Avian Mycobacteriosis

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The Organisms

There are many species of mycobacteria, but *Mycobacterium avium* (MA), serotypes 1, 2, 3 and 8, *Mycobacterium genavense* (MGE), and *Mycobacterium tuberculosis* (MTB) are the most common organisms that infect birds. These bacteria have some unusual characteristics that make the diseases that they cause difficult to diagnose and treat. Mycobacteria grow slowly and thus the disease they cause will often develop slowly. Because they live in the cells of infected birds, they are difficult to kill and thus infected birds must be treated for many months. Finally, they have a tough cell wall that makes them resistant to many disinfectants and the environment. Therefore, once a premise is contaminated, disinfection is difficult. Because of their staining characteristics, these organisms are sometimes referred to as acid-fast organisms. When the species of organism is not known, the disease is often referred to as avian tuberculosis.

Infection and Disease

Probably all species of birds are suceptible to mycobacterial infection. However, infections are relatively uncommon. When outbreaks do occur, they are most frequent in collections of captive waterfowl, zoo birds, grey-cheeked (*Brotogeris pyrrhopterus*) and canary-winged parakeets (*B. versicolorus*), certain species of tropical doves, Australian finches, and in densely housed bird populations.

The route of exposure depends on the organism. Birds contract MTB directly from people by inhalation of aerosolized bacteria. By contrast, MA and MGE are contracted by ingestion of the organisms. MA appears to be ubiquitous in the environment. The factors that determine if a bird will or will not contract MA and MG are not known, but probably include a genetic susceptibility and the number of organisms to which the bird is exposed.

Mycobacterial disease can be localized or diffuse. Localized lesions are uncommon and are generally found on the face, skin, or leg and are generally caused by MTB. MA and MGE generally cause a widely disseminated disease. Following ingestion, they first colonize cells in the the intestines. Here changes may be so severe as to interfere with digestion. From the intestines, mycobacteria spread widely. Any organ system can be affected, but the liver, spleen, lung, air sac, skin and bone marrow are most commonly involved.

Affected organs may contain yellow to grey-tan, soft nodules or be diffusely enlarged. Amyloidosis of the kidney and liver is a common complication of MA infections and may contribute to the clinical signs. Microscopically, mycobacterial infections take on 2 primary forms but may contain elements of both. In the first, classical tubercles containing a central necrotic area surrounded by macrophages, multinucleated giant cells, histiocytes and plasma cells are found. In these lesions, bacteria may be scarce. At the other extreme, lesions are composed of extensive sheets of bacteria-laden histiocytes. The specific organism, the species of the host infected, the host's immune response and the stage of infection all contribute to the nature of the lesion.

Historical and Physical Findings

The clinical picture caused by mycobacterial infections is extremely diverse. Most commonly, however, birds present with a chronic slowly progressive disease. Owners may report a gradual weight loss, reduced

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vocalization, inappetence, weakness, lethargy, lameness and feather ruffling. Birds may show decreased exercise tolerance or overt breathing difficulties. Swellings in, or under, the skin may be the first sign of disease. Poor feathering, an abnormal moult, an increased volume of urine, and diarrhea may all be presenting complaints. Mycobacteriosis should always be suspected in birds proven to be highly susceptible to infection, in birds originating from flocks where mycobacterial infections have been previously identified and in birds that fail to respond adequately to routine antibiotic therapy. Mycobacteriosis occurs predominately in birds 2 to 5 years of age but can occur at any age.

Diagnosis

Historical and physical findings are rarely specific for mycobacteriosis and these diseases must be differentiated from other chronic granulomatous diseases such as psittacosis and aspergillosis, as well as neoplasia, visceral gout and internal parasites. A complete blood count, chemistry profile, parasitological examination of the feces, fecal gram and acid-fast stains and radiographs should be done on a bird suspected to have a mycobacterial infection. Assessable masses should be aspirated or biopsied.

Examination of the white blood cell count will often show significant changes. White cell counts are commonly elevated and may be extraordinarily high. Anemia is variably present. Serum chemistry changes are generally nonspecific, but may reflect liver involvement. In some stages of the disease the serum albumin may fall and the globulin fraction increase.

