

Mycobacteriosis

Fish Tuberculosis,
Picine Tuberculosis,
Swimming Pool Granuloma,
Fish Tank Granuloma,
Fish Handler's Disease,
Fish Handler's Nodules

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Etiology

Mycobacteriosis is a chronic or acute, systemic, granulomatous disease that occurs in aquarium and culture food fish, particularly those reared under intensive conditions. Mycobacteriosis results from infection by several species of *Mycobacterium*, aerobic, Gram-positive, pleomorphic rods which are members of the order Actinomycetales and family Mycobacteriaceae. Mycobacteria are widespread in the environment, particularly in aquatic reservoirs. The two most important species causing mycobacteriosis in fish and humans are *Mycobacterium marinum* and *Mycobacterium fortuitum*. Other species known to cause mycobacterial disease in fish include *M. chelonae*, *M. neoaurum*, *M. simiae*, and *M. scrofulaceum*.

Mycobacterium marinum was first recognized in 1926 from the liver, spleen and kidney of tropical coral fish kept in the Philadelphia Aquarium. *M. marinum* can grow prolifically within fibroblast, epithelial cells and macrophages. In the past, human outbreaks of *M. marinum* were sporadic and most commonly associated with contaminated swimming pools. Chlorination practices used today have greatly minimized the frequency of outbreaks from these sources. In the last decade, a small but steady increase in the frequency of *Mycobacterium marinum* infections in cultured or hatchery confined fish and human cases associated with fish aquaria has been noted.

Geographic Distribution

Mycobacterium marinum is ubiquitous and is found worldwide in bodies of fresh water, brackish water and salt water. One survey found that more than 67% of water specimens collected from natural, treated and animal contact sources contained mycobacteria, including *M. marinum*.

Transmission

The source of *Mycobacterium marinum* infection is contaminated water sources. In fish, transmission can occur by consumption of contaminated feed, cannibalism of infected fish or aquatic detritus or entry via injuries, skin abrasions or external parasites. In viviparous fishes, transovarian transmission has also been reported. Snails and other invertebrate organisms have been shown to play a role in the transmission of *Mycobacterium*.

In humans, breaks in the skin serve as an entry point for the organism during contact with contaminated water sources or infected fish. This is most common during cleaning or maintenance of aquariums. Direct inoculation may occur following injury from fish fins or bites. Less commonly, exposure can occur from contact with natural water sources during fishing, boating or swimming. Most infections occur in persons who keep an aquarium at home, but *M. marinum* infection may be an occupational hazard for certain professionals, such as aquaculturists, fish processors, or pet shop workers.

Mycobacterium marinum can remain viable in the environment (soil and water) for two years or more or in carcass and organs up to one year. This can lead to the possible indirect transfer of the organism, as was reported in a case of exposure from a bathtub where the family's tropical fish tank was frequently cleaned and an outbreak of mycobacteriosis in lizards kept in a contaminated fish aquarium.

Disinfection

Mycobacterium marinum can have greater resistance to disinfectants and require longer contact times for most disinfectants to be effective; 5% phenol, 1% sodium hypochlorite (low organic matter and longer contact times), iodine solutions (high concentration of available iodine), glutaraldehyde and formaldehyde (longer contact time) are considered effective.

Infections in Humans.

Incubation Period

In humans the incubation period is 2 to 4 weeks, but may take up to nine months to develop disease.

Clinical Signs

Mycobacteriosis infection most commonly manifests as a cutaneous disease which can be quite variable, slow developing and symptomatically non-specific. Small erythematous papules develop into granulomas, abscesses or ulcers which may persist for months. Skin lesions may be single but are often multiple, clusters; lesions may spread proximally along the line of the lymphatics. Lesion location varies depending on exposure. Elbows, knees and feet are most commonly reported in swimming-bath related cases and hands and fingers in aquarium owners. Deep tissue infections are possible and can cause considerable damage to the underlying tissues, tendons and bone, such as chronic proliferation of the synovial tissue, erosion of the joints, damage to tendons. Extensive scarring and adhesions, especially of the hand and wrist can lead to compromise function. Severe sequelae can involve disseminated dermatitis, arthritis, bursitis, osteomyelitis, and tenosynovitis. Systemic dissemination is rare but several cases have been reported in immunocompromised persons and can result in death.

Communicability

There is no evidence of person-to-person transmission of mycobacteriosis.

