DRUGS:

Theory and Use in the Avian Trade

by Robert Clipsham, DVM
Simi Valley, California

Drugs are simultaneously both the greatest aid and hazard in the avian trade today, after the two major categories of husbandry and nutrition. Drugs, of which antibiotics are the most commonly employed, are both widely used and abused. Antibiotics, cortisone compounds, chemotherapeutics and cardiac drugs are responsible for many animals and humans being alive that would have otherwise died. Drugs are tools, they are not magical, nor are they necessarily tolerant of poor handling in the body.

Axioms:

All drugs are toxins.
All toxins are drugs.
All drugs are poisons at the right time and dose.

This paper is a general discussion of drugs and antibiotic use. It is not an instruction guide for their use. I am providing the information so that better care can be given by bird owners. If questions occur, we encourage you to call your local avian veterinarian.

Many drugs have low toxicity potential in all species, some in a few, some only at certain ages or stages of reproduction, and some are very critical at all times due to the interactions with body systems.

The following rules will give you guidelines to use if a question exists beyond your current knowledge:

1. Drugs cannot improve poor sanitation, eliminate stress, improve nutrition or upgrade husbandry. If these conditions are not corrected, treatment will only *slow down the problem at best.*
2. Antibiotics are for bacterial diseases. Antifungals are for fungal problems. Disinfectants are for non-living objects. DO NOT put any chemical or drug into a body merely to be giving treatment. Most drugs treat only a limited scope of diseases.
3. There are NO cost effective drugs currently available for viruses. This includes antibiotics.
4. In general, the more available the drug, the less effective it is due to past exposure to the organism, abuse and resistance factors.
5. Do not treat any animals with any drug that you do not have first hand knowledge of *in that particular species in that specific dose form.*
6. If the first drug fails to succeed, do not waste valuable time on a second guess. The animal's health, immune system and recovery rate are all being reduced each day that it does not start healing. This translates into more work, overhead cost, delayed sales and higher risk of animal deaths.
7. Separate and isolate all birds showing disease signs. Reduce the risk rate of involving more birds.

FUNDAMENTALS OF ANTIBIOTICS

History

Most common current antibiotics have been developed over the past 50 years (1935). Tremendous amounts of research have been applied both for medical and economic reasons. Human medicine closely regulates the distribution, sale and use of drugs. The same producers are under much less stringent restrictions for animal use.

Due to availability from domestic and foreign sources and the advent of generic brands, virtually all prescription veterinary drugs are available from both legal and illegal sources.

The numbers of drugs available are greater each year due to research. This is necessary due to ever increasing resistance to older drugs and the need to decrease potential side effects. Generally the newer the drug, the higher the cost due to increased development time. Veterinary drugs are almost entirely a spin off of human drug production and are a very small market in themselves.

Biochemical Activity

Antibiotics fall under one of two

categories; bacteriocidal or bacteriostatic. Bacteriocidal (cidal) drugs kill bacteria by blocking a vital process in the cell necessary for life. This process can be done in many different ways and accounts for the reason why many different drugs exist. This class is generally preferred over bacteriostatics because of the more rapid and assured ability to remove infectious agents. Bacteriostatic (static) drugs only stop the cell from reproducing and *does not kill* the bacteria already present. This class of drugs relies on the body's immune system to remove the disease. Therefore, it now becomes clear why good diet, sanitation, husbandry and stress reduction are so important in curing sick animals. The following chart reveals the class distinctions of many common antibiotics.

Bacteriocidal	Bacteriostatic
Penicillins	Tetracycline
Ampicillin	Erythromycin
Amoxicillin	Sulfarmides
Gentamicin	Chloramphenicol
Streptomycin	Nitrofurans
Tribrissen (bactrim)	Tylan
Nitrofurans	

All antibiotics rely on being absorbed into the bacterial cell to be effective. All antibiotics are designed to mimic some chemical structure that the bacteria uses naturally. The antibiotic chemical structure is only similar enough to fit into the "lock" but not similar enough to let the biochemistry keep on working. It becomes a "defective part" and the bacteria is disrupted either by destruction or not being able to reproduce and eventually dies of "old age."

The exact way that this occurs is different for each class of antibiotics. It can cause leakage of bacterial cell contents by inhibiting the formation of the rigid cell wall, the pliable inner cell membrane, preventing bacterial protein production which is required for growth, or inhibition of DNA or FNA production.

