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Fish Mycobacteriosis: Review

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Abstract: Fish mycobacteriosis is a chronic disease caused by a group of bacteria (simple single-celled organisms) known as mycobacteria, which affects both in culture and wild setting fishes. It includes both slowly and rapidly growing mycobacterial species that includes *M. marinum* and *M. fortuitum*. These two mycobacterial species also have a significant public health impact among human beings. Transmission to human beings includes during handling of fish that is infected by mycobacteria and during cleaning of aquiram and materials already contaminated by fish that have been infected by mycobacteriosis. External clinical sign is rare but it forms a granulomatous lesion on kidney, liver and spleen during post mortem diagnosis. Fish that are infected by mycobacteriosis can't fit for human consumption and this in turn decreases trade on fish which leads to economic loss in farms. Laboratory confirmation of mycobacteriosis is based on acid-fast microscopy of suspected pathological material. There is no widely accepted treatment for it rather than depopulation which cause a large economic loss in fish farms and facility disinfection as control and protection methods.

Key words: Economic Loss・Fishes・Fish Mycobacteriosis・Public Health Impact

INTRODUCTION

Fish mycobacteriosis is known as piscine tuberculosis, which is a chronic progressive disease caused by several species of the genus mycobacterium [1]. This disease also affects many species of wild and cultured fishes inhabiting both fresh water and marine environments [2]. Fish mycobacteriosis is a systemic infectious disease that is typically a sub-acute to progressive condition caused by different mycobacterium species, includes *Mycobacterium marinum*, *Mycobacterium fortuitum*, *Mycobacterium chelonae* and *Mycobacterium abscessus* [3].

Some fish may show no external signs of disease. But, other fishes show a clinical sign like anorexia, emaciation, listless, lethargic and they may separate from other fishes and seek out corner of the holding facility, abdominal distention, skeletal deformities, stunting defects and pale gills are observed [4]. In addition to fish infection, mycobacteria are capable of causing both localized and disseminated infections in man [5]. Seafood related environmental mycobacteria mostly pose risks to fish handlers, aquarium hobbyists and even raw fish consumers [6].

Mycobacteriosis affects a wide range of fresh water and marine fish species, suggesting a ubiquitous distribution and has the potential to profoundly impact the fishery sector as a whole and its economic consequences include mortality, morbidity and effects of subclinical infection [7], such as decreased feed efficiency, decreased growth rates and decreased marketability of fish [8]. Fish mycobacteriosis has substantial economic consequences especially in the aquaculture and fisheries industry as infections may significantly decrease production and trade [9].

The diagnosis of mycobacterial disease in fish is possible on the basis of the discovery of granulomas during autopsy in native preparates or during histopathological examination by staining the smears according to Ziehl-Neelsen test (ZNT) as Acid fast-rods (AFR), which occur independently or in clusters [10].

There are no widely accepted treatment for fish mycobacteriosis. But some antibiotic treatment are applied to decrease local trauma and to decrease wound infection for long time. And this antibiotic treatment are based on strain susceptibility of the fishes. Drugs like rifampicin, streptomycin and erythromycin have been shown to have some effectiveness against an

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undescribed mycobacterium species in yellowtail (*Seriola quinqueradiata*) [11] and ethambutol, isoniazid or rifampicin are occasionally used for treating high-value specimens in aquaria [12]. Having a separate, physically isolated, quarantine for new arrivals can greatly reduce the risk of disease outbreaks affecting brood stock and production animals [13]. Therefore, the objective of this to provide up-to-date information about review is fish mycobacteriosis.

Fish Mycobacteriosis

General Characteristics: Fish mycobacteriosis is among the major diseases of fish which is caused by many species of the genus mycobacterium which is serious and often lethal disease of fish, affecting a wide range of species globally both in culture and wild settings of fish species [14]. Mycobacteria are a heterogeneous group of bacteria in terms of their genotypic features and disease association [15]. These causative mycobacteria have a general characteristic like they are, pleomorphic, aerobic, gram-positive, acid-fast, non-motile rods, 0.2-0.6 ìm in diameter and 1-10 ìm long in the genus mycobacterium, the only genus in the family mycobacteriaceae [2].

There are more than 120 recognized species of mycobacteria [16]. The mycobacterium comprises obligate pathogens that cause serious human and animal diseases, opportunistic pathogens and saprophytic species [17]. Mycobacterial species are capable of causing serious and costly diseases in most vertebrates including humans (most notably Tuberculosis, Leprosy and Buruli ulcer), livestock (Bovine tuberculosis) and fish, which is commonly reported in aquaculture and the fish aquaria trade [18].

Etiology: There is no single etiological agent of mycobacteriosis. Instead several species and strains have been identified [19]. Classically, mycobacteria causing fish disease are divided into slow growing mycobacterial (SGM) and rapid growing mycobacterial (RGM) species [20]. This includes *M. marinum* and the rapidly growing *M. fortuitum*, *M. chelonae* and *M. abscesses* [21]. *Mycobacterium fortuitum* and *M. chelonae* usually cause superficial lesions via skin wounds, pulmonary disease and cervical lymph node infection may also occur. *Mycobacterium marinum* infections are cutaneous with the hands being commonly affected in human [22]. Many other species of mycobacterium have been isolated from fish, including *M. smegmatis, M. neonarum, M. simiae, M. scrofulaceum, M. poriferae* and *M. triplex* like organism [23]. Generally, the following table (Table 1) shows other mycobacterial species identified from different fish species.

Epidemiology

Transmission: Fish mycobacteriosis is a disease which is considered to be linked to deficiencies in hygiene, overcrowding or malnutrition. However, outbreaks are known to have occurred in rearing premises where water quality values remained within optimal ranges [24]. Transovarian transmission in viparous fish [30] and direct transmission from water contact have been suggested [31]. Mycobacterium transmission is often precipitated by a stressor, but specific factors causing the outbreak are seldom discovered and depend on host factors, environmental factors and the mycobacterium species involved [2].

