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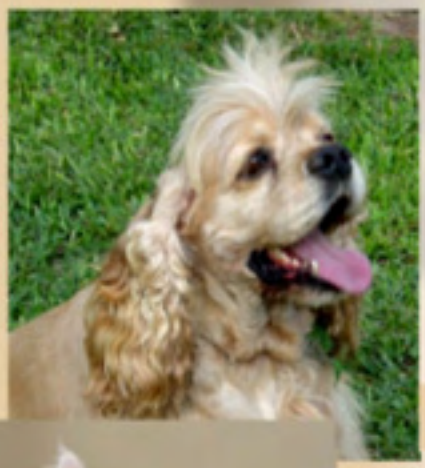

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RESUMEN

animales de compañía

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ANTIBIOTIC THERAPY IN EXOTIC PETS

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Antibiotics are part of a broader group of chemicals called *antimicrobials*. An *antimicrobial* is any drug that kills *microbes*. Microbes can be any microscopic organisms such as bacteria, protozoa, viruses and fungi. The term *antibiotic* is reserved for those drugs which are derived from living organisms. Penicillin, which is a drug produced from the mold *penicillium*, and tetracycline, which is produced from a fungus called *Streptomyces*, are both antimicrobials, but more specifically, they are also both antibiotics.

It is now possible to make synthetic antibiotics. So, by true definition, these synthetic antibiotics are not actually antibiotics, even though they are used to kill bacteria. Instead, they are classified as antimicrobials, since they are not derived from living organisms.

The terminology gets even more perplexing nowadays because medicine is continually discovering new antibiotics which are closely related to existing antibiotics. Thus, qualifiers are added to the various names of the new antibiotics. The cephalosporins are a good example. The newer drugs are classified as *second generation* and *third generation* cephalosporins.

BACTERIA

There are many different types of bacteria. Depending on the species being treated, different bacteria play significantly different roles. For instance, rabbits can act as asymptomatic carriers of Bordetella, but, in Guinea Pigs, the Bordetella can be lethal.

In reptilian and avian medicine the majority of the significant bacterial pathogens are in the G(-) group. Common examples include *Pseudomonas, E. coli* and *Klebsiella.* There are many different species and sub-species within each group.

In addition to the G(-) and G(+) groups, there is another important classification which should be mentioned. Bacteria can be further separated into types based on whether or not they utilize oxygen for growth and reproduction. Those bacteria which need oxygen to live are called *aerobic*, and those which do not require oxygen are called *anaerobic*. Some bacteria can live in either environment.

There are a few bacteria which do not fit well into any of the above groups. These are clinically important bacteria which, in some cases, not only cause serious disease in birds, but can also infect people as well. Examples of these unusual bacteria would include *Mycoplasma*, *Rickettsia* and *Chlamydia*, the latter being responsible for Psittacosis in birds and people.

Not all bacteria respond to antibiotics in the same fashion. For example, bacteria of the genus *Pseudomonas* can be killed with an antibiotic called gentamicin, but they are not even slowed down by penicillin. In a similar thought, not all antibiotics are equally effective against all bacteria. Penicillin is used to kill the bacteria which causes Strep Throat in people, but may be totally ineffective against a G(-) bacteria which causes sinusitis in birds.

Bacteria can change their susceptibility to antibiotics over time. This means that a specific type of bacteria may be vulnerable to a given antibiotic initially, but may develop a resistance to the same drug weeks to months later. Oddly enough, if that same bacteria is isolated from that antibiotic for a period of time, it may eventually become vulnerable once again. Salmonella bacteria are a classic example of an organism that can rapidly form resistant patterns to antibiotics. hence, that is the reason that it is often considered unwise to treat fulminate salmonella infections.

It is because of these variables that the decision to administer antibiotics to any animal, or human, is not a haphazard event. Due to the differences between the individual antibiotics and the ever changing response by the disease causing bacteria, a sound understanding of the infectious processes and the antimicrobials used for their treatment is mandatory.