Both 'cidal and 'static antibiotics can use any of the mentioned methods against bacteria. E.g.: both tetracycline (static) and gentamicin (cidal) will prevent protein synthesis in the cell's ribosomes at the 30-S subunit site. However, tetracycline does so by preventing transfer RNA at the site while gentocin distorts the site and causes a "misreading" of the messenger RNA so improper amino acids are placed in the wrong sequence and make non functional proteins.

Each drug has its own specific method of action. Antibiotics can not be classed neatly beyond certain *major* generalities.

Bacteria are also classified according to cell wall type. They are either Gram positive or Gram negative. These classes are set by their staining characteristics with Gram's stain. Pink for negative, purple for positive. This difference is due to certain chemical layers being much thicker in Gram positive (G+) bacteria, than Gram negative (G−) ones. This also explains why certain antibiotics are considered to be primarily G+ or G− drugs, or occasionally both. The disrupting ability of the drug is either dependent or not involved with the specific chemical structure of that thicker G+ coat.

Another concept of antibiotic treatment is that even though one *type* of bacteria is responsible for an infection it is made up of a *population* of billions and *billions of individuals.* The end result all the single bacteria have on the body is to produce a "sick bird." Treating a sick animal really means treating billions of bacteria with slightly different abilities. The end result hopefully is to remove them all, but not all bacteria will respond the same. The drugs do not kill all bacteria a little bit each day until the last day when they all die. The drugs actually kill the very weakest the first day (the most susceptible), the moderately strong ones in the middle of the treatment and only kill the strongest (most resistant) bacteria after they have been subjected to the effects of the drug for the greatest number of days. *This is why you cannot treat for only 2 or 3 days or every other day and be successful!*

The last concept that must be understood to appreciate the limitations of antibiotics is that nearly all bacteria are *extracellular* (outside of the animal's cells) and moving freely around the blood system, brain, organs, etc. Bacteria rarely have a preference where they cause infections. Some bacteria are intracellular because they must survive and cause disease. This is important because of the theory of *selective toxicity,* which means that antibiotics are far more toxic to bacteria than to animal cells, either because they penetrate animal cells poorly or the animal cell does not use that chemical. This is important if an infection is an intracellular one but the particular antibiotic penetrates animal cells poorly. Viruses are always intracellular. Therefore, antibiotics are not generally in contact with viruses and *are for bacteria only.*

Diagnosis

Most bacterial infections are *suspected* by observation or examination. They are *diagnosed* by culture and sensitivity (C/S).

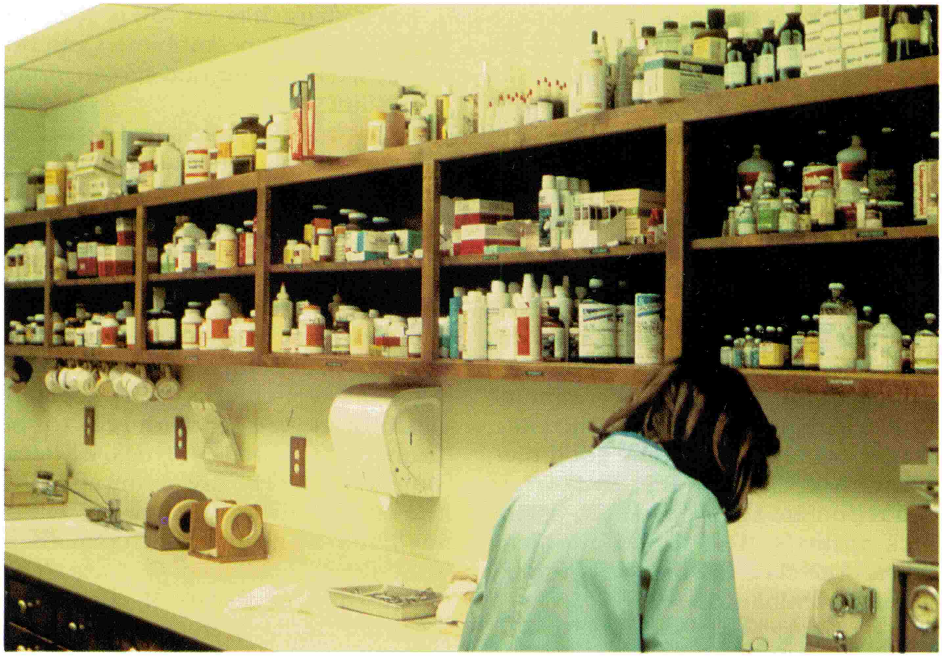
This generally involves using a *sterile* swab and wiping the suspected area (mouth, stool, organ, etc.) and transferring it onto an artificial media plate (agar) and allowing it to grow in a warm environment (incubator) at approximately normal animal temperature (90° to 110°F). When enough bacteria are present to be seen with the naked eye, they are transferred to a second agar plate on which small paper discs are placed. These discs are soaked with very precise amounts of different antibiotics (one type per disc). The sensitivity plate is allowed to grow again for another day and then examined to see which drug(s) prevented the bacteria from growing on or around it. The areas (circles) of clean agar are measured in centimeters and compared to charts published by the drug manufacturer to see if it is large enough to do an effective job in the body. Different charts are used for different types of bacteria.