Transmission among fishes includes ingestion of mycobacteria is probably the major source of infection, including fish that have recently eaten dead tank mates [32]. Cannibalism and eating contaminated feed and thereby ingesting the infectious agent that are infected by mycobacteriosis are also the main routes for the transmission of mycobacterium in fish. The oral route of transmission suggests food presents a risk for exposure [33].

Transmission to human were mostly include due to inadequate chlorination of swimming pool water, while cleaning aquariums without wearing protective gloves and less commonly infection occurs after fish hook injuries or by direct contact of previously damaged skin with raw fish, oysters or other spiny sea animals [34]. Mycobacterial lesions in the digestive tract, gill and skin are the main source for releasing infectious materials into the water column. In addition, once the fish dies and decomposes, release of infective bacteria from infected tissues increases [6]. Although, infection may be caused by direct injury from the fish fins or bites most are acquired during the handling of the aquariums such as cleaning or changing the water [35].

Geographic Distribution: Fish mycobacteriosis is a sub-acute to chronic wasting disease known to affect nearly 200 fresh water and salt water species [36]. Outbreaks are most common in tropical aquarium fish, wild stocks of fish including cod, halibut, striped bass, north-east Atlantic mackerel and yellow perch. Intensively most common in culture warm water fish species, hatchery-confined fish, such asChinook salmon, cultured

Table 1: List of other mycobacterial species identified from different fish species

Bacterial Species	Fish Species	References
M. abscessus	Zebra fish (*Danio rerio*) Medaka (*Oryzias latipes*), Milk fish (*Chanos chanos*)	[24]
M. avium	Dwarf Cichlid (*Apistogramma cacatuoides*)	[25]
M. gordonae	Gold fish (*Carassius auratus*), Guppy (*Poecilia reticulate*), Angel fish (*Pterophyllum scalare*)	[26]
M. haemophilum	Zebra fish (*Danio rerio*)	[3]
M. neoaurum	Chinook salmon (*Oncorhynchus tschawytscha*)	[27]
M. simiae	Black acara (*Cichlasoma bimaculatum*)	[28]
M. triplex-like	Striped bass (*Morone saxatilis*)	[29]

striped bass, fresh water ornamental fish and sturgeon [14]. Maycobacterium *marinum* is widely distributed in aquatic environments such as natural water (still or stagnant, salty or fresh), fish tanks and swimming pools [20]. Host factors likely play a role as demonstrated by the differing susceptibility of medaka and zebra fish to *M. marinum* [37].

Mycobacterial fortuitum is highly distributed in Venezuala in silver mullet fish species [4]. Mycobacteria in aquatics are natural pathogens of ectotherms includes frogs and fish and their optimal growth temperature range is 25-35°C [38]. Although, mycobacteriosis is considered to be precipitated by stress, specific factors leading to disease outbreaks are seldom defined and appear to vary between systems. *Mycobacterium fortuitum* has also been implicated in cases of cattle and sheep mastitis [39], canine pulmonary and subcutaneous abscesses [40], feline cutaneous granulomas as well as the mouse neurological disorder, `Spinning disease' [41].

Clinical Sign: Fish mycobacteriosis is predominately a chronic disease that may not produce external clinical signs but, tissues of the fish may be involved, including eyes, gills, visceral organs, musculature and fins. External clinical signs are nonspecific and include scale loss and dermal ulceration, pigmentary changes, abnormal behavior, spinal defects, emaciation and ascites [42]. Emaciation, external lesions, bulging of the eyes and reduced growth have all been associated with this disease. Internally, grayish-white nodules (granulomas) may be visible in the spleen, kidney or liver of severely affected fish [13].

Granulomas are primarily found in the spleen, liver and kidney during earlier stages of the disease, but may spread to all organs in more advanced cases and infection has been suggested to be terminal. However, this may be highly dependent on the mycobacterial species and host [43]. Fish with late-stage disease often develop ulcerations and other external lesions that may have some diagnostic value [44].

In human *M. fortuitum* and *M. chelonae* usually cause superficial lesions via skin wounds, but pulmonary disease and cervical lymph node infection may also occur [22]. In humans, *M. marinum* causes granulomatous inflammation and nodular or diffuse granulomas of the skin, subcutaneous tissues and tendon sheaths of fingers and hands. Invasive septic arthritis and osteomyelitis may occur in immune compromised hosts, causing chronic skin lesions, congestion of the whole finger and hand and tenosynovitis [45]. Granulomatous skin lesions are seen at the entrance site of *M. marinum*, thus the lesions are predominately located on the hands and forearms [20].

Pathogenesis

Pathogenic Mechanism of Mycobacteriosis: After fish ingests pathogenic mycobacterial cell in the intestine cause infection in intestine and liver. As they are intracellular, immune system of the host is suppressed by preventing proper mobilization and action of macrophages then spread throughout the body and spread infection and promote host cell death until host dies itself [46]. With the exception of *M. ulcerans*, pathogenic mycobacteria in vertebrates are predominately intracellular parasites of phagocytes [47]. The lesions swell and develop into ulcerations, often leading to granuloma. In some instances, infection spreading to the lymphatics lead to a sporotrichoid pattern of infection. Some long-term effects of lesions are tenosynovitis, osteomyelitis, arthritis and a compromised immune system [42].

Scale loss, fin necrosis, abdominal distention, multiple skin ulcers and lesions were comprised of small nodules. Dermal aggregates extended into the epithelial layer. Lymphocytes as well as pigment cells were aggregating around the lesions resulting in heavy melanization of the skin. In mycobacteriosis, the most severe granulomas are predominately located in the liver and the spleen of the fish [32]. Granulomatous inflammation is the classic histopathological manifestation of fish mycobacteriosis [48].

