

Practical Antibiotic Therapy

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This presentation will be a brief review of antibiotics and how to manage common infections. The first half will focus on characteristics of drug classes, and the second half will have tips on using antibiotics successfully in dogs and cats.

When I work with students, I find they are often at a loss on how to choose an antibiotic for a case. It's not easy for them to look up information quickly, and they lack the clinical experience that we take for granted. However, instead of just telling them what to use, I ask them a few questions:

1. What organism do you think is causing the infection?
2. What tissue or organ do you want the antibiotic drug to reach?
3. Are there any safety concerns (such as other disorders present), or cost or compliance issues with the clients?

From there, we can usually narrow our choices down and select an appropriate drug. If there's time, the student can use textbooks or the Internet (such as VIN) to help answer the questions. I also ask students how they will know if the antibiotic is working, i.e. how do they plan to follow up the case?

I sometimes ask students if they think antibiotics are overused in veterinary medicine. Usually they say yes, but they are not sure why. Although I go over inappropriate antibiotic use in general, I also tell them that every animal and every client is unique. Even when it's scientifically "correct" not to use antibiotics, sometimes other factors override.

From my observations, I've formed some opinions about why antibiotics are overused:

1. Practitioners were taught by other veterinarians, usually employers or mentors, to give antibiotics routinely.
2. There's a sense that antibiotics are well-tolerated, easy to give, and they "won't hurt, might help".
3. Since pets can't talk and much disease is hidden, antibiotics are given "just in case".
4. Antibiotics are believed to prevent infection, for example in surgery.
5. Some illnesses such as viral infections can lead to secondary bacterial infections.
4. Clients expect or even demand antibiotics for their pets, and will be unhappy and go elsewhere if a veterinarian refuses to prescribe.

These reasons may be valid but when subjected to strict scientific evidence and proof of efficacy, a lot of these are not major concerns. As an example, several scientific studies have shown that if antibiotics are given routinely in elective, sterile surgical procedures (such as spays), the post-op infection rate is higher than if no antibiotics are given. In teaching students, I try to emphasize evidence-based medicine rather than just passing along my experiences or anecdotes. In the absence of scientific evidence, we try to come up with rational solutions to infections and the use of antibiotics.

Disclaimer: although these doses have been double-checked and proofread, it's possible that typos or errors have crept in. Please confirm all dosing information before use.

Antibiotic classes

Penicillins

Most penicillins are active against gram-positive organisms. Both aerobic and anaerobic bacteria may be susceptible, but there are many resistant organisms.

Penicillin G (benzyl penicillin) is effective for streptococcal infections and leptospirosis. Because it's an older drug and injectable only, it's not commonly used. Doses range from 20,000 to 40,000 units/kg every 6-8 hours.

Ampicillin and **amoxicillin** are oral or injectable and are usually effective for *E. coli*, *Proteus*, *Pasteurella*, *Borrelia*, strep, and lepto. Ampicillin is an inexpensive and convenient injectable drug that can be used IV, IM, or SC. The dose is 22 mg/kg every 6-8 hours. Amoxicillin oral is dosed at 22 mg/kg every 8-12 hours.

Amoxicillin/clavulanate (Clavamox, Pfizer) is my preference when oral penicillins are indicated. The standard label dose works well, although it can safely be given 3 times a day instead of twice to maintain plasma concentrations.

Ticarcillin has a broad spectrum and is especially effective against *Pseudomonas*. It is available alone (**Ticar**) or combined with clavulanate (**Timentin**). The dose is 22-44 mg/kg every 6-8 hours but can even be increased in severe infections. We commonly dilute with saline to compound a topical antibiotic for bacterial otitis externa or media (especially *Pseudomonas*).

Tips: penicillins are very safe even if overdosed. They are absorbed better on an empty stomach.

Cephalosporins

There are many types of cephalosporins available with various activities against gram-positive and gram-negative bacteria. Most do not have an anaerobic spectrum.

Cephalexin is a popular oral drug. It is usually effective against staph, strep, *E. coli*, *Klebsiella*, and *Proteus* while ineffective against *Pseudomonas* and anaerobes.