Agar plates differ also. Some will grow almost any bacteria. Some are intentionally made to only allow certain kinds of bacteria to grow to speed up identification of the organism. The Valley Veterinary Clinic uses a plate split in half to grow both G+ and G− on one side and only G− types on the other. The agars can also have pigments which some bacteria will use to help color code certain types.

Some bacteria will only grow in very extreme conditions. Some require very cold incubators (cryophillic), some need special added artificial nutrition, reduced oxygen levels (partial anerobes), carbon dioxide only (obligate anerobes) or normal room air atmosphere (aerobes).

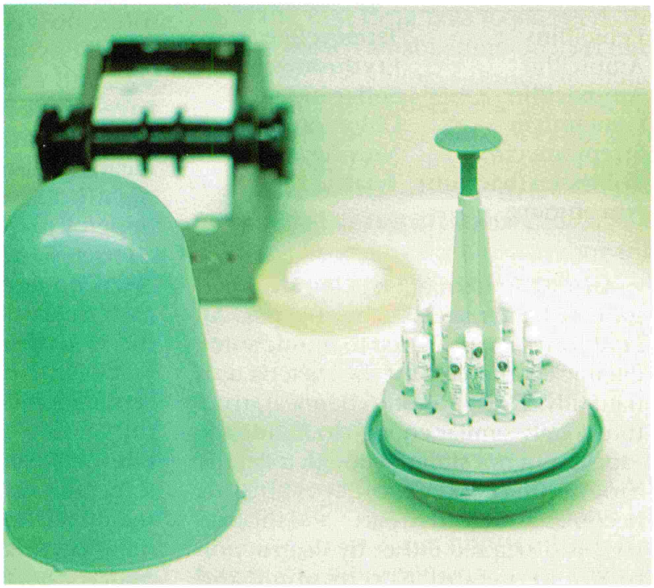
Bacteria have differing appearances on agar plates such as large colonies (single bacteria grown into one round spot containing millions), small, dry, mucoid, odors or colors.

It now becomes obvious that if a swab were placed on all different types of agars at all different temperatures with all different kinds of gases, it would be easy to identify an infection. But the costs are high so it is not done routinely and most bacteria grow very easily on one or two agar types with normal room air. ***This commonly explains why obviously sick animals may not grow anything on a culture.***



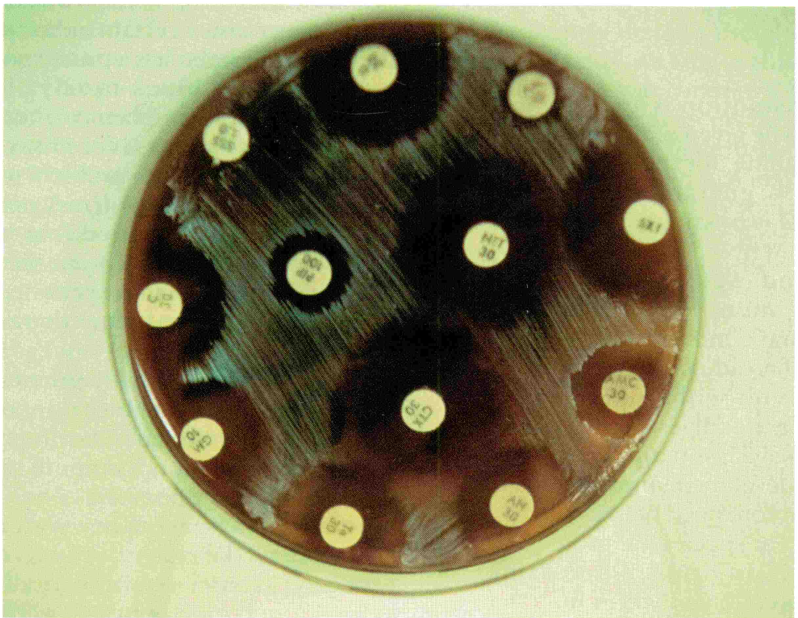
Photos by R. Clipsham, DVM

Drug inventory in clinic pharmacy.