Diagnostic Tests

Diagnosis can be difficult and is often delayed. A thorough clinical history can provide clues including skin injuries associated with fish, aquariums or possibly swimming pools. Tissue biopsy for histology and culture is important. Histological appearance will vary and depend on the age of the lesion. Early lesions may reveal acid-fast bacteria, polymorphonuclear leukocytes, and histocytes, whereas older lesions consist of lymphocytes, epithelioid cells and some Langhans' giant cells, usually without caseation. A definitive diagnosis may be obtained by a positive culture under optimal growth conditions. *M. marinum* grows best on Lowenstein-Jensen media at 30-33°C (rather than at 37°C) in 7 to 21 days. Colonies are cream in color and turn yellow when exposed to light. PCR tests have also been developed.

Treatment

Many *M. marinum* infections have a slow, spontaneous resolution over periods of 1 to 6 years. Antibiotic therapy may be warranted to prevent progression to deep infection. Antibiotic agents that have been shown to be active against *M. marinum* in vitro include ethambutol, rifampicin, streptomycin, trimethoprim-sulfamethoxazole, tetracyclines, clarithromycin, azithromycin, and some of the quinolones. Depending on the extent and severity of the infection, antimicrobial therapy duration may vary from two weeks to 18 months. Corticosteroids should be avoided or used minimally to avoid exacerbating the condition. Deep infections typically requires both antibiotic and surgical treatment. Debridement of the necrotic tissues such as synovectomies, tenosynovectomies, arthrodesis may be necessary. Amputation may be required in order to

control the infection despite appropriate antimicrobial therapy and repeated debridements.

Prevention

Prevention of mycobacteriosis involves avoiding contact with contaminated water sources or infected and cleaning and disinfection procedures. Gloves should be worn with working with or touching fish, the aquaria water or equipment. A heavy glove may be necessary if contact with fish with sharp spines is anticipated. Avoid contact with fresh or salt water sources, including aquaria, if there are open cuts scrapes, or sores on your skin. Wash hands thoroughly with soap and water after fish processing or aquaria cleaning. Ensure regular and adequate chlorination of swimming pools to kill any bacteria that may be present.

Morbidity and Mortality

The incidence of *Mycobacterium marinum* in the U.S. is low. A survey in the U.S. from 1993-1996, reported the geographic distribution and national average of 198 *M. marinum* cases annually.

M. marinum infections can result in significant morbidity. Skin lesions can be chronic and leave scarring upon healing. Delay of diagnosis is common, and invasion into deeper structures such as synovia, bursae, and bone occurs in approximately one third of reported cases. Deep infections can lead to sequelae including loss of joint mobility from osteomyelitis and severe cases may need amputation of appendages to control infection. An estimated 40% of patients with deep disease, treated conservatively with antimicrobial therapy, still required surgical debridement to control the disease process. Systemic disease from *Mycobacterium marinum* is rare, but most commonly affects persons with immunocompromised conditions.

Infections in Animals

Species Affected

All species of fish (freshwater, brackish water and salt water) are susceptible to mycobacteriosis and it has been described from a wide variety of aquarium fish. Outbreaks are most common in tropical aquarium fish. Members of several freshwater families [Anabantidae (bettas and gouramis), Characidae (tetras and piranhas) and Cyprinidae (danios and barbs)] appear to be particularly susceptible.

Mycobacteriosis has been found in wild stocks of fish including cod, halibut, striped bass, North-East Atlantic mackerel, and yellow perch. Intensively culture warm water fish species are also very susceptible. There has been an increase in frequency of *M. marinum* infection in cultured or hatchery-confined fish, such as chinook salmon, cultured striped bass, freshwater ornamental fish, salmon, sturgeon and bass.

Mycobacterium marinum infection has been reported to occur in some reptiles. A collection of Egyptian spiny-

tailed lizards (*Uromatyx aegyptius*) were affected after being housed in an unsterilized tank previously used for fish.

Incubation Period

The incubation period is variable, ranging from years of development to sudden death.

Clinical Signs

Signs of mycobacteriosis in fish are variable and often resemble other diseases. Disease may be acute or chronic. Some fish may show no external signs of disease. The chronic form of the disease is most commonly seen. Affected fish can be anorexic, emaciated, listless and lethargic; they may separate from other fishes and seek out corner of the holding facility. Nodular skin lesions, ulcerations or hemorrhages can occur following rupture of an internal muscular lesion. Additional signs may include exophthalmos (bulging eyes), abdominal distention and skeletal deformities, such as spinal curvature or stunting defects and pale gills. Some fish may develop fin and tail rot. Fading of cutaneous pigmentation is also common. The acute form of the disease occurs rarely. It is characterized by rapid morbidity and mortality with few clinical signs.