Doses range from 20-40 mg/kg every 8 hours. Staph pyoderma responds to 30 mg/kg every 12 hours.

Cefpodoxime (Simplicef, Pfizer) has a similar spectrum as cephalexin but has a longer half-life and is only given once a day. The dose is 5-10 mg/kg daily. In our hospital, cefpodoxime has replaced much of the cephalexin usage.

Cefazolin is an injectable that is often used for surgical prophylaxis. At the time of anesthetic induction (when an IV catheter is placed), a single IV dose of 22 mg/kg is effective and may be repeated every 1-2 hours in a long operation. Cefazolin may also be given IV, IM, or SC every 6-8 hours for various infections (not anaerobic).

Cefoxitin is injectable like cefazolin but more expensive. It has a wider gram-negative and anaerobic spectrum, and may be useful in life-threatening infections. The dose is 22-33 mg/kg every 6-8 hours.

Tips: like penicillins, cephalosporins are safe even if overdosed and should be given often enough to maintain plasma levels.

Aminoglycosides

These injectable or topical antibiotics are mainly effective for gram-negative infections. They do not work in anaerobic conditions. There are many examples in this class, but two are most commonly used.

Gentamicin can be used for staph, E. coli, Proteus, and some other gram-negative aerobes. Nephrotoxicity is a concern if used at high doses, for long periods of time, or if other renal issues. Ototoxicity is reported with some topical ear drops and ointments. To maximize bacterial killing and reduce the risk of nephrotoxicity, gentamicin is recommended at 4.4-6.6 mg/kg once a day IV, IM, or SC.

Amikacin has a broader spectrum than gentamicin and is less toxic, so it is my preferred drug. It has better efficacy against Pseudomonas. The dose is 15-20 mg/kg once a day IV, IM, or SC.

Tips: if an animal is receiving aminoglycosides, do a urinalysis every day and especially look for casts in the sediment. Discontinue at the first sign of kidney damage. These drugs are synergistic with penicillins and cephalosporins. A common broad-spectrum combination is amikacin once daily and ampicillin every 6 hours, both IV. Do not combine in the same syringe, as they have a different pH and are incompatible.

Tetracyclines

These antibiotics are broad-spectrum and the first choice for several organisms, including Ehrlichia, Anaplasma, Borrelia, Rickettsia, Bordetella, and Mycoplasma. They are also used along with penicillins for leptospirosis.

Tetracycline is generally used orally at 22 mg/kg every 8 hours. It is well-tolerated but may stain dental enamel in very young animals (or if given during late pregnancy).

Doxycycline is preferred in most cases as it is given once or twice a day at 5-10 mg/kg. It causes more GI upset (vomiting) than tetracycline and should be given with

food. A slow IV infusion can be used. Esophagitis occurs when capsules or tablets are swallowed dissolve in the esophagus. Do not break open capsules. Give a syringefull of water after each dose (very important in cats).

Tips: Doxycycline has anti-inflammatory properties and is effective for osteoarthritis in addition to being an antibiotic. It may be used when tick-borne infections are suspected, but a positive response does not prove the diagnosis.

Macrolides

Macrolides are effective for some gram-positive bacteria and Chlamydomphila, Mycoplasma, and Campylobacter.

Erythromycin commonly causes GI side effects (vomiting) and is rarely used.

Azithromycin is a derivative with more of a gram-negative aerobic and anaerobic spectrum. There's a wide range of doses and intervals reported. In dogs, 5-10 mg/kg once or twice a day is a reasonable starting dose but in cats 5-10 mg/kg every other day or every 3 days (due to longer half-life) is recommended.

Tylosin powder is useful in some cases of inflammatory bowel disease or chronic diarrhea in dogs and cats. A dose of 5-10 mg/kg once or twice a day may help (accurate dosing is difficult).

Lincosamides

These drugs have similar activities as macrolides. Gram-positive aerobes and anaerobes are susceptible as well as some protozoa such as Toxoplasma.

