Fish Tank Exposure and Cutaneous Infections Due to *Mycobacterium marinum*: Tuberculin Skin Testing, Treatment, and Prevention

Felicia M. T. Lewis, Bryan J. Marsh, and C. Fordham von Reyn
Infectious Disease Section, Department of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire

In the present study, 8 patients with soft tissue infection due to *Mycobacterium marinum* are described, and contemporary data on treatment are reviewed. Six patients had positive cultures, all patients had cutaneous exposure to fish tanks, 7 had sporotrichoid lesions, and 2 had deep infection. All 7 tested patients had tuberculin skin test reactions ≥10 mm. Six patients with disease limited to the skin were successfully treated with 2-drug combination therapy, including clarithromycin, ethambutol, and rifampin. Optimal treatment should include 2 drugs for 1–2 months after resolution of lesions, typically 3–4 months in total. Deeper infections may require more prolonged treatment and surgical debridement. Positive tuberculin reactions may be due to infection with *M. marinum*. Persons with open skin lesions or immunosuppression should avoid cutaneous contact with fish tanks.

*Mycobacterium marinum* is a slow-growing environmental mycobacterium that was first isolated from dead fish in a Philadelphia aquarium in 1926 [1] and was identified as a human pathogen in 1951 after isolation from granulomatous skin lesions in patients from Sweden. *M. marinum* is distributed widely in aquatic environments [2], especially in relatively still or stagnant water, such as in fish tanks and swimming pools, and in naturally occurring bodies of water [3, 4]. Infection is acquired by direct inoculation with the bacterium through broken skin in an aquatic environment. Adequate chlorination has drastically reduced the number of cases acquired from swimming pools, and recent reports emphasize acquisition from fish tanks but do not offer recommendations for prevention [3, 5–10].

Although more potent antimicrobials are now available for the treatment of *M. marinum* infection, only limited numbers of cases are available on which to analyze the effects of newer antimicrobials on the outcome of treatment. Large series typically include reviews of cases treated by numerous providers, rather than cases treated by the authors. In addition, although recent studies have emphasized the influence of asymptomatic infection with environmental nontuberculous mycobacteria (NTM), such as *Mycobacterium avium* complex (MAC), on the tuberculin skin test [11], detailed data have not been presented on the effect of symptomatic infections with NTM, such as *M. marinum*, on the tuberculin skin test. We present our personal experience with 8 cases of soft-tissue infection due to *M. marinum* and emphasize the mode of acquisition and implications for prevention, the effect on tuberculin skin testing, and responses to combination antibiotic therapy, including macrolides. We also review other recent studies on treatment to provide recommendations for current management of infections due to *M. marinum*.

**METHODS**

Medical records at the Dartmouth-Hitchcock Medical Center and records of skin test studies from the Infectious Diseases Section, Department of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, were reviewed for cases of infection due to *M. marinum*.
tious Disease Section were reviewed from May 1990 to 2000 to identify patients with a diagnosis of skin or soft tissue infection due to *M. marinum*. Data then were abstracted from patient records and reports of laboratory tests. All case patients were seen by one of the authors. Case patients were accepted for inclusion if culture of a cutaneous lesion was positive for *M. marinum* or if a patient without a culture performed had a characteristic chronic cutaneous lesion with sporotrichoid spread and a plausible aquatic exposure history. The literature on treatment of *M. marinum* was reviewed by use of MEDLINE for the period 1966–2002 using the following keywords: “*M. marinum*,” “fish tank granuloma,” “swimming pool granuloma,” and “aquarium granuloma.”

Intradermal skin tests were approved by the Dartmouth Committee for the Protection of Human Subjects and were performed with 0.1 mL *M. avium* sensitin (MAS; 10/2; State Serum Institute) and 0.1 mL (5 TU) *Mycobacterium tuberculosis* PPD (Connaught Laboratories). Skin tests were performed at the time that patients were seen by one of the authors. Tests were administered intradermally by use of the Mantoux technique and were read by trained personnel 48–72 h after placement, as described elsewhere [11]. Cultures for *M. marinum* were performed by use of both solid medium (Middlebrook 7H11; Lowenstein-Jensen) and broth medium (Middlebrook 7H9; MB/BacT) at both 30°C and 35°C when a sufficient sample was available.

