# Mycobacterial Lesions in Fish, Amphibians, Reptiles, Rodents, Lagomorphs, and Ferrets with Reference to Animal Models

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**KEYWORDS**

• Fish • Amphibians • Reptiles • Rodents • Lagomorphs
• Ferrets • Mycobacteria

Mycobacteriosis is a serious disease across many animal species and has been described in the scientific literature since the 1880s. Approximately more than 120 species are currently recognized in the genus *Mycobacterium.*[1] Mycobacteria differ greatly in their ecology, from the obligate pathogen *Mycobacterium tuberculosis*, which is a leading cause of human mortality worldwide, to saprophytic soil residents such as *M terrae*.[2]

A number of classification schemes have been used to characterize this bacterium. Historically, Mycobacteria were divided in three groups for the purposes of diagnosis: (1) the *M tuberculosis* complex (MTC), which includes *M tuberculosis*, *M bovis*, *M africanum*, *M microti*, *M canetti*, *M caprae*, *M pinnipedii*, and for some authors, *M marinum* and *M ulcerans*; (2) *M leprae*, which causes Hansen's disease or leprosy; and (3) mycobacteria other than the *M tuberculosis* complex (MOTT) or nontuberculous mycobacteria (NTM), comprising *M avium*, *M intracellulare*, *M marinum*, *M ulcerans*, *M lepraemurium*, and atypical mycobacteria.[3–5]

The Runyon classification (introduced by Ernest Runyon in 1959)[6] of nontuberculous mycobacteria is based on the rate of growth, production of yellow pigment, and whether this pigment was produced in the dark or only after exposure to light. Fast growers require less than 7 days to produce colonies on solid agar, whereas slow growers may require weeks to months. Both fast- and slow-growing species may be

The authors have nothing to disclose.
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Vet Clin Exot Anim 15 (2012) 25–40
doi:10.1016/j.cvex.2011.10.001 **vetexotic.theclinics.com**
1094-9194/12/$ – see front matter 

nonpigmented, photochromogenic (form pigment in response to light), or scotochromogenic (form pigment in the absence of light).[2,5]

The status of *M marinum* and *M ulcerans* is currently under examination. They are both closely related to *M tuberculosis*; however, are not considered part of the MTC group. *M marinum* cannot be distinguished from *M ulcerans* by ribosomal gene sequencing because they are so closely related that taxonomists argue if these two microorganisms really represent a single species. *M ulcerans* appears to have recently evolved from *M marinum* by reductive evolution and plasmid acquisition. Currently molecular evaluation is greatly expanding what is known about relatedness of all these organisms and assisting in rapid identification.[5,7–10] Both *M marinum* and *M ulcerans* are faster growing than *M tuberculosis* and more closely related than other mycobacterial species, which makes them useful models for studying the pathogenesis of *M tuberculosis*.[4]

Diagnosis of mycobacteriosis requires detection of acid-fast bacteria in exudates, fine-needle aspirates, or tissue biopsy specimens; culture; or detection using polymerase chain reaction (PCR) techniques. Isolation by culture and biochemical analysis has been the traditional method used in the identification of mycobacteria. However, mycobacteria tend to be slow-growing organisms (compared to other bacteria) and biochemical analysis is not only time consuming but also does not definitively distinguish between various species. Molecular methods (PCR and DNA sequencing) are proving to be a rapid and common method of identification. The list of recognized mycobacterial isolates and species continues to grow, reflecting the advancement and acceptance of molecular characterization of species.

## ZOONOTIC POTENTIAL OF MYCOBACTERIA

Many of the mycobacterial species isolated from animals have a zoonotic potential.[11] This has been well documented with *M marinum* and this organism is classically associated with dermatologic lesions in aquarists.[12–14] *M abscessus*, *M fortuitum*, and *M chelonae* are also responsible for skin and soft tissue infection in humans.[14]

The zoonotic potential of *M genavense* and *M haemophilum*, mycobacterial pathogens requiring special conditions for laboratory culture, have also been described.[15] *M genavense* is an atypical, difficult to grow bacterium that has been isolated from organ transplant recipients or from patients concurrently infected with human immunodeficiency virus. It is the most commonly recognized cause of mycobacterial infections in pet birds.[5] Human infections by *M haemophilum* frequently are associated with septic arthritis, osteomyelitis, and pneumonia, generally restricted to immunocompromised patients.[12,15] Zebrafish appear to be particularly vulnerable to *M haemophilum*.

*M kansasii*, a member of the atypical group of mycobacteria, has been reported to produce chronic pulmonary disease resembling tuberculosis and chronic granulomatous dermatitis in humans.[16–18] It has been recognized as an infection in a Chinese soft shell turtle (*Pelodiscus sinensis*) and from the aqueous environment of ornamental fish tanks.[17,19]

Buruli ulcer caused by *M ulcerans*, a previously uncommon emerging disease, has recently been reported as the second most frequent mycobacterial disease in humans after tuberculosis in some countries. This bacterium is found in association with rivers, swamps, and wetlands. The mode of transmission remains unclear, although vectors such as aquatic insects, adult mosquitoes, or other biting arthropods are suspected. It has been isolated from fish and an Indian flap-shelled turtle (*Lissemys punctata punctata*).[20,21]