Lincomycin is not commonly used as resistance is a problem.

Clindamycin is effective for a wider range of organisms and has a good tissue distribution. The dose for dogs is 5.5-33 mg/kg twice a day. Pyoderma responds to 11 mg/kg once a day. The lower dose range is ok for skin/soft tissue infections while the higher doses are better for difficult infections such as bone (osteomyelitis) or toxoplasmosis. The dose for cats is 11-33 mg/kg once a day. However, cats respond well to 5.5-16.5 mg/kg twice a day.

Tips: because of good tissue penetration and anaerobic spectrum, clindamycin is ideal for abscesses and periodontal disease. Higher doses are more expensive and not often needed.

Nitroimidazoles

The main drug in this category is **metronidazole**. The spectrum includes anaerobic bacteria and protozoa such as Giardia. It also has anti-inflammatory effects which may explain its popularity for nonspecific diarrhea and colitis. The dose range is commonly 10-20 mg/kg twice a day or 20-40 mg/kg once a day. Do not exceed 50 mg/kg/day, as CNS adverse effects are common.

Sulfonamides

These are the oldest antibacterials but still have some use, especially for coccidia. When combined with **trimethoprim** or **ormetoprim (Primor, Pfizer)** the spectrum is against gram positive and gram negative aerobes along with a few anaerobes. However, side effects and toxicity make this drug combination less popular today. Keratoconjunctivitis sicca can develop within 1 week of starting treatment. Hepatotoxicity, bone marrow suppression, immune-mediated disease, and hypothyroidism are among the adverse effects reported even at normal doses. 15 mg/kg twice a day or 30 mg/kg once a day are common doses for TMS, while Primor can be dosed according to label instructions.

Sulfadimethoxine (Albon, Pfizer) is useful at the label dose of 27.5 mg/kg once a day for 10-14 days for coccidiosis.

Tips: trimethoprim/sulfa is occasionally used at our hospital for canine prostatitis in large dogs when alternate drugs are too expensive for clients to afford. Otherwise, very rarely used.

Fluoroquinolones

Quinolones are mainly effective against gram-negative aerobic bacteria along with a few gram-positives. There is little anaerobic spectrum. Tissue distribution is wide and the doses can be flexible for stubborn infections. Resistance is a growing problem, possibly due to overuse as a “routine” choice for simple infections. The main indication for use is difficult gram negative organisms such as Pseudomonas or Klebsiella. A complete discussion is beyond the scope of this brief review, as there are many human and veterinary quinolones on the market.

Ciprofloxacin recently became a generic human drug and the cost is much lower. Veterinarians have started using cipro as a low-cost alternative to veterinary quinolones. However, absorption and tissue drug levels are not predictable in dogs, and much less research has been done on safety and efficacy in animals. A starting dose of 10 mg/kg once a day is commonly used, although up to 30 mg/kg daily has been reported.

Enrofloxacin (Baytril, Bayer) has both oral and injectable forms and has been widely used for many years. The flexible dose for dogs is 5-20 mg/kg once a day. Although the original dose label was twice a day, and the current label supports dividing the daily dose into half twice a day, better efficacy is generally seen with once daily dosing. In cats, enrofloxacin use should be limited to necessary cases, as retinal lesions including blindness can be an adverse effect. High doses or prolonged treatments seem to be risk factors. The dose should never exceed 5 mg/kg once a day in cats.

Orbifloxacin (Orbax, Schering-Plough) is an alternative quinolone with slightly less tissue distribution. The flexible dose is 2.5-7.5 mg/kg once a day.

Marbofloxacin (Zeniquin, Pfizer) is available as an oral tablet but not injectable. The flexible dose for dogs and cats is 2.75-5.5 mg/kg once a day. Adverse effects in cats do not seem to be a concern, although theoretically any quinolone can be dangerous.

Tips: Ideally quinolone use would depend on a bacterial culture/sensitivity test that included minimum inhibitory concentrations (MICs). By using values from the drug label (such as volume of distribution and tissue drug levels) and MICs, flexible dosing

can be calculated to ensure adequate antibiotic effects. Without MICs, the exact dose to choose for an infection is based more on clinical experience.

