Health Care Provider Supplemental Guide to "Talk to Your Health Care Provider About Antibiotics"

1 Antibiotic resistance doesn't mean your body is resistant to antibiotics. It means the bacteria that make you sick are changing so that some antibiotics can't kill them.

- **ASK YOUR HEALTH CARE PROVIDER how this happens and what it might mean for you.**

Each year in the U.S., at least 2 million people are infected with antibiotic-resistant bacteria, and at least 23,000 people die as a result[1]. The time between the discovery of a new drug and the development of resistance to that drug is gradually decreasing[1].

Teaching points for patients:

A few bacteria have random mutations that make them resistant to certain antibiotics. If one of those antibiotics is used, it will kill the bacteria without the mutation, but the mutated, resistant bacteria will survive and take the place of the non-mutated bacteria that were killed.

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2 About 30% of the antibiotics we take in the U.S. are not needed.

- **ASK YOUR HEALTH CARE PROVIDER if you really need an antibiotic and what you can do to feel better if you don't.**

At least 30% of prescriptions provided in U.S. doctors' offices and emergency departments are unnecessary, based on national guidelines for common conditions[1].

- 90-98% of acute rhinosinusitis cases are viral. Even when caused by bacteria, antibiotics may not help[2].
- Viruses cause >90% of acute bronchitis. Treatment of uncomplicated acute bronchitis with antibiotics is not recommended[3].
- Only 5-10% of pharyngitis cases in adults are caused by Group A Streptococcus[4]. Group A Streptococcus is increasingly resistant to clindamycin and azithromycin[5].
- Antibiotics are not recommended for most uncomplicated bacterial diarrhea infections in healthy people. There's no evidence that they shorten the duration of enteric disease caused by salmonella[6]. Antibiotics are not recommended for cases of Shiga toxin-producing E. coli because they have been shown to increase the risk of hemolytic uremic syndrome[7, 8]. Antibiotics are recommended for moderate to severe cases of Shigella dysentery, with the antibiotic of choice in these cases governed by local antibiotic sensitivity patterns[9].

When a patient doesn't need an antibiotic, offer evidence-based symptomatic treatment as appropriate for the clinical situation. Some symptomatic treatments that might be effective for your patients are analgesics/antipyretics[10], throat lozenges or sprays (except for intranasal zinc and zinc gluconate products due to risks of hyposmia and anosmia)[11, 12], cromolyn sodium[13], ipratropium bromide[14], a combination of antihistamine and decongestants (as opposed to antihistamines alone)[15], nasal suctioning for infants, and avoidance of irritants such as cigarette smoke. Other symptomatic treatments that have been shown to be less effective, but still potentially beneficial to patients include honey[16] and saline nasal drops/spray/irrigation[17].

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3 Even if you haven't taken an antibiotic, resistant bacteria can spread to you or your family.

- **ASK YOUR HEALTH CARE PROVIDER about antibiotic resistance in your community and how it could affect you and your treatment.**

Humans and animals are both capable of spreading antibiotic resistance through multiple pathways.

Bacteria naturally develop antibiotic resistance when humans are given antibiotics to treat infections[1]. Recent studies have found that 75% of the multi-drug resistant bacterial infections found in hospitalized children were present before they were admitted, suggesting they acquired the bacteria in their community[2]. Travelers to/from both high-income and low-income countries are at risk of both acquiring and spreading antibiotic resistant bacteria during their travels. The most common are Enterobacteriaceae, such as Salmonella, E. coli, and Klebsiella[3].

Animals have also been known to both acquire antibiotic resistant bacteria from their environment and transport antibiotic resistant bacteria to new places when they travel. In addition to developing antibiotic resistance through the use of antibiotics, animals can also pick up resistant bacteria through the soil and their food[4]. The animals then shed the resistant bacteria in their manure. Plants can pick up the resistant bacteria when the manure is used as fertilizer or if the manure enters nearby streams and rivers[4]. The resistant bacteria are then transmitted to humans through the ingestion of these plants or contaminated water[4].

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4 Bronchitis and sore throats are almost always caused by viruses. Antibiotics won't help because they don't treat viral infections.

- **ASK YOUR HEALTH CARE PROVIDER how to make your cough, sore throat, and other symptoms better and what might suggest a bacterial infection like strep throat.**

Viruses cause more than 90% of acute uncomplicated bronchitis[1]. Colored (e.g. green) sputum does not indicate a bacterial infection[1]. When talking to patients, it is recommended to label acute bronchitis as a "chest cold" or "viral upper respiratory infection" to decrease the patient's request for antibiotics[1]. You are also encouraged to talk with patients about the expected course of illness and cough duration, which is typically 2-3 weeks[1].

Antibiotics for acute uncomplicated bronchitis have been shown to provide only minimal benefit, reducing the cough or illness by about half a day, and have adverse effects including allergic reactions, nausea and vomiting, and Clostridioides difficile infection[1]. All major guidelines on bronchitis, including those from the American College of Chest Physicians, recommend against using antibiotics for acute bronchitis for otherwise healthy patients unless the patient has a known pertussis infection[1]. An important focus of the history and examination is determining if pneumonia is present. The benefits of using antibiotics for patients with bronchitis who are elderly, frail, or have multiple comorbidities have not been extensively studied, and as a result no guidelines have been established for those populations[2].