Spleen of naturally infected gold fish (*Carassius auratus*) showed necrosis and depletation of the haemopiotic tissues. Spleen of the experimentally infected at the day 60 post-infection with *M. fortuitum* showed considerable increase in the melano macrophage centers numbers with excessive melanosis and filled with hard tubercles [49]. Spleen and kidneys usually contained the highest concentration of mycobacterial tuberculi (Visceral nodular/granulomatous lesions) in many species of fish [48].

Generally, the predominant pathological hallmark of mycobacterial infections in fish is the infiltration of lymphoid cells and macrophages with granuloma formation by which both the granulomatous tissue and surrounding areas produce a positive reaction with periodic acid-schiff method staining. The nodules are granulomas of varying size which is visible in infected tissue consists of clumps of epitheloid cells surrounded by a connective capsule of varying thickness and areas of necrosis are often seen in the centre [32]. Granulomatous lesions were found in the skin, eye and internal organs and in the oral cavity of some individuals could be related to infections derived from the eroded mucosa and mycobacterial infection in zebra fish is acquired primarily through the intestinal tract [50].

Diagnosis: Diagnosis of mycobacteriosis of fish requires examination of any visible external and internal organs and tissues changes through appropriate necropsy techniques, sampling and the processing of diagnostic samples by an appropriately qualified laboratory typically diagnosed based on microscopic evaluation of tissues processed for histopathology. The pathologist evaluates the tissues for the presence of granulomas. Part of this evaluation is to perform a special stain Ziehl-neelsen acid fast stain (ZNAFS) on the tissues. However, the mycobacteria cannot always be detected in tissue sections, depending perhaps on species, abundance and the growth phase of the pathogen [51]. This stain specifically stains the mycobacteria due to the structure of the bacterial cell wall. Different biochemical evaluations of the infection can be done using the approved techniques. In some laboratories culture of the bacterium requires a special medium and the bacterium may take several weeks to grow on the agar plate [52].

Immunohistochemistry (IHC) was found to be effective in the detection of mycobacterial antigens in tissue at the early stages of disease where conventional histological staining methods failed. The specific reaction by IHC was visible as a golden brown colour within the cytoplasm of phagocytic cells. Mycobacteria are identified by staining the smears according to Ziehl-neelsen (Z-N) as AFR, which occur independently or in clusters [10]. The Immunohistochemistry (IHC) method proved to be more sensitive than ZN staining since positive regions were observed in the liver of infected fish by IHC which could not be seen or were only faintly observed stained with ZN stain. Definitive identification of the type strains is however may not possible using these conventional methods mentioned above. An alternative approach to the identification of mycobacteria is the application of molecular techniques like Polymerase chain reaction (PCR) using small sub unit ribosomal Ribo nucleic acid (SSsRNA) (16sRNA) primer [53].

Laboratory confirmation of mycobacteriosis is based on acid-fast microscopy of suspected pathological material [54]. Primary isolation of fish mycobacteria is best achieved using Ogawa and Lowenstein-Jensen media subcultures develop at 28°C within 3-5 days on these media. On Ogawa medium, the cultures appear creamy in the dark but brilliant yellow color when exposed to light. Mycobacteria may also be isolated occasionally on general-purpose bacteriological media such as Tryptic soy agar (TSA) or Brain heart infusion agar (BHIA) provided that a large inoculum is used. All fish mycobacterium have been cultured at 20-30°C for 2 to 30 days. The isolates are strongly acid-fast, rod-shaped, weakly gram-positive, cord forming, non-motile and non-spore forming [10].

As differential diagnosis Nocardia species, which are weakly acid-fast and rod shaped make complain. However, Nocardia is unique in that it will be visible in tissue as branching rods and rare in fish as these organism tend to associate with soils rather than water, but it is seen occasionally and the lesions it causes would be characterized as granulomatous. Histology will differentiate the two infections that the branching rods characteristic of Nocardia should be easily seen in the infected tissues [23].

Treatment: There are no widely accepted treatments for mycobacteriosis in fishes. The treatment of mycobacteriosis in fish is not widely advocated for several reasons which includes the generally resistant nature of Non tuberculus mycobacteria (NTM) infections to antibiotics [55]. There is also the risk of treatment creating invisible carriers of disease as well as the potential zoonotic risk to staff [6, 56]. Antibiotic susceptibility testing on fish isolates is rarely performed and resistance appears to be highly dependent on the infecting species and strain [11]. Oral treatment was chosen as this method ensures control of the quantity of antibiotics used for each fish with minimal quantities reaching the waterways and little effect on water quality [57].

A combination of antibiotic therapy based on sensitivity pattern for adequately long periods of time is necessary to ensure complete wound healing and to prevent recurrence [58]. There is no established treatment of choice for *M. marinum* infection due to a naturally multi-drug resistant species and its treatment is based primarily on the personal experience and preference of individual investigators without the benefit of large studies [59]. Ultimately, the only cure for *M. fortuitum* infection may be surgical debridement, especially if the infected area is extensive and the infection involves an implant, which is normally removed [60]. Generally, the treatment strategies are also evolving simultaneously with different ant mycobacterial drug therapy including isoniazid, ethionamide, thiacetazone, rifampin, rifabutin, rifapentine, pyrazinamide, streptomycin, kanamycin, amikacin, capreomycin, gentamicin, tobramycin and ethambutol among others [61].

Prevention and Control: Understanding this disease and its implications from an ecosystem perspective will require strong interaction of fish health professionals with traditional fisheries ecologists and epidemiologists [62]. Avoid handling fish or cleaning fish tanks or should wear heavy, waterproof gloves when handling or processing fish and cleaning home aquariums or fish tanks. Everyone should wash their hands thoroughly with soap and water after contact with fish or processing fish. It is also important to ensure the regular and adequate chlorination of swimming pools and fish tanks to kill any bacteria that may be present [63].