Nitrofurans

The main example of this class of antibacterials is **nitrofurantoin**. It does not reach therapeutic plasma or tissue concentrations but is excreted in the urine. It has a good gram-negative spectrum and is dosed at 2.2-4.4 mg/kg every 8 hours. It is occasionally used once a day long-term for difficult urinary tract infections.

Managing common bacterial infections

Which bacteria are which? Here is a brief review:

Gram positive, aerobic: Staph, Strep, Enterococcus, Nocardia, Corynebacteria
Gram negative, aerobic: E. coli, Proteus, Klebsiella, Pseudomonas, Pasteurella,
Bordetella, Salmonella, Campylobacter
Gram positive, anaerobic: Clostridium, Peptostreptococcus, Actinomyces
Gram negative, anaerobic: Bacteroides, Fusobacterium, Porphyromonas

Skin Infections - Pyoderma

The most common bacteria involved in skin infections is Staph intermedius, so effective antibiotics would kill Staph and have good skin distribution. Cefpodoxime, cephalexin, Clavamox, and clindamycin are most commonly used in our hospital. Resistance can be seen with clindamycin but is rare with the other drugs. Quinolones are also effective, but generally are reserved for severe pyoderma (mixed infection) or if another infection is present. The number one reason for treatment failure or recurrence is short duration. I routinely treat skin infections for 21 days minimum, and never less than 14 days even if a very mild problem. Some deep infections require continuous treatment for 6-8 weeks.

Bone infections

Osteomyelitis can be serious and an attempt should be made to do a culture/sensitivity before starting antibiotics (and other procedures such as surgery). Clindamycin, Clavamox, or cefpodoxime can be used empirically. Diskospondylitis isn't cultured directly but urine or blood cultures often are positive. Cefpodoxime or cephalexin are reasonable first choices.

Respiratory tract infections

The upper respiratory tract in dogs and cats is rarely infected primarily. More often viruses, stress, or other factors contribute to opportunistic infections. Clavamox or cephalexin work well for kittens and puppies with nonspecific signs such as runny nose.

Kittens with upper respiratory disease can be treated with azithromycin, which is more expensive but available as a convenient liquid.

Infectious tracheobronchitis (kennel cough) is often self-limiting and doesn't require antibiotics. However, *Bordetella bronchiseptica* can be moderate to severe and should be treated with antibiotics that penetrate into respiratory mucus. The best choice is doxycycline, followed by clindamycin or azithromycin. Quinolones are an alternative. Do not reach for Clavamox or cephalosporins for *Bordetella* – these drugs do not transfer from the bloodstream into the trachea and bronchi.

Pneumonia (lower respiratory infection) is not as common and should be cultured if possible (transtracheal wash, bronchoalveolar lavage). Broad-spectrum combinations are useful, such as combining a quinolone with Clavamox.

Dental infections

Periodontitis is the most common infection in animals and people and is best treated with dental hygiene (cleaning, brushing, etc.). In some instances, systemic antibiotics can be useful in decreasing the bacterial load and reducing inflammation. We do not routinely use antibiotics along with our dental procedures. However, in certain cases we dispense clindamycin with instructions to give 3 days before and 7 days after a dental cleaning or therapy. Clavamox, metronidazole, and doxycycline may be useful in some types of periodontitis or oral cavity infection but clindamycin is almost always the first choice due to tissue penetration and efficacy against the organisms.

Intestinal infections

If the organism can be identified, specific therapy is possible. *Giardia* is treated with metronidazole or fenbendazole (or both) while coccidia is usually susceptible to sulfa drugs. *Campylobacter* may respond to erythromycin or clindamycin, and quinolones may be effective. Mild cases of *Salmonella* do not require antibiotics, but if systemic signs are present Clavamox, quinolones, or trimethoprim/sulfa may help. Clostridial diarrhea is difficult to diagnose but usually responds to Clavamox, metronidazole, erythromycin, or tylosin.

