

A Practical Guide to Diagnosis and Treatment of Infection in the Outpatient Setting
Avoiding Unnecessary Use and Misuse of Antibiotics

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The first in a series of articles to educate primary care physicians about the proper, judicious and equitable use of antibiotics in the outpatient setting.

Overuse of antibiotics is rampant in our community and across the country. This serves to accelerate the rate of development of multi-drug resistant (MDR) organisms. Using antibiotics in situations where they are not necessary also increases the cost burden on the healthcare system, not from the antibiotics themselves, but from the treatment of infections caused by these MDR organisms and the additional morbidity caused by adverse reactions to the drugs themselves.

Using the wrong or inferior antibiotics or using incorrect dosing thereof to treat certain bacterial infections can lead to prolonged illness and treatment failure. Delayed diagnosis may also result. Some doctors, not willing to put forth the effort to run the patient through a diagnostic regimen, simply prescribe an antibiotic hoping that whatever the problem is it will resolve. Many times, oral antibiotics are not potent enough to control the more serious bacterial infections, but are prevalent enough in body fluids and tissues to interfere with cultures, rendering them falsely negative.

A sound understanding of a few general principles should aid primary care doctors to avoid the pitfalls of antibiotic misuse. Please consider the following.

Take the time to make the correct diagnosis before prescribing an antibiotic.

This necessitates a return to the basics taught in our medical schools and residencies: 1) obtain a detailed history, 2) perform a thorough physical examination, 3) think through a differential diagnosis, and 4) order tests appropriate for the differential diagnosis.

Unfortunately, enormous patient loads force many doctors to rush through each patient, giving only superficial attention to each of the above four steps. As a result, many patients with viral illnesses, or illnesses that are not infectious in origin at all, are administered antibiotics unnecessarily. Better attention to historical details, physical exam, and a little extra effort to obtain appropriate confirmatory tests would prevent primary care physicians from making this error.

One place to start would be to recognize when an infection is bacterial and when it is viral. As a general rule, bacterial infections have a tendency to be focal, produce pus (or purulent respiratory secretions), and if severe enough, generate leukocytosis. Viral infections, on the other hand, have a tendency to be more generalized, produce no pus, rarely produce leukocytosis (with the exception of infectious mononucleosis) and many times cause leucopenia. A good rule of thumb for dealing with upper respiratory tract infections is to remember that streptococcal infections (i.e., strep throat) never causes rhinorrhea. So, if a patient presents with a sore throat and runny nose, you can be assured that it is viral and that patient does not need antibiotics. If there is any uncertainty, rapid streptococcal kits are available which can give a result while the patient waits.

If a bacterial infection is diagnosed, know which antibiotics are first line for that infection and use them.

First line drugs are more efficacious than second or third line agents. The better the efficacy, the shorter the course of antibiotics that is usually required and the lower the rate of treatment failure. For example, Levaquin is often used to treat cellulitis. However, less than 50% of *Staphylococcus aureus* (the most common cause of cellulitis) is sensitive to Levaquin, and therefore it is less efficacious than the first line drugs dicloxacillin (an anti-staphylococcal penicillin), cephalexin (a first generation cephalosporin) or clindamycin.

First line drugs also have a tendency toward a relatively narrow spectrum of antimicrobial activity. The more narrow the spectrum an antibiotic has, the fewer groups of bacteria to which it will apply selective pressure to mutate into resistant forms. As in the example of cellulitis, Levaquin has broad *gram negative* coverage, something that is not needed in the treatment of this predominantly gram positive infection. The Levaquin will, however, affect the gram negative gut flora and increase the likelihood of developing strains that are less sensitive to quinolones.

The bottom line: know what the first line drugs are, and use them. A discussion of first line drugs for specific infections will be presented in subsequent articles.

Use correct doses – look them up if uncertain.

Under-dosing of antibiotics encourages development of resistant strains of microorganisms. A simplistic way of looking at it is that a microorganism causing a given infection may not be a pure clone, but rather a heterogeneous population that includes sub-strains with varying levels of sensitivity to the antibiotic being employed. As a general rule, the concentration of antibiotic in the infected tissue must exceed the MIC (minimum inhibitory concentration) of the causative agent by eight fold to successfully subdue the infection. Under-dosing an antibiotic leads to lower tissue concentrations which may still be enough to eradicate the most sensitive (those with the lowest MICs), and most numerous subpopulation, but not enough to kill of the more resistant strains (those with the higher MICs). Thus, the more resistant strains survive and become the more dominant population.