Communicability

Transmission of *M. marinum* among fish is poorly understood. The most probably route of primary infection is either oral (when an infected fish dies and is consumed by other fish in the population), or thorough injuries in the skin (if the number of bacteria in the environment is high or if the fish has a poorly functioning immune system).

Diagnostic Tests

Diagnosis of mycobacteriosis depends on clinical and histological signs and identification of the bacterial pathogen. Smears from scrapings of the cut surface of the spleen, kidney or skin lesions should be made and stained with Kinyoun modification of the Ziehl-Neelsen stain. Use of fluorescing dyes are also recommended.

Gross and histologic lesions of necrogranulomas containing acid-fast bacilli give strong clues towards the involvement of *Mycobacterium*.

Isolation of the pathogen can provide definitive diagnosis. Attempts can be difficult due to the fastidiousness of the pathogen. Cultures should be incubated for 2 to 30 days at 20-30 °C, since *M. marinum* is a slow grower. Visible growth will require seven or more days of incubation. The cell and colony morphology is not distinctive. Identification may occur on the basis of biochemical characteristics, however these tests are cumbersome and time consuming.

PCR-based methods may be an alternative for diagnosis. Enzyme-linked immunosorbent assays have not been developed for fish.

Treatment

Drug therapy in fish is of limited value for this disease and vary in their degree of success. Treatment will not eliminate *Mycobacterium* from affected fish colonies. Parenteral and oral administration of sulphasoxazole with doxycycline or minocycline, bath treatment or intraperitoneal injections of kanamycin or streptomycin or incorporation of isoniazid or rifampin in the feed may be possible treatments.

Infection is only completely controlled by culling the affected fish population and disinfecting tanks and equipment associated with these animals.

Prevention

Prevention measures involve sanitation, disinfection and destruction of carrier fishes. Fish should be obtained from farms known to be free of diseases. Imported fish should require a period of quarantine. If trash fish or dead fish carcasses are used as a source of protein in the feed for fish, it should be heated at 76°C for 30 minutes to kill any pathogenic mycobacteria. Dead fish should be destroyed by burning or burying in quicklime.

There are no vaccines for fish mycobacteriosis.

Morbidity and Mortality

The incidence of mycobacteriosis in aquarium fish has been reported to range from 10-22%. In natural fish populations, 10-100% of fish may be infected. Disease outbreaks in cultured fish appear to be related to management factors, such as the quality and quantity of nutrient and water supplied.

Post-Mortem Lesions

Mycobacteriosis lesions occur along the gut or in the skin and gills. Gross or microscopic grayish-white miliary granulomas may be found scattered, grouped or coalescing within any number of organs. Lesions can be hard or soft, range from 80-500 µm in size, and may have a caseous necrotic center. The spleen, kidney and liver are the most commonly affected. Peritonitis and edema may be apparent. In severe cases, visceral organs will be swollen and fused by whitish membranes around the mesenteries. Large caseous necrotic areas

Internet Resources

Material Safety Data Sheets – Public Health Agency of Canada, Office of Laboratory Security
<http://www.phac-aspc.gc.ca/msds-ftss/index.html>