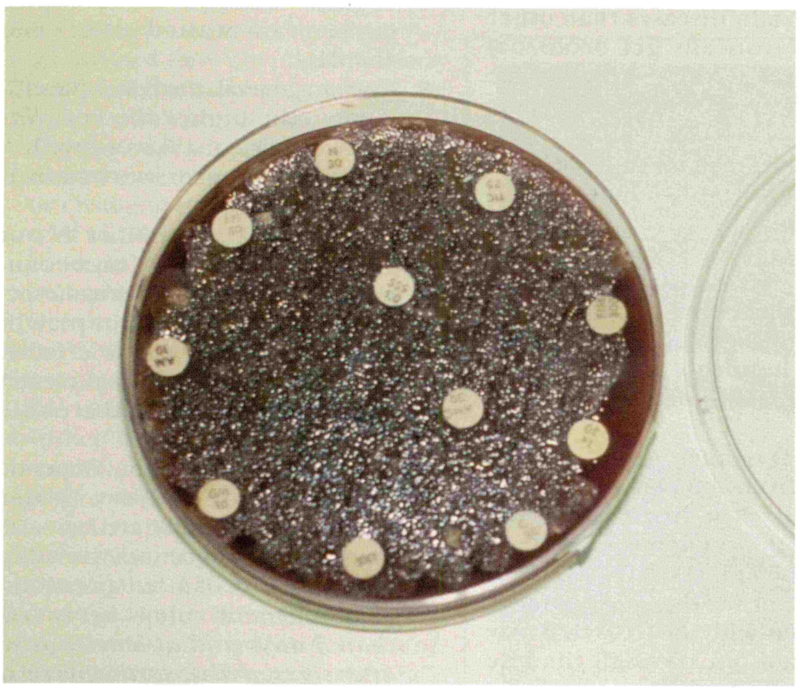


Drug sensitivity disc dispenser.

Culture plates with diagnostic media tubes in incubator.



Wide range of drug sensitivities.



Complete antibiotic resistance on sensitivity test plate. Note lack of inhibition zones.

Treatment

The decision to treat and with what to treat is the result of balancing many aspects including:

1. What type of animal and age.
2. What type of bacteria.
3. What organs are damaged or normal.
4. Length of illness.
5. Where is the infection in the body.
6. How many animals and how easily can they all be treated.
7. What groups of drugs might work.
8. Cost of drug(s).
9. How many drugs.
10. How long to treat.

Continued on page 34

Continued from page 33

The ideal solution is a cheap, safe drug that can be given orally, preferably without handling, for the shortest time with a 100% guarantee of normal healing. This is possible but generally not the case. Why?

1. Type and Age: Babies are, in general, more sensitive to some drugs, have more relative water weight than adults, may be fed by a parent who will also ingest the drug, may not digest well at all and tend to have less natural resistance (poorly developed immune system) and therefore need help faster.

   Different species are more risky with certain drugs, some drink more water than others or no water at all, some have shorter digestion periods or are just more likely to have certain diseases than other species (toucans get protozoal infections while cockatoos are prone to E. coli septicemia). Some species seem to succumb to illness much faster than others and time is more important than cost on a short term basis.
2. Bacterial Type: Some species or strains of bacteria tend to have more potent effects than others and are more dangerous. Some produce toxic chemicals and must be stopped very quickly to save the bird.
3. Organ Damage: All drugs are passed from the body somehow. Generally, the liver breaks the chemical down into harmless waste, the kidneys may pass it out with the urine, the intestines may pass it out with the feces or it may be passed out through the bile ducts.

   If an organ is damaged such as the kidneys and a specific drug such as gentamicin is used, which is removed by the kidneys, the drug will build up in the body beyond safe levels and drug toxicity will follow. The same occurs with liver damage and tetracycline and chloramphenicol or kidney damage with erythromycin, neomycin and sulfas.
4. Length of Illness: The longer the damage, the faster the cure is needed *but* the longer the damage, the less able the body is *generally* able to tolerate drug side effects. A choice may need to be made between speed and safety.
5. Infection Location: Certain organs utilize certain drugs better. Certain drugs never enter certain areas of the body. The brain has a protective mesh that will block nearly all drugs except chloramphenicol. You may desire to use a liver transformed drug for a liver problem to concentrate it there *or* you may not if the liver is so damaged that it cannot tolerate it at all. The answer lies in blood test results, experience and knowledge of the drugs available.
6. How Many Animals: The greater the number, the harder to treat (time and money). The best treatment is generally by mouth or injection but large numbers of wild animals may require water treatment (the least effective generally) in order to treat them all.
7. What Drug Group is Best: Check organ function for safety and check cultures for sensitivities. A wasted guess means wasted money and animals.
8. Cost: In general, the better the efficiency, the higher the cost *but* many old drugs still work well. A sensitivity test may save hundreds of dollars.
9. How Many Drugs: More is not always better. Some drugs counteract each other. Some drugs (especially in the same group) will double the risk of side effects. Some drugs actually make each other more potent and are safe (synergists).
10. How Long A Treatment: Depends on method of delivery (water treatments generally are twice as long as oral or injections), severity of disease, risk of more spread and cost. A general rule is *never less than 5 days and at least 3 days after signs of disease disappear if the drug is safe.*