Strep throat: Diagnostic studies are usually not indicated for children under the age of 3 years because of the relative rarity of streptococcal pharyngitis in the group[3]. Testing for group A Streptococcus (GAS) pharyngitis by a rapid antigen detection test should not be performed when there are overt signs that the pharyngitis is viral in nature, as indicated by features such as rhinorrhea, cough, oral ulcers, and/or hoarseness[3]. When testing is performed in children and adolescents, negative tests should be backed up with a throat culture, while positive tests do not need to be followed up due to the high specificity of the test[3]. Negative results for adults do not need to be followed up because of the relative rarity of GAS in adults[3].

Don't forget to consider pertussis, for which antibiotics are indicated. Pertussis starts with symptoms similar to a viral upper respiratory tract infection, such as nasal congestion, runny nose, and sore throat[4]. As the illness progresses over the next 2-6 weeks, pertussis patients classically have coughing attacks that terminate with a "whoop" and can be followed by vomiting[4], although adolescents and adults might not present with this classic picture. An increasing number of pertussis cases are being reported in immunized people and populations with high immunization rates[5].

Over-the-counter medications are often recommended as first-line treatment for acute cough. However, a Cochrane review on over-the-counter medications for acute cough in the community setting found a paucity of good data; existing trials are of low quality and report conflicting results[5].

When a patient doesn't need an antibiotic, offer evidence-based symptomatic treatment, as appropriate for the clinical situation. Some symptomatic treatments that might be effective for your patients are analgesics/antipyretics[6], throat lozenges or sprays (except for intranasal zinc and zinc gluconate products due to risks of hyposmia and anosmia)[7, 8], cromolyn sodium[9], ipratropium bromide[10], a combination of antihistamine and decongestants (as opposed to just using antihistamines)[11], nasal suctioning for infants, and avoidance of irritants such as cigarette smoke. Other symptomatic treatments that have been shown to be less effective, but still potentially beneficial to patients include honey[12] and saline nasal drops/spray/irrigation[13].

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5 Your favorite antibiotic might not be the best one for your illness.

- **ASK YOUR HEALTH CARE PROVIDER how he or she chooses the best antibiotic for you and what kind of bacteria your health care provider is treating.**

Azithromycin tends to be a favorite, especially for patients with sinusitis. However, studies show that more than 40% of bacteria that cause acute bacterial sinusitis are resistant to macrolides such as azithromycin[1]. For uncomplicated bacterial sinusitis with reliable follow up, watchful waiting for 10 days after the onset of upper respiratory symptoms is encouraged[1, 2].

Teaching points for patients:

Dispel the strong vs. weak antibiotic myth. It's not that an antibiotic is "strong" or "weak". It's a matter of which is best for your infection. Some antibiotics are good for some types of infections; others are good for other infections. It depends on the organism. Health care providers choose the right antibiotic based on a knowledge of which types of bacteria usually cause a particular illness and what the levels of resistance are in the community. In some cases, a culture might be needed.

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6 Don't save antibiotics to take the next time you get sick, and don't share them with other people. Tell your health care provider if you have already taken antibiotics for your illness.

- **ASK YOUR HEALTH CARE PROVIDER why taking antibiotics without a prescription can do more harm than good.**

Teaching points for patients:

- Antibiotics can interfere with the results from bacterial cultures, making it more difficult to correctly diagnose and treat the illness[1].
- Antibiotics can interact with other medications, including hormonal contraceptives[2].
- Some antibiotics should not be taken by pregnant women.
- Research has shown that there is a higher rate of antimicrobial resistance in communities that frequently use nonprescription antibiotics[3].

- The leftover antibiotic might not be the correct antibiotic for the current illness, or might not be the correct dose[3].
- Patients who take leftover antibiotics are more likely to delay seeing a health care provider about the problem, possibly leading to more severe illness[1].
- 95% of the 450,000 cases of poisoning in children under the age of six reported to US poison control centers between 2001 and 2008 were caused by the accidental ingestion of unused prescription medications.

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7 Side effects are common with antibiotics.

- **ASK YOUR HEALTH CARE PROVIDER what side effects to look for and which ones are serious.**

Antibiotics cause 16% of emergency department visits that are related to adverse drug events[1]. Among children aged 19 years old and younger, antibiotics were the most common drug class implicated for these emergency department visits[1]. Approximately four out of five of these visits were due to an allergic reaction[2]. The decision to start antibiotic therapy should include a discussion with the patient of the side effects of the drug, including what steps to take if they suspect an adverse drug event.

Antibiotic use leaves patients vulnerable to antibiotic-associated diarrhea, which occurs in up to 35% of those taking antibiotics[3]. Furthermore, there are 500,000 cases of *Clostridioides difficile* infection in the United States every year, resulting in approximately 30,000 deaths[4]. Avoiding unnecessary antibiotic use, as well as proper selection of antibiotics based on guidelines and resistance patterns, can help patients avoid *C. difficile* infections.

