positively framing the diagnosis and using specific instructions for symptom relief (including over-the-counter medications when indicated) are associated with more patient-parent alignment with the proposed treatment plan. The provider should be clear about the diagnosis of a viral syndrome, express empathy about the severity of symptomatology (and the impact that a sick child can have on the family), and express relief that antibiotics are not needed. Rather than categorically stating that antibiotics are not indicated, the clinician can explain how he or she has
arrived at this decision and why this is a good thing. In some cases a short reminder of the potential harms antibiotics can cause (e.g., diarrhea, allergic reaction, rash, resistant bacteria) can be helpful.

A clear description of techniques for symptom management (e.g., bulb suction, nasal saline, nasal irrigation, humidifying treatments, honey for cough relief in patients over 1 year of age, antipyretics for fever, analgesia for pain, bronchodilators when appropriate) can improve parent-patient approval of the provider’s recommendations. Anticipatory guidance regarding the expected course of the illness can also prevent further parental distress and concern for alternative diagnoses.

Educating patients and families regarding their disease process and appropriate treatment can have a positive effect on future interactions. By investing time in teaching our patients, their improved knowledge about common viral illnesses and risks of antibiotics can shape their expectations and health-care demands in the future.

Lastly, systems-based interventions such as antibiotic stewardship programs have proven effective in modifying physician behavior and greatly reducing the incidence of unnecessary antibiotic prescribing. Electronic medical record integration with clinical decision making tools, formulary restrictions, regular audits and feedback to individual providers about prescribing behavior relative to peers, publicly displayed commitment letters about reducing unnecessary antibiotic prescriptions, and delayed prescribing strategies (e.g., “watch and wait”) have all been shown to radically reduce harmful and unnecessary antibiotic use.

**Additional References:**

**Resources:**
2. Get Smart campaign from CDC has links to information for families and providers about appropriate antibiotic use. http://www.cdc.gov/getsmtart/