The other way of prevention and control is rapid removal of dead fish to minimize transmission through cannibalization, as well as removal of any moribund animals, which might act as reservoirs of infection [33]. Control of mycobacteriosis in culture settings is extremely difficult once an epizootic has occurred. In most cases eradication or depopulation of infected animals followed by disinfection of the culture system is the only acceptable means [64]. Quarantine and biosecurity also the main way of prevention and control [23]. Having a separate physically isolated system for new arrivals can greatly reduce the risk of disease outbreaks affecting brood stock and production animals. Maintain animals in quarantine for a minimum of several weeks to ensure proper feeding and health of the population. Fish showing clinical sign of disease should be immediately removed and quarantined to reduce the risk of pathogen transfer [13].

Ethanol, benzyl-4-chlorophenol-phenylphenol (*Lysol*) and sodium chlorite have been found to rapidly kill *M. marinum* in water and other commonly used disinfectants such as N-alkyl dimethyl benzyl ammonium chloride (*Roccal-D, Micronex*) and potassium peroxymonosulfate (*Virkon-S*) are ineffective even after extended contact times. Sodium hypochlorite was an effective sterilizing agent provided the contact time was longer than 10 min [65]. However, disinfection is not always successful due in large part to the resistance of many species of mycobacteria to common disinfectants in wild fisheries. Management is faced with both the potential of transmission to humans from infected fish as well as the difficult task of determining population level impacts which may vary with species of host and bacteria as well as environmental factor [62].

In generally, control of mycobacteriosis in aquaria typically requires destruction of affected stock and disinfection of holding tanks and plumbing. There is no vaccines available to prevent this disease in fish. Major limitations in fish vaccine developments are less understanding of fish immunology, many vaccines unlicensed, not cost effective (expensive) and stressful on administration [66].

Economic Impact: Mycobacteriosis is a common chronic infection of fish and its prevalence may reach as high as 15% in some fish populations [32]. The economically significant consequences of these infections include mortality, morbidity and effects of subclinical infection such as decreased feed efficiency, decreased growth rates and decreased marketability [7]. The acute form of the disease occurs rarely and it is characterized by rapid morbidity and mortality with few clinical signs [4].

Acute disease has been reported in association with high bacterial loads [67]. Therefore, if one fish in a population is diagnosed with the condition, then the entire population must be considered exposed and potentially infected. In addition, factors that promote the establishment of mycobacteria within a given aquaculture system also need to be identified to decrease chance of exposure.

The zoonotic nature of the organism and the massive economic losses in the aquaculture industry caused by this disease plus the lack of effective treatment cause a major economic loss in fish farm [45]. There is no widely accepted treatment for fish infected with mycobacteria, so depopulation of an infected group is strongly recommended. Fish mycobacteriosis is often chronic with limited mortality, but in certain circumstances infections may be acute and result in severe loss in cultured fish [54].

Public Health Impact: Certain mycobacterial species (Particularly *M. marinum* and *M. fortuitum*) can cause contagious skin infections in humans (Under particular conditions) transmitted from fish [8]. Aquatic mycobacteria pose significant zoonotic concerns [68]. The majority of mycobacterial species derived from the water environment of fish ponds were first isolated and described as the aetiologic agents of human diseases [69]. Humans become infected while working with the contents of aquaria with infected fish [70]. The consumption of insufficiently heat treated fish foods is a presumed source of potentialy pathogenic mycobacteria for patients infected with Human immune virus (HIV) [71]. The following two mycobacterial species have a most significant health impact or public health significance in humans.

***Mycobacterium marinum*:** *Mycobacterium marinum* is ubiquitous and is found worldwide in bodies of fresh water, brackish water and salt water. All species of fish are susceptible to mycobacteriosis and it has been described from a wide variety of aquarium fish [14]. *Mycobacterium marinum* is an aerobic, environmental, waterborne mycobacterium that belongs to Runyon's classification group I photo chromogenic non-tuberculous mycobacteria which is usually found in non-chlorinated water occupying many aquatic environments commonly infecting fish and amphibians in a worldwide distribution [68].

Mycobacterium marinum causes the most common chronic bacterial disease in ornamental fish and it can affect both the temperate and tropical species in freshwater and marine environments [6]. It has an intermediate growth rate with an optimum growth temperature of 28-30°C. It is found in aquatic environments worldwide typically causing chronic systemic infections in fish.

Transmission to humans occurs through contact of previously damaged skin with contaminated, predominately still water aquariums, inadequately chlorinated swimming pools, through injuries inflicted by fish hooks and through cuts while handling raw fish [20]. *Mycobacterium marinum* is a well-known human pathogen producing granulomatous lesions in skin and peripheral deep tissues [68].

The Centers for disease control and prevention (CDC) in the United States of America (USA) included *M. marinum* on their list of 'Emerging infectious diseases' from 2008 [63]. The following table (Table 2) shows human cases acquired from fish by *M. marinum* in five countries listed below from 1992 to 2005 studied by USA foodborne and topically acquired infections by mycobacteria.

Mycobacterium marinum infection is also called 'Fish tank granuloma 'or 'aquarium granuloma' or 'swimming pool granuloma'. However, infections related to swimming pool bathing has substantially fallen due to construction improvements and the chlorination of water. *Mycobacterium marinum* infection is opportunistic and occurs ~ 2 weeks after direct inoculation of the organism either from fish fins and bites or from the handling of aquariums [77]. *Mycobacterium marinum* in mouse macrophages has also been shown to escape phagosomes and spread directly from cell to cell via actin-based motility [78].

For people with immune system deficit (i.e.Human immune virus (HIV), cancer patients undergoing chemotherapy, *M. marinum* infection can become severe [59]. Inflammatory nodules or abscesses can develop in severely immunosuppressed patient usually in a sporotrichotic type of distribution [79]. Disseminated infection, lung involvement and other systemic manifestations including bacteraemia is usually seen in immune compromised patients, but is considered very rare [77].