COMMON ANTIMICROBIALS

The purpose of antimicrobial therapy is to assist in eliminating the disease causing bacteria from the ill host. The word «assist» is used deliberately because antibiotics play only a part in this goal. It is important to realize that the host's own immune system must also contribute to fighting off the disease. Antibiotics are not as effective in an immunocompromised host, as is the case with human A.I.D.'s patients. This is especially true in reptiles, since many herps are in serious condition by the time they are taken to the veterinarian, and their immune system is often weakened by the disease, antibiotics alone may not be as effective as they would be in a less compromised animal.

Antibiotics can be divided into two groups based on their mechanism of action, or the way they work. Antibiotics can be classified as either *bactericidal*, if they actually kill the bacteria that they are targeting, or *bacteriostatic*, if they act by inhibiting the bacterial replication only, and don't actually kill the organism. In some of the severely immunocompromised patients it is often best to use antibiotics which are bactericidal rather than bacteriostatic. Because of the mechanisms by which the two different types of drugs work, bacteriostatic antibiotics should not be mixed with bactericidal drugs.

Since there are relatively few antimicrobials commonly used in exotic practice it is worth presenting a brief overview of the general classes of drugs. By understanding the basics of antibacterial therapy the practitioner will be more aware of the benefits and potential side-effects of the various drugs available. The abbreviations after the drug category is for recommended patient use. (R - rabbits; Rd - rodents; F - ferrets; A - avian; Rp - reptiles)

Chloramphenicol
(R, A, Rd, F)

Chloramphenicol is a broad-spectrum (has a wide range of antibacterial effectiveness), bacteriostatic antibiotic. It exerts its antibacterial effects against aerobic G(-) and G(+) organisms, some anaerobic bacteria, *Chlamydia*, *Rickettsia* and *Mycoplasma*. Of the G(-) bacteria, it is very effective against *Salmonella*, has some antibacterial activity against *E. coli* and is impotent against *Pseudomonas*.

Chloramphenicol can be administered to a patient by various routes, but most commonly it is given either by injection into the muscle, or orally with a dropper directly into the mouth. It is well absorbed by either route, but there is a greater concentration of the drug in the plasma and tissues with injectable therapy. Chloramphenicol also has the advantage of reaching relatively high concentrations in some of the internal organs such as the kidneys, liver, heart and central nervous system where other antibiotics may not be as effective .

A big disadvantage of chloramphenicol is that it is bacteriostatic. There is some belief that it may be bactericidal at higher concentrations. As mentioned previously, this may not be an ideal drug for patients that are immunocompromised, such as the snake with a severe respiratory infection that has been housed at sub-optimal temperatures. Since chloramphenicol is bacteriostatic it should not be used in combination with bactericidal drugs.

As a last note, since chloramphenicol has a potential for causing human toxicity (aplastic anemia), there is a tendency to steer away from prescribing this drug to out patients. Staff members should always take necessary precautions when handling the drug.

Tetracyclines (eg. Chlortetracycline, Oxytetracycline, Doxycycline)
(Rd, A)

The tetracyclines, like chloramphenicol, are bacteriostatic at standard doses. They, too, have a wide spectrum of activity against aerobic and anaerobic G(-) and G(+) bacteria. The tetracyclines also have excellent effectiveness against the unusual bacteria such as *Mycoplasma* and *Chlamydia*. Of all the tetracyclines, perhaps doxycycline has the most potential for clinical use in exotics, especially in birds and rodents.

The tetracyclines can be administered by either the oral route, including both direct administration with a dropper or mixed into the feed, and via injection. It should be pointed out, however, that tetracycline is poorly absorbed after oral dosing. This is in part due to the fact that ions such as calcium, magnesium and iron interfere with absorption from the intestinal tract. In mammals concurrent consumption of milk has been shown to decrease absorption of tetracycline by as much as 70%.