Preventive Treatment

Preventive medicine is the foundation for low cost, high quality management. Preventive medicine does not mean relying on drugs to balance poor health practices.

Preventive treatment has two phases:

1. To prevent the further spread of actual disease. *It is much easier to prevent an infection from entering the body than to remove one.*
2. Routine annual, semiannual, etc. program for conditions which are always present and impossible to eliminate. Example: worming programs, parasite control and psittacosis.

Regular use of antibiotics without reason or cause, especially at improper amounts, too few or intermittent number of days, and under less than optimal conditions (cold weather, breeding season, poor acceptance of drug or dirty equipment) will lead to *antibiotic resistance.*

This is the ability of the *bacteria (not* the bird) to withstand or ignore the antibiotic being used, in spite of the fact that it used to work well.

This occurs because in the past, either in that aviary, or aviaries where the birds came from, the bacteria were exposed to drugs that did not kill them but only allowed them to be exposed. The bacterial population either had:

1. The susceptible ones killed off and the strongest (most resistant) ones allowed to survive because of doses too low or days too few. This is *forced population selection.*
2. The bacteria learn how to survive the antibiotic by dropping the chemical need for the replaced molecule that the antibiotic has mimiced (by-pass), adopting a new chemical pathway instead of the antibiotic mimiced, the bacteria can learn to make enzymes to destroy the antibiotic molecule dropping of the target site completely or changing the permeability of the wall to that drug (not absorbed by bacteria anymore). These are examples of *genetic mutation.*

Genetic resistance can be transferred between different bacteria of the *same type* in a population via small packets of DNA called plasmids. These are absorbed by other bacteria and a bacteria *never exposed to that drug is reprogrammed.* G– bacteria can also pass resistance to other bacteria of *different kinds* of bacteria via small packets called RTF (resistance transfer factor) plasmids and *often contain programming for resistance to multiple drugs* when the gene taken in is inserted into the chromosome.

Some drugs are close enough in molecular structure that resistant bacteria have a mechanism similar enough for other resistances as well.

The bottom line is that natural selection has already guaranteed that antibiotic resistance will occur. Indiscriminate and incorrect use of drugs will speed up that process. This causes the need for more diagnostic work, more expensive drugs and more needless loss of life and dollars.

Legal Aspects

Most drugs are, by law, only for prescription use to prevent the development of "andromeda strain" bacteria in humans and animals. However, since the availability of drugs is so wide spread, the best that one can frequently do is to use effective drugs intelligently. As long as this use is under a licensed veterinarian's supervision, the veterinarian incurs the legal burden if an improper diagnosis or treatment occurs. Any individual may legally treat his own birds in any matter with any available drug that he feels fit.

However, if a non-licensed person prescribes and/or treats another person's birds and the diagnosis or treatment does not succeed, the prescriber may be liable for illegal practice of veterinary medicine. If the bird has a disease of public health significance (psittacosis), then the legal liabilities increase. The actual incidence of this is low but given the current social climate and the incidence of civil lawsuits, it appears to make good sense to have a qualified medical opinion to back up a non-licensed person, should the need for medication arise.

GLOSSARY

Agent — Causer of disease
Antibiotic — Chemical substance which has ability to stop bacterial infection
Antimicrobial — Any drug which prevents or cures any infection
Bacteriocidal — Bacterial killing substance
Bacteriostatic — Substance which stops bacterial reproduction
Carrier — Individual which harbors an infection but does not suffer the disease
Disease — Absence of health
Germ — Any microscopic organism capable of causing disease
Health — State of normal biology
Infection — Presence of smaller organism within a larger one (host)
Morbidity — Incidence of death in a group of individuals
Shedder — Infected carrier which passes organism out of body to others ●