***Mycobacterium fortuitum*:** *Mycobacterium fortuitum* is a rapidly growing, atypical and non-tubercular mycobacteria affecting wide range of animals including humans. In fish, it is one of the etiologic agents causing piscine-tuberculosis or mycobacteriosis a fatal disease characterized by the development of gray-white nodular structures and presence of single or multiple granulomatous lesions on several parenchymal organs [80]. *Mycobacterium fortuitum* is a natural fish pathogen. It induces apoptosis in head kidney macrophages of fish especialy in cat fish (*clarias*) species [81]. *Mycobacterium fortuitum* is a commonly isolated organism from respiratory specimens in clinical laboratories in many countries [82].

Table 2: Data of human cases infected by *M*. marinum from fish in different countries

Bacteria	Country	No.of cases	Year	Reference
M. marinum	USA	653	1993-1996	[72]
	France	63	1996-1998	[73]
	Spain	35	1991-1998	[74]
	Israel	20	1992-1999	[75]
	Taiwan	3	2004-2005	[76]

Mycobacterium fortuitum is one of the RGM which are distinguished from other NTM by their ability to form colonies in less than 1 week and their in vitro resistance to anti mycobacterials [83]. The optimum growth temperature of these organisms lies between 30-33°C [84]. *Mycobacterium fortuitum* is pathogenic to animals and humans neither the molecular pathogenesis of this organism nor the virulence determinants have been identified [85]. Although the pathogenesis of *M. fortuitum* pulmonary infection in patients is unclear and have confirmed its association with lipoid pneumonia and the evidence of identical *M. fortuitum* strains among all the sputum and intestinal fluid specimens in patient. Lipoid pneumonia is caused by aspirating fat like compounds of animal, vegetable or mineral origin [86]. Some of studies concluded that *M. fortuitum* have an advantage for survival in a lipid environment [87].

In human, *M. fortuitum* associated with breast infections which cause breast abscess [88]. Many patients with *M. fortuitum* detected from lower respiratory tract specimens were found to have underlying lung diseases, including old pulmonary tuberculosis, lung cancer, interstitial lung disease and other NTM pulmonary diseases. Thus, *M. fortuitum* from respiratory tracts has been considered to indicate mere colonization or transient infection [89].

REFERENCES

1. Beran, V., L. Matlova, L. Dvorska, P. Svastova and I. Pavlik, 2006. Distribution of mycobacteria in clinically healthy ornamental fish and their aquarium environment: Journal of Fish Diseases, 29(7): 383-393.
2. Gauthier, D.T. and M.W. Rhodes, 2009. Mycobacteriosis in fishes: a review. The Veterinary Journal, 180(1): 33-47.
3. Whipps, C.M., S.T. Dougan and M.L. Kent, 2007. Mycobacterium haemophilum infections of zebrafish (*Danio rerio*) in research facilities: FEMS Microbiology Letters, 270(1): 21-26.
4. Pérez, T.A.T., D.A. Conroy and L. Quiñones, 2001. Presence of acid-fast bacteria in wild and cultured silver mullets (Mugil curema) from Margarita Island, Venezuela: Interciencia, 26(6).
5. Lewis, F.M.T., B.J. Marsh and C.F. Von Reyn, 2003. Fish tank exposure and cutaneous infections due to Mycobacterium marinum: Tuberculin skin testing, treatment and prevention: Clinical Infectious Disease. 37: 390-397.
6. Decostere, A., K. Hermans and F. Haesebrouck, 2004. Piscine mycobacteriosis: a literature review covering the agent and the disease it causes in fish and humans: Veterinary Microbiology, 99(3-4): 159-166.
7. Zanoni, R.G., D. Florio, M.L. Fioravanti, M. Rossi and M. Prearo, 2008. Occurrence of *Mycobacterium* spp. in ornamental fish in Italy: Journal of Fish Diseases, 31(6): 433-441.
8. Kibruyesfa, B., 2017. Fish Mycobacteriosis with Special Reference to Pathology, Diagnosis and Human Health: Overview. World Journal of Fish and Marine Sciences, 9(2): 09-16.
9. Nomakorinte, G., L.M. Anita and M.H. Tiny, 2018. Non-tuberculous Mycobacterium species causing mycobacteriosis in farmed aquatic animals of South Africa: Journal List Microbiology, 18: 18-32.
10. Diamant, A., A. Banet, M. Ucko, A. Colorni, W. Knibb and H. Kvitt, 2000. Mycobacteriosis in wild rabbitfish Siganus rivulatus associated with cage farming in the Gulf of Eilat, Red Sea: Diseases of Aquatic Organisms, 39(3): 211-219.
11. Kawakami, K. and R. Kusuda, 1990. Efficacy of rifampicin, streptomycin and erythromycin against experimental Mycobacterium infection in cultured yellowtail: Nippon Suisan Gakkaishi Bulletin of the Japanese Society of Scientific Fisheries, 56(1): 51-53.
12. Chinabut, S., 1999. Mycobacteriosis and nocardiosis: viral, Bacterial and Fungal Infections, pp: 319-340.
13. Astrofsky, K.M., M.D. Schrenzel, R.A. Bullis, R.M. Smolowitz and J.G. Fox, 2000. Diagnosis and management of atypical *Mycobacterium* spp. infections in established laboratory zebra fish (Brachydanio rerio) facilities: Comparative Medicine, 50(6): 666-672.
14. Enzensberger, R., K.P. Hunfeld, T. Elshorst-Schmidt, A. Böer and V. Brade, 2002. Disseminated cutaneous Mycobacterium marinum infection in a patient with non-Hodgkin's lymphoma Infection.