Medical Microbiology
<http://www.gsbs.utmb.edu/microbook>

The Merck Veterinary Manual
<http://www.merckvetmanual.com/mvm/index.jsp>

References

- Acha PN, Szyfres B (Pan American Health Organization [PAHO]). Zoonoses and communicable diseases common to man and animals. Volume 1. Bacterioses and mycoses. 3rd ed. Washington DC: PAHO; 2003. Scientific and Technical Publication No. 580. Salmonellosis; p. 233-251.
- Aiello SE, Mays A, editors. The Merck veterinary manual. 8th ed. Whitehouse Station, NJ: Merck and Co; 1998. Mycobacterial infections other than tuberculosis [monograph online]. Available at: <http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/52312.htm>. Accessed 28 Jun 2006.
- Aiello SE, Mays A, editors. The Merck veterinary manual. 8th ed. Whitehouse Station, NJ: Merck and Co; 1998. Fish health management: bacterial disease [monograph online]. Available at: <http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/170414.htm>. Accessed 28 Jun 2006.
- Austin B, Austin DA, editors. Bacterial fish pathogens. Praxis Publishing Ltd., Chichester, UK.
- Avaniss-Aghahani E, Jones K, Holtzman, A, Aronson T, Glover N, Boian M, Froman S, Brunk CF. Molecular technique for rapid identification of mycobacteria. J Clin Microbiol. 1996;34:98-102.
- Bhaty MA, Turner DPI, Chamberlain ST. *Mycobacterium marinum* hand infection: cases reports and review of literature. Br J Plast Surg. 2000 Mar;53(2):162-165.
- Chinabut S. Mycobacteriosis and nocardiosis. In Woo PTK, Bruno DW, editors. Fish diseases and disorders, Volume 3. 1999. CAB International: Oxford, UK. pp 319-331.
- Chomel BB. Zoonoses of house pets other than dogs, cats and birds. Pediatr Infect Dis J. 1992;11(6):479-487.
- Decostere A, Hermans K, Haesebrouck F. Piscine mycobacteriosis: a literature review covering the agent and the diseases it causes in fish and humans. Vet Micro. 2004;99:159-166.
- Dobos KM, Quinn FD, Ashford DA, Horsburgh CR, King CH. Emergence of a unique group of necrotizing mycobacterial diseases. Emerg Infect Dis. 1999;5(3):367-378.
- Edelstein H. *Mycobacterium marinum* skin infections: Report of 31 cases and review of the literature. Arch Int Med. 1994;1359-1364.
- Enzensberger R, Hunfeld KP, Elshorst-Schmidt T, Boer A, Brade V. Disseminated cutaneous *Mycobacterium marinum* infection in a patient with non-Hodgkin's lymphoma. Infection. 2002;30(6):393-395.
- Holmes GF, Harrington SM, Romagnoli MJ, Merz WG. Recurrent, disseminated *Mycobacterium marinum* infection caused by the same genotypically defined strain in an immunocompromised patient. J Clin Microbiol. 1999;37(0):3059-3061.
- Jernigan JA, Farr BM. Incubation period and sources of exposure for cutaneous *Mycobacterium marinum* infection: case report and review of the literature. Clin Infect Dis. 2000;31:439-443.
- Krauss H, Weber A, Appel M, Enders B, Isenburg HD, Schiefer HG, Slenczka W, von Graevenitz A, Zahner H. Zoonoses: infectious diseases transmissible from animals to humans. 2003. Washington DC; ASM Press. pp 214-215.
- Lahey T. Invasive *Mycobacterium marinum* infections. Emerg Infect Dis. 2003;9(11):1496-1498
- Lehane L, Rawlin GT. Topically acquired bacterial zoonoses from fish: a review. MJA. 2000;173:256-259.
- McMurray DN. Mycobacteria and Nocardia. [monograph online]. In Baron S, editor. *Medical Microbiology*. 4th ed. New York: Churchill Livingstone; 1996. Available at: <http://gsbs.utmb.edu/microbook/ch033.htm> Accessed 28 Jun 2006.
- Novotny L, Dvorska L, Lorencova A, Beran V, Pavlik I. Fish: a potential source of bacterial pathogens for human beings. Vet Med.- Czech, 2004;49(9):343-358.
- Parent LJ, Salam MM, Appelbaum PC, Dossett JH. disseminated *Mycobacterium marinum* infection and bacteremia in a child with severe combined immunodeficiency. Clin Infect Dis. 1995;21(5):1325-1327.
- Post G. Textbook of fish health, 2nd ed. TFH Publications: Ascot. pp65-68.
- Public Health Agency of Canada, Office of Laboratory Security. Material Safety Data Sheet - *Mycobacterium* spp. (other than *M. tuberculosis*, *M. bovis*, *M. avium*, *M. leprae*) 1996 Sept. Available at: <http://www.phac-aspc.gc.ca/msds-ftss/msds102e.html>. Accessed 28 Jun 2006.
- Sanguinetti M, Posteraro B, Ardito F, Zanetti S, Cingolani A, Sechi L, De Luca A, Ortona L, Fadda G. Routine use of PCR-reverse cross-blot hybridization assay for rapid identification of *Mycobacterium* species growing in liquid media. J Clin Microbiol. 1998;36:1530-1533.
- Stamm LM, Brown EJ. *Mycobacterium marinum*: the generalization and specialization of a pathogenic mycobacterium. Microbes Infect. 2004 Dec;6(15):1418-1428.
- van der Sar AM, Abdallah AM, Sparrius M, Reinders E, Vandenbroucke-Grauls CMJE, Bitter W. *Mycobacterium marinum* strains can be divided into two distinct types based on genetic diversity and virulence. Infect Immun. 2004;72(11):6306-6312.
- Vazquez JA, Sobel JD. A case of disseminated *Mycobacterium marinum* infection in an immunocompetent patient. Eur J Clin Microbiol Infect Dis. 1992;11(10):908-911.