Birds on an oral prescription of a tetracycline drug should be watered with de-ionized or soft water to prevent interference with the absorption of the drug. Likewise, during treatment, any oral vitamin or mineral supplements should be suspended until after treatment is finished. If vitamins are needed for balanced therapeutics during treatment the vitamins and minerals can be supplemented with injectable preparations.

There are tetracycline medications in Europe which yield effective drug levels for up to six days after a single intramuscular injection. These European preparations are not available in the United States. Similar injectable tetracycline products which are used here in the U.S. have undesirable side effects and should be used with caution.

The tetracyclines are the drugs of choice for the treatment of Psittacosis. Chlortetracycline in the feed or Doxycycline via an oral dropper are both very effective in the control of this serious disease. The European preparation of injectable tetracycline has also been used with success.

For mycoplasma infections in rodents, doxycycline is an excellent choice as it is readily accepted in the oral form by the tiny patients.

Penicillins (eg. Penicillin, Amoxicillin, Carbenicillin, Piperacillin)
(*R, A, Rp)

The penicillins are bactericidal in rapidly growing or replicating organisms. Quiescent bacteria are resistant. The original penicillins are effective against the G(+) bacteria and *Pasteurella*. A G(+) bacteria called *Staphylococcus aureus* produces an enzyme called penicillinase which destroys penicillin.

Oxacillin is an example of newer group of narrow spectrum penicillinase-resistant penicillins now available for treatment of Staph bacteria. Ampicillin, amoxicillin and hetacillin are extended spectrum penicillins with some activity against G(-) bacteria, but like the original penicillins, they are destroyed by penicillinase.

The newest penicillins on the market are also narrow spectrum, but they are very effective against the G(-) bacteria, including *Pseudomonas aeruginosa*, a bacteria which can cause serious disease. Carbenicillin and piperacillin are examples of these newer penicillins. These later two drugs are very effective when used in combination with the aminoglycosides, having a synergistic effect.

The penicillins are poorly absorbed after oral administration. Studies to date indicate that the penicillins are the most effective when they are administered by injection. Since most of the gut flora in rabbits and rodents are of the G (+) type, using penicillins can often times have lethal effects. Other than using injectable penicillin in rabbits with refractory abscesses under careful observation, it is generally unacceptable to use penicillins in rodents.

Cephalosporins (eg. Cephalexin, Cefachlor, Cefotaxime and Ceftazidime)
(A, Rp)

Cephalosporins are very similar to the penicillins. They are bactericidal, effective against rapidly growing bacteria and ineffective against resting bacteria. Their spectrum encompasses both the G(-) and G(+) bacteria. Like the penicillins newer cephalosporins have been developed which have more specialized roles. The *first generation* cephalosporins, such as cephalexin, have an antibacterial spectrum similar to amoxicillin. The *second generation* drugs are more effective against the G(-) bacteria. Cefachlor and cefuroxime are examples in this group. The *third generation* cephalosporins, such as cefotaxime (Claforan®) and Ceftazidime (Fortaz®), also have activity against some of the hard to kill bacteria such as *Pseudomonas*.

Oral administration is only effective with a few of the first generation cephalosporins. The newer drugs require injectable therapy to be effective.

Aminoglycosides (eg. Gentamicin, Amikacin)
(R, A, Rd, F, Rp)

The aminoglycoside antibiotics are considered to be among the best for the treatment of serious G (-) infections, including those caused by some of the *Pseudomonas* species. All of the antibiotics in this class are bactericidal, but they have little effect against the G(+) bacteria, and are ineffective against the anaerobes.

Coupled with the extreme effectiveness of the aminoglycosides is an inherent danger of severe toxic side-effects. Of significance are the effects of the aminoglycosides on the kidneys, the ears and the neuromuscular system. Kidney damage, hearing loss and loss of balance, and neuromuscular blockade, as evidenced by weakness, paralysis and death have all been reported in animals. Amikacin is slightly less toxic that gentamicin, but at the same time, it is also not as potent and generally requires a higher dose.