15. Nasr, E.B., A. Tavakoli, M. Salehi and M. Tazhibi, 2006. Detection of rifampin resistance patterns in Mycobacterium tuberculosis strains isolated in Iran by polymerase chain reaction single strand conformation polymorphism and direct sequencing methods: Memory Institute Oswaldo Cruz., 101: 597-602.
16. Devulder, G., M.P. De Montclos and J.P. Flandrois, 2005. A multigene approach to phylogenetic analysis using the genus Mycobacterium as a model: International Journal of Systematic and Evolutionary Microbiology, 55(1): 293-302.
17. Bland, C.S., J.M. Ireland, E. Lozano, M.E. Alvarez and T.P. Primm, 2005. Mycobacterial ecology of the Rio Grande: Applied and Environmental Microbiology, 71(10): 5719-5727.
18. Colorni, A., R. Avtalion, W. Knibb, E. Berger, B. Colorni and B.Timan, 1998. Histopathology of sea bass (*Dicentrarchus labrax*) experimentally infected with Mycobacterium marinum and treated with streptomycin and garlic (*Allium sativum*) extract: Aquaculture, 160(1-2): 1-17.
19. Kent, M.L., C.M. Whipps, J.L. Matthews, D. Florio, V. Watral, J.K. Bishop-Stewart, M. Poort and L. Bermudez, 2004. Mycobacteriosis in zebrafish (*Danio rerio*) research facilities: Comparative Biochemistry and Physiology Part C: Toxicology and Pharmacology, 138(3): 383-390.
20. Griffith, D.E., T. Aksamit, B.A. Brown-Elliott, A. Catanzaro, C. Daley, F. Gordin, S.M. Holland, R. Horsburgh, G. Huitt, M.F. Iademarco and M. Iseman, 2007. An official ATS/IDSA statement: diagnosis, treatment and prevention of nontuberculous mycobacterial diseases: American Journal of Respiratory and Critical Care Medicine, 175(4): 367-416.
21. Noga, E.J., 2010. Mycobacteriosis in Fish Disease: Diagnosis and Treatment, pp: 204-208. John Wiley & Sons, Oxford.
22. Lucas, S.B., 1989. Mycobacteria and the tissues of man: In Clinical Aspects of Mycobacterial Disease, pp: 107-176. Academic Press, London.
23. Ruth Francis-Floyd., 2011. Mycobacterial Infections of Fish: SRAC Publication. No. 4706.
24. Teska, J.D., L.E. Twerdok, J. Beaman, M. Curry and R.A. Finch, 1997. Isolation of Mycobacterium abscessus from Japanese medaka: Journal of Aquatic Animal Health, 9(3): 234-238.
25. Lescenko, P., L. Matlova, L. Dvorska, M. Bartos, O. Vavra, S. Navratil, L. Novotny and I. Pavlik, 2003. Mycobacterial infection in aquarium fish. Veterinarni Medicina, 48(3): 71-78.
26. Pate, M., V. Jencic, M.Zolnir-Dovc and M. Ocepek, 2005. Detection of mycobacteria in aquarium fish in Slovenia by culture and molecular methods: Diseases of Aquatic Organisms, 64(1): 29-35.
27. Backman, S., H.W. Ferguson, J.F. Prescott and B.P. Wilcock, 1990. Progressive panophthalmitis in chinook salmon, Oncorhynchus tshawytscha (Walbaum): a case report; Journal of Fish Diseases, 13(5): 345-353.
28. Lansdell, W., B. Dixon, N. Smith and L. Benjamin, 1993. Communications isolation of several mycobacterium species from fish: Journal of Aquatic Animal Health, 5(1): 73-76.
29. Rhodes, M.W., H. Kator, I. Kaattari, D. Gauthier, W. Vogelbein and C.A. Ottinger, 2004. Isolation and characterization of mycobacteria from striped bass Morone saxatilis from the Chesapeake Bay: Diseases of Aquatic Organisms, 61(1-2).
30. Stoskopf, M.K., 1993. Bacterial diseases of freshwater tropical fishes: Fish Medicine, pp: 882.
31. Frerichs, G.N., 1993. Mycobacteriosis: nocardiosis: Bacterial Diseases of Fish, 1: 219-233.
32. Noga, E.J., J.F. Wright and L. Pasarell, 1990. Some unusual features of mycobacteriosis in the cichlid fish Oreochromis mossambicus. Journal of Comparative Pathology, 102(3): 335-344.
33. Whipps, C.M., J.L. Matthews and M.L. Kent, 2008. Distribution and genetic characterization of Mycobacterium chelonae in laboratory zebrafish Danio rerio: Diseases of Aquatic Organisms, 82(1): 45.
34. Stamm, L.M. and E.J. Brown, 2004. Mycobacterium marinum: the generalization and specialization of a pathogenic mycobacterium: Microbes and Infection, 6(15): 1418-1428.
35. Bhatty, M.A., D.P. Turner and S.T. Chamberlain, 2000. Mycobacterium marinum hand infection: case reports and review of literature. British Journal of Plastic Surgery, 53(2): 161-165.
36. Bowser, P.R., 1999. Diseases of fish: Cornell University, Ithaca, New York, pp: 18-25.
37. Broussard, G.W. and D.G. Ennis, 2007. Mycobacterium marinum produces long-term chronic infections in medaka: a new animal model for studying human tuberculosis. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 145(1): 45-54.
38. Hurst, L.C., P.C. Amadio, M.A. Badalamente, J.L. Ellstein and R.J. Dattwyler, 1987. Mycobacterium marinum infections of the hand. The Journal of Hand Surgery, 12(3): 428-435.