Radiographically, liver and spleen enlargement are common but nonspecific findings. Small intestines thickening is difficult to demonstrate, but is highly significant if observed. One or more soft tissue masses in the air sacs or lungs are suggestive of mycobacterial granulomas but will need to be differentiated from *Aspergillus* granulomas. Lesions of the long bones occur infrequently, but are highly suggestive of mycobacterial infections. Ultrasonography may be used to define masses in the abdomen or air sacs, evaluate intestinal thickness and differentiate between causes of liver enlargement.

Acid-fast stains of the droppings are not very sensitive, but the presence of acid fast organisms in clusters in several areas of the slide is diagnostic. Biopsy of diseased organs is often diagnostic, but because organisms may be few, they will sometimes be missed. Bone marrow aspirates provide an easy but only intermediately sensitive assay.

Intradermal skin testing has been useful in poultry, but is unsatisfactory in most other species. Some infected birds produce antibody to the mycobacteria that they are infected with, others do not. Recent work in my laboratory suggests that birds that are able to respond to the infection and limit their bacterial load will have antibody. Birds with heavy bacterial loads do not produce antibody.

Polymerase chain reaction (PCR) technology appears to have considerable potential in the diagnosis of mycobacterial disease. Humans with MA infections are generally bacteremic and we suspect that the seronegative birds may also be. If true, a combination of serology and PCR of processed blood samples may prove a powerful diagnostic combination.

Culturing the organism is a complex and often unrewarding process. Mycobacteria are grown on special media and take weeks to months to be identified. Complicating the issue further, many mycobacteria cannot be routinely isolated by standard methods.

Risks of Bird to Human Transmission

MTB, MGE, and the MA serotypes infecting birds are all potential human pathogens. MTB is of greatest concern, as the bird probably contracted this organism from one of its owners and MTB readily infects healthy humans. MA infections are common in patients with AIDS and are generally a complication of the advanced and near terminal stages of this disease. Children may also be at increased risk for MA infections. The source of MA for humans has not been conclusively defined, but probably represents low level environmental exposure and not direct bird to human transmission. MGE, like MA, is a disease of the immunosuppressed, although it is far less common an infection than MA in humans. Both MA and MGE infections in pet birds appear to pose little risk to the healthy population in general. However, when a

mycobacterial infection is diagnosised in a pet bird, the owners should be warned of the potential zoonotic nature of this disease and should be asked to consult with a physician before a decision on treatment or euthanasia is made. It should also be emphasized to the owner that infected birds pose a significant risk to other birds in their home. The author does not recommend treating birds with MTB.

Treatment

Controlled clinical trials optimizing treatment protocols for mycobacterial infections in birds have not been done. Case reports, however, suggest that treatment can be successful in many cases. Successful treatment of any mycobacterial infection requires a combination drug therapy to prevent the development of resistance, prolonged therapy (6 to 12 months), and an adequate immune response from the host (Table).

Environmental contamination posses a major problem for the re-introduction of species into a facility where mycobacterial infected birds have been previously held. Extensive cleaning of indoor facilities and cages and disinfection with inorganic chlorine solutions may be effective. It is questionable if pastures and outdoor enclosures with dirt floors can ever be properly sanitized.

Suggested Reading

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Table 1: Treatment Protocols for *Mycobacterium avium* Infections in Cage Birds

Drugs[a]	I	II	III	IV
Protocol 1[b]	Ciprofloxacin 20 mg/kg q 12h PO or Enrofloxacin 15 mg/kg q 12h for 10 days, PO or [Imc]	Clofazimine 1.5 mg/kg q 24h, PO	Cycloserine 5 mg/kg q 12h, PO	Ethambutol 20 mg/kg q 12h, PO
Protocol 2[d]	Clofazimine 6mg/kg, q 24h, PO	Ethambutol 30mg/kg q 24h, PO	Rifampin 45mg/kg q 24h, PO	
Protocol 3[d]	Ciprofloxacin 80mg/kg q 24h, PO or Enrofloxacin 30mg/kg q 24h, PO	Ethambutol 30mg/kg q 24h, PO	Rifampin 45mg/kg q 24h, PO or Rifabutin 15mg/kg q 24h PO	

[a] All treatments are for a minimum of six months unless otherwise noted.
[b] Rosskopf et al., 1991.
[c] Repeated intramuscular injections will lead to muscle necrosis.
[d] VanDerHeyden, 1994.