Even patients on a correct therapeutic dose may show some signs of mild or impending kidney damage while on aminoglycosides. Typically, there is an increase in water consumption by the patient and a concurrent polyuria. This is reversible if caught early and the drugs are discontinued.

The aminoglycosides act synergystically with the penicillins and the cephalosporins. This means that, when used together, the combination of the drugs has a greater effectiveness than when either of the drugs are used alone. For example, by combining an aminoglycoside with a penicillin the antibacterial spectrum includes both the aerobic and anaerobic G(+) and G(-) bacteria, as well as the serious *Pseudomonas* species.

The aminoglycosides are only available in the injectable forms. They can be administered subcutaneously, intramuscularly or intravenously. They are not available as an oral medication.

Sulfa drugs (eg. Sulfadimethoxine, Trimethoprim-sulfamethoxazole)
(R, A, Rd, F, Rp)

The most common sulfa drug used in non-domestic medicine, trimethoprim-sulfamethoxazole, is actually a combination of two separate drugs. The two drugs used in combination like this have a synergistic action against bacteria, thus making the combination bactericidal. It has a broad spectrum of effectiveness, including some of the serious G(-) bacteria such as *Klebsiella*.

Since this drug is partially eliminated from the body through the kidneys it should be used with caution in dehydrated patients. It has also been shown to cause anemias in some patients and allergic reactions in others.

Trimethoprim-sulfamethoxazole is available either as an injectable antibiotic or in a highly palatable oral form. In addition to its effectiveness as an antibiotic, it also has some use as a treatment for protozoal infections caused by coccidia.

Quinolones (Ciprofloxacin, Enrofloxacin)
(R, A, Rd, F, Rp)

The quinolones are relatively new drugs and have recently gained popularity in exotic medicine. In my opinion, these drugs, especially enrofloxacin (Baytril®) are grossly overused. Ciprofloxacin and enrofloxacin are broad spectrum, bactericidal antimicrobials. They are effective against many of the G(+) and G(-) bacteria, including the penicillinase producing *Staphylococcus* and some of the *Pseudomonas* species. In addition, they are very effective against the *Mycoplasmas*.

Since these are relatively new antimicrobials there is still a lot of information regarding their side-effects that is not known. Some of the reported side-effects to date include gastrointestinal upset, seizures in some animals and joint defects in young or growing animals. It is not recommended to use quinolones in patients which are still in their growth stage.

Ciprofloxacin, a human drug, is only available in a tablet form and must be dissolved in water and dosed orally. Enrofloxacin was designed strictly as a veterinary drug and is available as an oral suspension, a tablet form and as an injectable preparation, however, only the tablets and the injectable forms are available for use in the United States.

SELECTING AN ANTIBIOTIC

Without belaboring the point, by now it should be apparent that antibiotic drug therapy is not a simple task. The rest of this discussion will attempt to outline the strategy for proper antibiotic treatment in a sick patient.

There are a number of factors which need to be considered when selecting an antibiotic:

1. Cost of the antibiotics

Some of the newer antibiotics and antimicrobials are extremely expensive. To some owners a few dollars may not be important, but to those that are on a budget, the difference in the cost of the antibiotics might make the difference between starting treatment or euthanizing the pet and buying a new one.

The cost differential can be quite large. The newer synthetic penicillin and cephalosporin antimicrobials can be as much as ten to fifteen times more expensive than their older counterparts. This may not amount to much when the treatment involves a small passarine, but the expense multiplies rapidly when the larger patients, such as some of the constrictors, are being medicated.

2. Intended route of administration of the antibiotic

As already pointed out, not all antibiotics are given to the patient in the same way. In some severe infections by far the best route of administration is via injection of the antibiotic directly into the ill patient. However, not all owners can afford to have the treatment performed by the hospital, and some people are unwilling to administer injections to their pet by themselves.

In many cases it is necessary to prescribe oral antibiotics. Remember, not all oral drugs have the same degree of absorption from the intestinal tract. And, just because the drug might be one that is absorbed, it doesn't mean that particular drug is the best drug to use for that particular problem.