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8 Billions of "good" bacteria live on your skin and inside your body and help keep you healthy. Antibiotics kill some of these good bacteria.

- **ASK YOUR HEALTH CARE PROVIDER about your risk of *Clostridioides difficile ("C. diff")* infection, yeast infections, or other problems caused by killing your good bacteria.**

Recently there have been many articles in the lay press describing research on the human microbiome, the collection of bacteria and other microorganisms that reside in or on a specific part of the body, such as the gut or the skin. The articles describe numerous correlations with and hypothesized effects of alterations in the microbiome, particularly the fecal microbiome, including obesity, inflammatory bowel disease, colon cancer, depression, Parkinson's disease, allergy, and autism. Antibiotics have been shown to deplete the bacteria in patients' gut microbiomes[1]. The clinical relevance of these studies is unclear, but your patients might ask you about them.

Diarrhea is a common side effect of antibiotics, with Clostridioides difficile being responsible for most of the severe cases of antibiotic-associated diarrhea potentially caused by the decreased microbial diversity in the gut[2]. A recent small study found that patients who underwent a round of antibiotics and then received an autologous fecal microbiota transplantation (i.e. taken from the patient's own feces) reestablished the intestinal microbiota composition that the patient had before antibiotic treatment[3]. As above, more research is needed, but your patients might ask you about these studies.

There has been a rise in the use of probiotics and prebiotics in the past decade[4]. According to the Mayo Clinic[5], **pre**biotics are intended to stimulate the growth of healthy bacteria in the gut. An example of a prebiotic is the complex carbohydrates found in many fruits and vegetables. Because these carbohydrates aren't digestible, they become food for the bacteria in the gut. **Pro**biotics are microbes that are directly added to the gut microbiome. An example of a probiotic is yogurt, which contains live organisms that become part of the gut microbiome when they are ingested. Prebiotics and probiotics are both proposed to aid the body's natural defenses by changing the gut microbiome.

Cochrane Reviews of short-term studies have shown probiotics to be useful in preventing antibiotic-associated diarrhea in the pediatric population[6] and, more broadly, preventing C. difficile diarrhea after taking a round of antibiotics[7]. The authors of both studies note the positive findings in these populations, but they also note the unknown long-term consequences of taking probiotics, especially in healthy populations.

Following antibiotic prescribing guidelines may help avoid use of an agent that is either too narrow, which might not kill the pathogenic bacteria, or too broad, which might kill good bacteria and also contribute to resistance.

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9 Vaccinations can prevent some bacterial infections in both adults and children, reducing the need for antibiotics.

- **ASK YOUR HEALTH CARE PROVIDER if you need any vaccines.**

Vaccines might reduce antibiotic use in at least four ways:

1. Reduction of bacterial disease. Vaccines can prevent illnesses such as pneumococcal and meningococcal diseases for which antibiotics are indicated. In California, the introduction of a pneumococcal conjugate vaccine prevented 35 antibiotic prescriptions per 100 vaccinated children, suggesting that 1.4 million antibiotic prescriptions per year in the US are prevented with pneumococcal conjugate vaccination[1]. When the vaccines prevent these diseases, they reduce the need for antibiotics to treat them, thus potentially decreasing antibiotic resistance in the community.
2. Reduction of inappropriate antibiotic use. Vaccines for viral diseases such as influenza prevent illnesses for which antibiotics might be given inappropriately[2].
3. Reduction of secondary bacterial infections. Vaccines for viral diseases such as influenza might prevent secondary bacterial infections for which antibiotics are indicated.
4. Reduction of hospitalization. Vaccines can prevent illnesses that lead to hospitalizations and exposure to the antibiotic-resistant bacteria that thrive in that setting.

Please refer to the ACIP Vaccine Recommendations and Guidelines for both children & adolescents and adults[3].

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10 Antibiotics can be lifesavers if you have a serious bacterial infection or sepsis.

- **ASK YOUR HEALTH CARE PROVIDER what symptoms might suggest that you have a serious bacterial infection or sepsis and what you should do if you don't get better or if you start to feel worse.**

In addition to understanding what clinical changes should prompt a phone call, follow-up visit, or other action, it's important for your patients to know the symptoms of sepsis and to act fast and seek immediate medical care if symptoms develop. According to the CDC, signs of sepsis include a high heart rate and either a fever or shivering[1]. Common symptoms include confusion or disorientation, shortness of breath, extreme pain or discomfort, and clammy or sweaty skin[1]. High risk populations include those who are 65 years or older, people with chronic conditions, and people with weakened immune systems[2]. People of lower socioeconomic status are also more susceptible to developing bloodstream infections, which can lead to sepsis[2].

A review of sepsis cases in New York State[3] found that the most common illness leading to sepsis was pneumonia (35% of cases), followed by urinary tract infections (25%). The same study found that 35% of patients had diabetes, 32% of patients had cardiovascular disease, 23% had chronic kidney disease, and 20% had chronic obstructive pulmonary disease (COPD).

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