39. Richardson, A., 1971. The experimental production of mastitis in sheep by Mycobacterium smegmatis and Mycobacterium fortuitum: The Cornell Veterinarian, 61(4): 640-646.
40. Fox, L.E., G.A. Kunkle, B.L. Homer, C. Manella and J.P. Thompson, 1995. Disseminated subcutaneous Mycobacterium fortuitum infection in a dog: Journal of the American Veterinary Medical Association, 206(1): 53-55.
41. Wilkinson, G.T., W. Kelly and D.e.n.i.s.e. O'boyle, 1978. Cutaneous granulomas associated with Mycobacterium fortuitum infection in a cat: Journal of Small Animal Practice, 19(1-12): 357-362.
42. Bruno, D.W., J. Griffiths, C.G. Mitchell, B.P. Wood, Z.J. Fletcher, F.A. Drobniewski and T.S. Hastings, 1998. Pathology attributed to Mycobacterium chelonae infection among farmed and laboratory-infected Atlantic salmon Salmo salar: Diseases of Aquatic Organisms, 33(2): 101-109.
43. Heckert, R.A., S. Elankumaran, A. Milani and A. Baya, 2001. Detection of a new Mycobacterium species in wild striped bass in the Chesapeake bay: Journal of Clinical Microbiology, 39(2): 710-715.
44. Herbst, L.H., S.F. Costa, L.M. Weiss, L.K. Johnson, J. Bartell, R.Davis, M. Walsh and M. Levi, 2001. Granulomatous Skin Lesions in Moray Eels Caused by a Novel Mycobacterium Species Related to mycobacterium triplex: Infection and Immunity, 69(7): 4639-4646.
45. Durborow, R.M., 1999. Health and safety concerns in fisheries and aquaculture: Occupational medicine (Philadelphia, Pa.), 14(2): 373-406.
46. Barker, L.P., K.M. George, S. Falkow and P.L. Small, 1997. Differential trafficking of live and dead Mycobacterium marinum organisms in macrophages: Infection and Immunity, 65(4): 1497-1504.
47. Sturgill-Koszycki, S., P.H. Schlesinger, P. Chakraborty, P.L. Haddix, H.L.Collins, A.K. Fok, R.D. Allen, S.L. Gluck, J.Heuser and D.G. Russell, 1994. Lack of acidification in Mycobacterium phagosomes produced by exclusion of the vesicular proton-ATPase: Science, 263(5147): 678-681.
48. Noga, E.J., 2000. The clinical work-up 10-29. Fish Disease Diagnosis and Treatment.
49. Marzouk, M.S.M., M.A. Essa, F.R. El-Seedy, A.M. Kenawy and D.M.A. El-Gawad, 2009. Epizootiological and histopathological studies on mycobacteriosis in some ornamental fishes: Global Veterinaria, 3(2): 137-143.
50. Harriff, M.J., L.E. Bermudez and M.L. Kent, 2007. Experimental exposure of zebrafish, Danio rerio (Hamilton), to Mycobacterium marinum and Mycobacterium peregrinum reveals the gastrointestinal tract as the primary route of infection: a potential model for environmental mycobacterial infection: Journal of Fish Diseases, 30(10): 587-600.
51. Gauthier, D.T., M.W. Rhodes, W.K. Vogelbein, H. Kator and C.A. Ottinger, 2003. Experimental mycobacteriosis in striped bass (*Morone saxatilis*): Diseases of Aquatic Organisms, 54(2).
52. Sanders, G.E. and L.E. Swaim, 2001. Atypical piscine mycobacteriosis in Japanese medaka (*Oryzias latipes*): Comparative Medicine, 51(2): 171-175.
53. Puttinaowarat, S., 1995. Detection of Mycobacterium spp. in culture by enzymelinked immunosorbent assay (ELISA) and polymerase chain reaction (PCR): Unpublished MSc. dissertation, University of Stirling, Stirling, UK.
54. Hedrick, R.P., T.McDowell and J. Groff, 1987. Mycobacteriosis in cultured striped bass from California: J. Wildlife Diseases, 23(3): 391-395.
55. Chang, C.T. and C.M. Whipps, 2015. Activity of antibiotics against Mycobacterium species commonly found in laboratory zebrafish: Journal of Aquatic Animal Health, 27(2): 88-95.
56. Haenen, O.L., J.J. Evans and F. Berthe, 2013. Bacterial infections from aquatic species: potential for and prevention of contact zoonoses: Revue scientifique et technique (International Office of Epizootics), 32(2): 497-507.
57. Austin, B. and D.A. Austin, 2012. Mycobacteriaceae representatives in bacterial fish Pathogens: Disease of farmed and wild fish, 5th ed. 89-99. Springer. Dordrecht. Netherlands.
58. Wallace Jr, R.J., V. Silcox and B.A. Brown, 1994. Taxonomy of rapidly growing mycobacteria: Clinical Infectious Diseases, 18(1): 121-122.
59. Edelstein, H., 1994. Mycobacterium marinum skin infections: Arch Intern Med., 154: 1359-1364.
60. Coney, P.M. and S. Thrush, 2007. Cutaneous Mycobacterium fortuitum complicating breast reconstruction: Journal of Plastic, Reconstructive & Aesthetic Surgery, 60(10): 1162-1163.
61. Nguyen, C., 2004. Mycobacterium marinum: New England Journal of Medicine, 350(9): e8.