**RESULTS**

**Clinical features.** Clinical features of the 8 patients are summarized in table 1. Four cases occurred in men and 4 in women (age range, 25–59 years; mean age, 45 years). All patients reported cutaneous contact with fish tanks at home or work before the onset of infection. In 1 instructive case (patient 2), a nurse working on a medical ward cleaned a fish tank on several occasions while she had an open lesion on her finger from a recent wart removal. Cultures were positive for *M. marinum* for all 6 patients who had cultures performed. One patient (patient 7) was diagnosed on the basis of a positive acid-fast bacillus (AFB) stain and typical clinical features. One patient (patient 8) was diagnosed on the basis of a typical cutaneous lesion with sporotrichoid spread and fish tank exposure. Overall, AFB stains were positive in 3 patients, and biopsy specimens showed granuloma formation in 6 patients.

Infections began on the finger or hand in all 8 patients, and, in 6 patients, remained confined to the skin. Deep tissue infection developed in 2 patients. Patient 5 had sporotrichoid spread (figure 1) and extensive deep infection, including osteomyelitis. Patient 7 developed tenosynovitis of the right index finger. Six patients (75%) demonstrated sporotrichoid spread with secondary nodules along proximal lymphatic channels. Three patients had significant underlying medical conditions, including both patients with deep infection extending to a site beyond the skin. Patient 5 who had extensive deep disease had psoriasis and was receiving treatment with prednisone. Patient 6 who had cutaneous disease had rheumatoid arthritis and was receiving treatment with plaquenil and non-steroidal anti-inflammatory agents. Patient 7 who had tenosynovitis had type II diabetes mellitus. Chest radiograph findings were negative for all 4 patients who had x-rays performed in this study (patients 1 and 5–7). Human immunodeficiency virus (HIV) risk factors were not noted in any patient, and HIV testing was not performed.

**Skin test results.** Seven patients had skin testing with PPD and MAS antigens. Of these 7 patients, all 7 (100%) had PPD reactions ≥10 mm in diameter, and 2 (29%) had reactions ≥15 mm in diameter. Three (50%) of 6 tested patients had MAS reactions ≥10 mm in diameter. Three patients had PPD and MAS reactions differing by ≤5 mm (nondominant), 2 had larger MAS reactions by ≥5 mm in size, and 1 had a PPD reaction that was greater by ≥5 mm. None of the patients were foreign born, and there was no known history of bacille Calmette-Guérin (BCG) immunization. Four patients had a history of a previous negative tuberculin skin test result, and 1 patient had a history of a previous positive tuberculin skin test result (patient 6).

**Treatment results.** Treatment regimens and outcomes are summarized in table 1. All 6 patients with cutaneous disease alone responded completely to antibiotic therapy with or without excisional biopsy. Four of these patients received therapy with clarithromycin and ethambutol for 3–6 months. Two received therapy with rifampin and ethambutol, one for 2 months and another for 14 months before resolution. Of the 2 patients who had extension of disease, patient 7 responded to 2 months treatment with of clarithromycin and ethambutol, and patient 5 with metastatic melanoma had not resolved after ~2 years of multiple excisions and a drug regimen that included clarithromycin, ethambutol, and rifabutin. For most patients, duration of therapy was typically 1–2 months after resolution of lesions.