Urinary tract infections

These may be simple or complicated. Acute cystitis is commonly caused by *E. coli* and usually responds to Clavamox or trimethoprim/sulfa. Quinolones can be effective but resistance is increasing. Staph infections are treated with Clavamox or cephalosporins. Less common bacteria are best treated based on culture/sensitivity lab results. Nitrofurantoin is a good “backup” drug for resistant infections. Pyelonephritis is more difficult to treat and culture is almost mandatory. Antibiotics should be given much longer for pyelonephritis (4-8 weeks) than for cystitis (1-2 weeks). Prostatitis is likewise difficult to treat and culture is best. The only antibiotics that reliably penetrate prostatic

tissue are macrolides (erythromycin, clindamycin), trimethoprim/sulfa, and quinolones. Therapy for prostatitis and even cystitis in male dogs should continue for 4 weeks.

Ocular infections

A recent finding is that some cats have hypersensitivity reactions to neomycin, which is one of the drugs in triple-antibiotic ointment or drops (also in Tresaderm, Merial and other ear and skin topicals). We have stopped using triple-antibiotic in cats but it is still useful for uncomplicated eye infections in dogs. Cats and dogs can be treated with topical oxytetracycline (Terramycin, Pfizer), chloramphenicol, erythromycin, tobramycin, and ciprofloxacin. Aminoglycosides (topical gentamicin) are rarely used in our hospital.

Other

Some infections need specialized treatment and consultation is best when choosing antibiotics. For example, the central nervous system is difficult to penetrate with drugs but CSF taps to try to obtain a sample for culture is invasive. Ear infections, especially chronic or recurrent cases, require a great deal of consideration in choosing topical and systemic drugs. Critical care patients (parvo, peritonitis, septicemia, etc.) have their own unique problems in antibiotic management.

References

The best textbook both for reference use and for practical information is Infectious Diseases of the Dog and Cat, edited by Craig E. Greene. The 3rd edition was published in 2006 and should stay current for the near future. Another comprehensive book for large and small animals is Antimicrobial Therapy in Veterinary Medicine, 3rd ed. by John F. Prescott. Smaller books include Saunders Handbook to Veterinary Drugs by Mark G. Papich (2nd ed, 2007) and The 5-Minute Veterinary Consult Clinical Companion, Canine and Feline Infectious Diseases and Parasitology, which is helpful for practitioners that like the “5-Minute” format. I don’t use that series personally, but students like the brief reviews.

For questions or additional resources, feel free to contact me anytime:

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I. WOLBACHIA

A. Description

1. Recently discovered endosymbiont, found in *Dirofilaria immitis* as well as many insects and arthropods
2. Gram-negative bacteria, first identified in 1967 but not recognized as *Wolbachia* in heartworms until 1995
3. Found in the lateral chords and reproductive tracts of adult female heartworms as well as all larval stages (including microfilariae)

B. Pathogenesis

1. Host (dog) may be exposed to *Wolbachia* by several routes:
 - a. released when adult worms or larvae die (host defense or drugs)
 - b. shed by female uterine contents and in microfilariae
 - c. excretory contents of adult worms
2. Antibodies formed in response to exposure to surface protein (WSP)
3. Potential problem with either *Wolbachia* antigen or WSP antibodies circulating throughout body--lungs, kidneys, liver, etc. exposed

C. Treatment

1. Organisms are readily cleared with doxycycline. Other reported effective drugs: rifampin, azithromycin. Not effective: chloramphenicol, erythromycin, ciprofloxacin. One study reported a protocol using doxycycline 20 mg/kg once a day for 30 days.
2. Therapy clears microfilariae, sterilizes and stunts growth of adults
3. Possible drawback to antibiotic treatment--may result in occult heartworm disease by blocking production of microfilariae

D. Future research

1. Development of diagnostic tests for *D. immitis* using WSP
2. Adulticidal treatment may be enhanced by treating *Wolbachia* with antibiotics--worms may be more susceptible to melarsomine if weakened by the clearing the endosymbionts