62. Jacobs, J.M., A. Lazur and A. Baya, 2004. Prevention and Disinfection of *Mycobacterium* sp. in Aquaculture: Maryland Sea Grant Extension Finfish Worksheet, pp: 9.
63. Shoemaker, C.A., 2009. Overview of zoonotic infections from fish and shellfish: In Program, abstracts and report of European Association of Fish Pathologists (EAFP). Workshop. Proc. EAFP International Conference, 14-19 September, Prague Czech Republic, pp: 6.
64. Conroy, G. and D.A. Conroy, 1999. Acid-fast bacterial infection and its control in guppies (Lebistes reticulatus) reared on an ornamental fish farm in Venezuela: The Veterinary Record, 144(7): 177-178.
65. Mainous, M.E. and S.A. Smith, 2005. Efficacy of common disinfectants against Mycobacterium marinum: Journal of Aquatic Animal Health, 17(3): 284-288.
66. Muktar, Y., S. Tesfaye and B. Tesfaye, 2016. Present status and future prospects of fish vaccination: a review. Journal Veterinary Science Technology, 2: 299.
67. Yanong, R.P., E.W. Curtis, S.P. Terrell and G. Case, 2003. Atypical presentation of mycobacteriosis in a collection of frogfish (Antennarius striatus): Journal of Zoo and Wildlife Medicine, 34(4): 400-407.
68. Petrini, B., 2006. Mycobacterium marinum: ubiquitous agent of waterborne granulomatous skin infections. European Journal of Clinical Microbiology and Infectious Diseases, 25(10): 609-613.
69. Levi, M.H., J. Bartell, L. Gandolfo, S.C. Smole, S.F. Costa, L.M. Weiss, L.K. Johnson, G. Osterhout and L.H. Herbst, 2003. Characterization of *Mycobacterium montefiorense* sp. nov., a novel pathogenic Mycobacterium from moray eels that is related to Mycobacterium triplex: Journal of Clinical Microbiology, 41(5): 2147-2152.
70. Antonio, D.B., J.J. Swanson, R.C. Cech, S. Mager, R.P. Doroshov and Hedric 2000. Prevalence of Mycobacterium in wild and captive delta smelt: California Fish Game, 86: 233-243.
71. Seiberras, S., D. Jarnier, S. Guez and C. Series, 2000. Mycobacterium marinum nodular lymphangitis: Presse Medicale, 29(38): 2094-2095.
72. Evans, J.J., O. Haenen and F. Berthe, 2009. Overview of zoonotic infections from fish and shellfish: European Association of Fish Pathologists, pp: 14-19.
73. Aubry, A., O. Chosidow, E. Caumes, J. Robert and E. Cambau, 2002. Sixty-three cases of Mycobacterium marinum infection: clinical features, treatment and antibiotic susceptibility of causative isolates: Archives of Internal Medicine, 162(15): 1746-1752.
74. Casal, D. and M. Casal, 2001. Multicenter study of incidence of Mycobacterium marinum in humans in Spain: The International Journal of Tuberculosis and Lung Disease, 5(2): 197-199.
75. Ucko, M. and A. Colorni, 2005. Mycobacterium marinum infections in fish and humans in Israel: Journal of Clinical Microbiology, 43(2): 892-895.
76. Tsai, H., S.S. Lee, S. Wann, Y. Chen, Y. Liu and Y. Liu, 2006. Mycobacterium marinum tenosynovitis: three case reports and review of the literature. Japanese Journal of Infectious Diseases, 59(5): 337.
77. Kiel, R.J., 2018. Mycobacterium marinum. (Accessed 17 April 2018). Htm. Http: //www. Emedicine. Com/med/topic1538.
78. Stamm, L.M., J.H. Morisaki, L.Y. Gao, R.L. Jeng, K.L. McDonald, R. Roth, S. Takeshita, J. Heuser, M.D. Welch and E.J. Brown, 2003. Mycobacterium marinum escapes from phagosomes and is propelled by actin-based motility: Journal of Experimental Medicine, 198(9): 1361-1368.
79. Bartralot, R., V. García-Patos, D. Sitjas, L. Rodríguez-Cano, J. Mollet, N. Martín-Casabona, P. Coll, A. Castells and R.M. Pujol, 2005. Clinical patterns of cutaneous nontuberculous mycobacterial infections: British Journal of Dermatology, 152(4): 727-734.
80. Talaat, A.M., M. Trucksis, A.S. Kane and R. Reimschuessel, 1999. Pathogenicity of Mycobacterium fortuitum and Mycobacterium smegmatis to goldfish, Carassius auratus: Veterinary Microbiology, 66(2): 151-164.
81. Datta, D., P. Khatri, A. Singh, D.R. Saha, G. Verma, R. Raman and S. Mazumder, 2018. Mycobacterium fortuitum-induced ER-Mitochondrial calcium dynamics promotes calpain/caspase-12/caspase-9 mediated apoptosis in fish macrophages: Cell Death Discovery, 4(1): 30.
82. Fowler, S.J., J. French, N.J. Screaton, J. Foweraker, A. Condliffe, C.S. Haworth, A.R. Exley and D. Bilton, 2006. Nontuberculous mycobacteria in bronchiectasis: prevalence and patient characteristics: European Respiratory Journal, 28(6): 1204-1210.

83. Daley, C.L. and D.E. Griffith, 2002. Pulmonary disease caused by rapidly growing mycobacteria: Clinics in Chest Medicine, 23(3): 623-632.
84. Baron, O., H. Mussaffi, M. Mei-Zahav, D. Prais, G. Steuer, P. Stafler, S. Hananya and H. Blau, 2014. Increasing nontuberculous mycobacteria infection in cystic fibrosis: Journal of Cystic Fibrosis, 14(1): 53-62.
85. Talaat, A.M., R. Reimschuessel, S.S. Wasserman and M. Trucksis, 1998. Goldfish, Carassius auratus, a Novel Animal Model for the Study of Mycobacterium marinum Pathogenesis: Infection and Immunity, 66(6): 2938-2942.
86. Marchiori, E., G. Zanetti, C.M. Mano and B. Hochhegger, 2011. Exogenous lipoid pneumonia. Clinical and radiological manifestations: Respiratory Medicine, 105(5): 659-666.
87. Hunter, R.L., M. Olsen, C. Jagannath and J.K. Actor, 2006. Trehalose 6, 6'-dimycolate and lipid in the pathogenesis of caseating granulomas of tuberculosis in mice: the American Journal of Pathology, 168(4): 1249-1261.
88. Cooke, F.J. and J.S. Friedland, 1998. Spontaneous breast abscess due to Mycobacterium fortuitum: Clinical Infectious Diseases, 26(3): 760-761.
89. Park, S., G.Y. Suh, M.P. Chung, H. Kim, O.J. Kwon, K.S. Lee, N.Y. Lee and W.J. Koh, 2008. Clinical significance of Mycobacterium fortuitum isolated from respiratory specimens: Respiratory Medicine, 102(3): 437-442.