**DISCUSSION**

The present study demonstrates that cutaneous exposure to fish tanks is the principal contemporary source of *M. marinum* infections in our inland area of the United States and is consistent with other recently published reports [6, 12]. Fish and shellfish injuries are responsible for a small proportion of cases in other studies, but acquisition from swimming pools is now unusual [6, 12, 13]. As demonstrated by patients 2 and 5 (who had psoriasis), fish tank–related infections may be related to immersion of an open cutaneous lesion. Despite the known
Table 1. Characteristics of 8 patients with *Mycobacterium marinum* infection.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age in years/sex</th>
<th>Type of exposure</th>
<th>Underlying disease or condition</th>
<th>Skin test reaction diameter, mm</th>
<th>AFB stain/culture</th>
<th>Infection type</th>
<th>Pathologic findings</th>
<th>Treatment regimen (duration)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25/M</td>
<td>Fish tank</td>
<td>None</td>
<td>ND</td>
<td>ND</td>
<td>+/+</td>
<td>Cutaneous, sporotrichoid</td>
<td>Mild acute inflammation</td>
<td>Rifampin and ethambutol (2 months); excisional biopsy</td>
</tr>
<tr>
<td>2</td>
<td>38/F</td>
<td>Fish tank</td>
<td>None</td>
<td>20</td>
<td>20</td>
<td>−/+</td>
<td>Cutaneous, sporotrichoid</td>
<td>Granuloma</td>
<td>Clarithromycin and ethambutol (4 months)</td>
</tr>
<tr>
<td>3</td>
<td>40/M</td>
<td>Fish tank</td>
<td>None</td>
<td>11</td>
<td>13</td>
<td>−/+</td>
<td>Cutaneous, sporotrichoid</td>
<td>Granuloma</td>
<td>Clarithromycin and ethambutol (3 months)</td>
</tr>
<tr>
<td>4</td>
<td>57/M</td>
<td>Fish tank</td>
<td>None</td>
<td>20</td>
<td>0</td>
<td>−/+</td>
<td>Cutaneous, sporotrichoid</td>
<td>Early histiocytic infiltrate</td>
<td>Clarithromycin and ethambutol (6 months)</td>
</tr>
<tr>
<td>5</td>
<td>55/M</td>
<td>Fish tank, Psoriasis, melanoma, prednisone therapy</td>
<td>None</td>
<td>11</td>
<td>9</td>
<td>−/+</td>
<td>Osteomyelitis, sporotrichoid</td>
<td>Granuloma</td>
<td>Ciprofloxacin, rifampin, ethambutol, clarithromycin, rifabutin, and amikacin; excision of nodules</td>
</tr>
<tr>
<td>6</td>
<td>36/F</td>
<td>Fish tank, Rheumatoid arthritis, hydroxychloroquine therapy</td>
<td>None</td>
<td>13</td>
<td>18</td>
<td>+/+</td>
<td>Cutaneous</td>
<td>Granuloma</td>
<td>Ethambutol and rifampin (14 months)</td>
</tr>
<tr>
<td>7</td>
<td>50/F</td>
<td>Fish tank</td>
<td>Diabetes mellitus</td>
<td>14</td>
<td>0</td>
<td>+/ND</td>
<td>Tendonitis, sporotrichoid</td>
<td>Granuloma</td>
<td>Clarithromycin and ethambutol (2 months); tenosynovectomy</td>
</tr>
<tr>
<td>8</td>
<td>59/F</td>
<td>Fish tank</td>
<td>None</td>
<td>13</td>
<td>ND</td>
<td>ND</td>
<td>Cutaneous, sporotrichoid</td>
<td>ND</td>
<td>Clarithromycin and ethambutol (6 months)</td>
</tr>
</tbody>
</table>

**NOTE.** AFB, acid-fast bacillus; MAS, *Mycobacterium avium* sensitin; ND, not done; +, positive; −, negative.
association of fish tanks with *M. marinum* infections our informal review of national aquarium supply stores indicates that instructions for home fish tanks do not typically recommend avoidance of water contact or the use of waterproof gloves for persons with open skin lesions.

*M. marinum* should be suspected when a characteristic skin lesion occurs 8–30 days (median, 21 days; 30 days in 35% of cases) after fish tank exposure [6]. Primary lesions typically present as a bluish-red papule, nodule, or plaque with a verrucous surface, most often at the site of a small abrasion or cut on the dominant hand [14, 15]. As in the present study, most patients have a sportotrichoid presentation on the upper extremity [15]. Lesions may have purulent drainage, and satellite lesions may appear and coalesce. Lesions are painful in fewer than one-half of cases [16], lymphadenopathy is rare and typically mild [3, 17], and systemic symptoms are distinctly unusual [18]. Infection is usually confined to the skin, because of preferential growth of *M. marinum* at temperatures <37°C.
However, as demonstrated here, deeper extension of infection may lead to tenosynovitis, arthritis, bursitis, and osteomyelitis [20–24]. Disseminated infection is rare and almost always occurs in immunosuppressed individuals [18, 25, 26].