In flock or herd situations, where treatment of a number of birds or rodents is necessary, it is often impossible to dose every animal individually either with a syringe or by an oral dropper. It may be necessary to medicate the feed or the drinking water. There are only a few antibiotics which are effective in either of these situations. Most oral antibiotics, especially those used in birds, are not capable of reaching high enough levels in the patient's blood stream when dissolved in the drinking water to do any good.

Another consideration for antibiotic selection is the nature of the disease being treated. For example, when treating birds with diseases that are transmissible to people, such as the case with Psittacosis, it is better to minimize bird-owner contact in order to decrease the personal health risk to the owner. Oral doxycycline is administered twice a day for 45 days. This means that the owner must come face to face with the bird at least 90 times during treatment. If injectable doxycycline is used the number of human-bird treatment interactions is reduced to just seven!

Certain disease conditions require specific routes of antibiotic administration. When a reptile develops an abscess the pus inside is not the same as that seen in a mammal. In reptiles the pus is coasted. Because of this, antibiotics do not penetrate the abscess well. This makes it difficult to achieve maximum effectiveness, even with the best antibiotics. It is often necessary to clean out, or curette, the abscess of the caseated pus prior to starting antibiotic therapy.

Even after the abscess is opened and cleaned, systemic antibiotics might still have difficulty reaching this site. Occasionally it may be necessary to apply topical flushes, solutions, ointments and creams to the abscess areas. With some exceptions, it is generally best to avoid any topical medication in avian patients, or any patient that frequently self-grooms.

A final route of administration worth mentioning is nebulization, a technique which is very useful in birds with pneumonia or air sacculitis. The antibiotic is dissolved into a carrier liquid such as sterile water or D.M.S.O. This is then placed into a canister and pressurized with either air or oxygen. The mixture is then micronized into a very fine mist which is readily inspired into the airways of the sick patient. The nebulizer should be able to produce particles no greater than 3 microns in diameter in order to penetrate the deeper airways.

3. The condition of the patient when it presents for treatment

Patients which are critically ill and immunocompromised may have different antibiotic requirements than those which present in early stages of disease. Also, because of some of the side-effects of the various antibiotics it may be necessary to stabilize the patient before starting treatment. An example would be a snake that is severely dehydrated from diarrhea. Starting this patient on gentamicin without consideration for his kidney function would be careless and potentially lethal. A better option would be to reestablish the snake's hydration with appropriate fluid therapy and start

it on an antibiotic which doesn't have the kidney effects of the aminoglycosides. The antibiotic therapy can always be altered at a later time once the animal is rehydrated and the laboratory results indicate that a change is warranted.

4. Bacterial Culture and Sensitivity

Regardless of the above criteria, the most important factor to be considered when selecting an antibiotic are the results of the bacterial *culture* and *sensitivity* data. Although these tests may not always identify what antibiotics are effective *in vitro*, they will identify those which may be ineffective. To me, that information is often times even more important.

5. Laboratory tests vs. shot-gun therapy

Cost or treatment is almost always a concern whenever a pet becomes ill. It would be ideal if the pet's owner could get the best possible treatment for the least possible cost. I recommend that you not spend, or not spend your client's money. Always offer the best options, and then if the client can't afford it, work down, cost wise, from there. You will never be criticized for offering the best medicine, but, you will be crucified for offering the worst.

When a client declines a recommended test or therapy, always, always document it in the record. I have been saved from many a bad situation by having dates, times and conversations clearly written in the patient's records.

Even when the client allows you to do everything that you suggest, you will still at times have treatment failure. I encourage you not to check your veterinary knowledge at the door just because it is an exotic pet. You need to consider reasons why your therapy hasn't been effective, such as atypical bacteria like chlamydia or mycoplasma, other causes such as fungi, yeast or viruses, and etiologies like toxins, other systemic diseases and so forth.

REFERENCE -

James W. Carpenter. Exotic Animal Formulary. Elsevier Inc. St. Louis, MO. 2005