Perhaps fueled by a desire to be frugal, considering the rising cost of healthcare, under-dosing of antibiotics is widespread. In the long run, however, it will become more costly if the rate of development of multi-drug resistance among pathogenic bacteria increases. Under-dosing of antibiotics also leads to treatment failures, which, for obvious reasons, also increases the cost of healthcare.

It behooves every practitioner who prescribes an antibiotic to take the time to look up recommended doses if s/he is not intimately familiar with the drug. If uncertain about renal function, or body weight, both of which influence the magnitude of antibiotic dose in most instances, it is better to err on the side of overdosing, rather than on the side of underdosing. With most antibiotics, little, if any, toxicity occurs when overdosed, but if underdosed, the risk of treatment failure and development of resistant strains increases.

Get a detailed drug allergy history.

An important part of the history that is almost always left incomplete is the drug allergy history. Without a full picture of the patient's antibiotic allergy history a physician might be prevented from using a first line drug which would treat a given infection more effectively than an alternative antibiotic and do it without much risk.

The key here is not only to find out to which drugs a patient has allergies, but to find out what reaction he or she had when the antibiotic was taken. Drug induced rashes like urticaria are in and of themselves basically harmless, albeit annoying. More serious reactions include anaphylaxis, Stevens-Johnson syndrome and angioedema of the upper respiratory tract. The different types of allergic reactions occur through different mechanisms, so drugs that cause a simple rash do not usually go on to cause anaphylaxis.

As a general rule, cephalosporins have a 10 to 20% cross allergenicity with penicillin. If using a cephalosporin in a patient who gets a simple rash when he takes penicillin means that there is a 10 to 20% chance of causing a rash, then the risk of giving that person a cephalosporin is acceptable – the worst that can happen is the patient might develop a harmless rash. If, however, the allergic reaction to penicillin was anaphylaxis, then 10 to 20% is too big of a risk and cephalosporins should be avoided.

Remember that what a patient thinks is an allergy may not be what we interpret as one. Stomach ache or nausea is *not* an allergic reaction, but should be labeled as gastrointestinal intolerance. In this case, other drugs within that same antibiotic class may be safely used. Some patients report cryptic reactions such as “I felt weird when I took Augmentin,” or “my fingertips tingled when I took Cipro.” Other patients relate that a family member was allergic to a certain antibiotic, therefore they assume that they are allergic to it as well. Allergic reactions are not considered to be hereditary.

Drug allergy histories like these would indicate that antibiotics within the same classes as those to which the patient is questionably allergic may be safely used. Obviously, if a patient is not asked specifically what kind of reaction he had to a certain antibiotic to which he claims to be allergic, first line drugs might be unnecessarily avoided. This could have an adverse affect on his response to therapy. If there is any question as to whether or not a patient is truly allergic to an antibiotic skin testing can be done, or a referral can be made to an allergist.

Interpret cultures correctly – treat the patient, not the lab result.

The mere presence of an organism in culture does not necessarily equate with infection. Bacteria are ubiquitous. If I run a culture swab along my normal-appearing forearm, the lab would likely report growth of a coagulase negative staphylococcus. Should I be started on Vancomycin? Of course not, there is no obvious infection. Yet many doctors react to sputum cultures, wound cultures, urine cultures and blood cultures in a knee jerk manner by starting antibiotics without any consideration as to whether this culture represents a *colonizer* and *contaminant*, or a *true pathogen*.

Each culture result must be interpreted together with other data points. A sputum growing *S. aureus* in someone with a mild dry cough, no fever, normal WBC and a clear CXR probably represents a colonizer and should *not* be treated. However, a culture growing pseudomonas obtained from a wound that is grossly purulent, malodorous, with red and inflamed surrounding skin probably does represent a true pathogen and *should* be treated. Never react to a culture alone, but always consider the whole patient.

Communicate effectively with the patient, especially when an antibiotic will *not* be prescribed.

Many doctors complain that the reason why they prescribe antibiotics for infections that are obviously viral is that the patients expect to leave their office with some treatment in hand. My personal experience as an infectious disease specialist has been to the contrary, however. If after a careful workup I believe that a certain patient has a nonbacterial infection, a detailed discussion of his/her diagnosis and explanation of why I do not believe that antibiotics are indicated always seems to satisfy them. So far no one has ever walked away unhappy. The vast majority of patients will accept your reasoning in such instances without resentment as long as you communicate clearly to them.

Effective communication with patients instills within them greater trust in their doctors. If they understand their medical problems better, they are more likely to accept the withholding of antibiotics in the appropriate situations.

Next in the series: Diagnosis and treatment of pharyngitis in the outpatient setting