Our experience demonstrates that infection with these organisms also is associated with sufficient tuberculin skin test reactivity to trigger consideration of treatment for latent tuberculosis. This issue has not been emphasized in recent studies. Jolly and Seabury [27] reported tuberculin reactions ≥10 mm in diameter in 14 (67%) M. marinum–infected patients tested with PPD-S, and Mollohan and Romer [7] reported positive reactions to the relatively nonspecific Vollmer patch test in 55 (77%) of 71 patients. In our study, all tested patients had tuberculin reactions ≥10 mm in diameter (some would be candidates for treatment of latent tuberculosis if they were in defined risk groups), and 2 had reactions ≥15 mm in diameter (both would be candidates for treatment of latent tuberculosis) [28]. Although one-half our patients did not have preinfection skin tests to prove unequivocally that their reactions were due to M. marinum, most healthy adults living in the United States have negative reactions to tuberculin [11], and infection with various NTMs often results in tuberculin reactivity [29]. Evaluation for tuberculosis always should be performed in those with positive tuberculin skin test results, and treatment should be provided on the basis of current guidelines [28]. However, positive tuberculin reactions in patients with M. marinum infection can be attributed to this infection and should not always be considered an indication for treatment of latent tuberculosis. The cross-reactions that we observed to tuberculin in patients with M. marinum infection were larger than tuberculin cross-reactions that we have observed in patients with MAC disease. This is consistent with genetic studies showing that M. marinum is closely related to M. tuberculosis [30].

Reactions ≥10 mm to the MAS skin test were observed in 3 (60%) of 5 patients. This is higher than the 30%–40% rate of MAS reactions expected in a general US population [11], but lower than the rate of positive PPD reactions in patients with M. marinum infection. This is consistent with the greater genetic difference between MAC and M. marinum. In the study by Jolly and Seabury [27], which used a different M. avium antigen, 14 (67%) of 21 patients had reactions ≥10 mm in diameter. In their study and the present study, most dual skin test reactions with these 2 antigens were nondominant (i.e., neither the PPD nor the MAS antigen produced a consistently larger reaction than the other). Distinction between infection with M. tuberculosis and M. marinum with a single tuberculin skin test, dual skin tests with tuberculin and an NTM antigen, or newer in vitro assays of IFN-γ production may not be possible [31].

There have been no controlled trials that compare treatment regimens for M. marinum infection, only case reports and case series. Recent treatment reports that include >10 patients are summarized in table 2. Combination therapy, typically with 2 drugs, as reported in several small series, appears to have a low failure rate in superficial infection and is generally recommended [2, 6, 32–37]. A review of 44 cases concluded that combination therapy with ethambutol and rifampin might be highly effective, on the basis of successful outcomes for 8 of 9 patients treated with this regimen [38]. Combination therapy, most commonly with clarithromycin plus rifampin, was used for 40 of 63 patients from France who were treated for an average of 3.5 months during 1996–1998 [12]. Surgical debridement or excision was required for 30 (48%) patients. Deep infection was present in 18 (29%) patients and was found to be the principal determinant of outcome. Infection resolved in 42 (93%) of 45 patients with localized infection versus 13 (72%) of 18 with deep structure infection. Monotherapy failed more often in deep than in cutaneous infections. Failure of clarithromycin-containing regimens was reported in only 2 (10%) of 20 patients with infection limited to the skin [12]. Success with azithromycin in combination with ethambutol and minocycline has been reported for the treatment of skin and soft tissue infection in 1 lung transplant recipient [39].

We believe that clarithromycin is the optimal first agent in combination treatment of M. marinum. Experience in the treatment of other NTMs suggests that azithromycin might be a reasonable alternative. Published series and our experience support ethambutol as a reasonable second agent, whereas in vitro studies and published clinical series suggest that rifampin also would be appropriate. There is not enough clinical experience from the treatment of infection with either M. marinum or other NTMs with any of the other agents that have demonstrated activity in vitro to judge their potential efficacy as second agents. Even if the organism is deemed susceptible to an antibiotic, we believe that monotherapy should be avoided because of the unreliability of susceptibility testing for this organism and the possibility of emerging resistance.

Published studies and our experience suggest that optimal combination therapy would therefore be clarithromycin and either rifampin or ethambutol. In a patient who cannot tolerate clarithromycin, the combination of rifampin and ethambutol may be considered, although our experience with patient 6 demonstrates that response to this regimen may sometimes be delayed. The optimal duration of therapy is not known, and results of published studies have been highly variable. The drugs recommended for treatment do not have prominent dose-related or time-dependent side effects. Thus, a reasonable approach is to treat with 2 agents for 1–2 months after the resolution of all lesions (typically 3–4 months in total) [35, 36]. Susceptibility testing is not routinely recommended and should be reserved for cases of treatment failure.

As evidenced by patient 5, treatment of deep or extensive
Table 2. Published studies on treatment of *Mycobacterium marinum* soft tissue infection.

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of patients</th>
<th>Duration</th>
<th>Specific therapy, no. of patients (% cured)</th>
<th>No. of patients</th>
<th>Duration</th>
<th>Specific therapy, no. of patients (% cured)</th>
<th>Surgery performed, no. of patients (% cured)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>[12]</td>
<td>66 (18)</td>
<td>Median, 3.5 months</td>
<td>Minocycline, 19 (NA); clarithromycin, 4 (NA)</td>
<td>40</td>
<td>Median, 3.5 months</td>
<td>Clarithromycin + rifampin, 20 (NA); cycline + clarithromycin, 11 (NA)</td>
<td>30 (NA)</td>
<td>Resolution in 55 (87%) of 66 overall but only 13 (72%) of 18 with deep infection</td>
</tr>
<tr>
<td>[13]</td>
<td>39 (NA)</td>
<td>NA</td>
<td>Minocycline 12 (NA); rifampin, 4 (NA)</td>
<td>7</td>
<td>NA</td>
<td>Clarithromycin + ethambutol, 7 (NA)</td>
<td>NA</td>
<td>Resolution within 2–4 months of treatment in most patients</td>
</tr>
<tr>
<td>[37]</td>
<td>38 (NA)</td>
<td>Mean, 15 weeks</td>
<td>TMP-SMZ, 19 (93); minocycline, 3 (100)</td>
<td>12</td>
<td>Mean, 15 weeks</td>
<td>TMP-SMZ + minocycline, 5 (100)</td>
<td>1 (100)</td>
<td>Of patients with adequate follow up, none worsened after treatment; only 2 failed to improve</td>
</tr>
<tr>
<td>[35]</td>
<td>31 (0)</td>
<td>Mean, 4 months</td>
<td>Minocycline, 14 (71); doxycycline, 3 (67); tetracycline, 1 (100); TMP-SMZ, 1 (100)</td>
<td>8</td>
<td>Mean, 5 months</td>
<td>Ethambutol + rifampin, 5 (100); other, 3 (100)</td>
<td>1 (NA)</td>
<td>Relapse in 2 patients after 4 months of minocycline; recommend treatment for 2 months after resolution for minimum of 6 months</td>
</tr>
<tr>
<td>[41]</td>
<td>12 (6)</td>
<td>Mean, 8 months</td>
<td>Doxycycline, 4–5 (100); TMP-SMZ, 2 (100); rifampin, 1 (100)</td>
<td>5–6</td>
<td>Mean, 8 months</td>
<td>Rifampin + ethambutol, 3–4 (100); rifampin, ethambutol, and ciprofloxacin, 1 (100)</td>
<td>12 (100)</td>
<td>Surgical series: resolution in all patients with long-term antibiotic therapy and debridement</td>
</tr>
</tbody>
</table>

**NOTE.** Includes studies with minimum of 10 patients published since 1966, not including case series from literature surveys. NA, not available; TMP-SMZ, trimethoprim-sulfamethoxazole.
disease, especially in an immunocompromised patient, can be challenging. Rifampin may be a preferred second or third agent in bone or joint infection, where this drug has been shown to improve outcome with infections due to other susceptible organisms [40]. It is possible that patients with disseminated infection or extensive deep infection, and the potential for a large burden of organisms, may benefit from treatment with 3 active agents, at least until clinical and microbiological response has been documented. Treatment of deep infection, especially in the immunocompromised host, typically requires surgical debridement. Multicenter controlled trials are needed to define the optimal regimen and duration of treatment for both superficial and deep infection.

In summary, fish-tank exposure is the source of most cases of cutaneous M. marinum infections and may be preventable through the use of waterproof gloves for persons with acute or chronic open skin lesions. Tuberculin skin test reactivity is common after infection with M. marinum and should not generally be attributed to tuberculosis. Treatment with a 2-drug regimen that includes a macrolide should be successful in most patients with disease limited to the skin.

Acknowledgments

We wish to thank Kaare Haslov (State Serum Institute, Copenhagen), for donation of M. avium sensiti skin tests, and Richard Waddell and Sue Tvaroha, for assistance with the study.

References