

Bacterial Soft Tissue Infections Following Water Exposure

Sara E. Lewis, DPM

Devin W. Collins, BA

Adam M. Bressler, MD

INTRODUCTION

Soft tissue infections following water exposure are relatively uncommon but can result in high morbidity and mortality. These infections can follow fresh, salt, and brackish water exposure and most commonly occur secondary to trauma. Although there are numerous microorganisms that can cause skin and soft tissue infections following water exposure, this article will focus on the 5 most common bacteria. The acronym used for these bacteria--AEEVM, refers to *Aeromonas* species, *Edwardsiella tarda*, *Erysipelothrix rhusiopathiae*, *Vibrio vulnificus*, and *Mycobacterium marinum*.

AEROMONAS

Aeromonas species are gram-negative rods found worldwide in fresh and brackish water (1-3). They have also been found in contaminated drinking, surface, and polluted water sources (3). *Aeromonas* are usually non-lactose fermenting, oxidase positive facultative anaerobes. There are 2 main groups, non-motile and motile. The motile group is made up of 8 species responsible for most human infections including *A. caviae*, *veronii* and *hydrophilia*, which account for greater than 85% (1,3).

Aeromonas species rarely cause infections in humans, but can be an especially serious threat to immunocompromised hosts. Reported risk factors include malignancy, liver cirrhosis, male sex, recent water exposure, and patients receiving medical leech therapy (2). Most reported infections occur in the warmer months in temperate climate regions.

Infections can lead to various clinical syndromes including diarrhea, soft tissue infections ranging from localized to myonecrosis, bacteremia, sepsis, and spontaneous peritonitis (1-3). While diarrhea is the most common clinical syndrome among patients exposed to *Aeromonas*, severe soft tissue infections and sepsis account for greater morbidity. If necrotizing fasciitis or myonecrosis occurs, surgical debridement is paramount to treatment. Mortality due to monomicrobial *Aeromonas* infection with sepsis has been reported to be up to 67% (2). In terms of antimicrobial susceptibility, *Aeromonas* is inherently resistant

to early generation penicillins and cephalosporins. Thus, standard treatments include fluoroquinolones (ciprofloxacin, levofloxacin), third and fourth generation cephalosporins (ceftazidime, cefepime), or potentially trimethoprim-sulfa (4). However, due to the potential of emerging resistance seen in *Aeromonas* species, susceptibilities should always be performed and antibiotics adjusted accordingly (3). It is important to maintain a high index of suspicion for *Aeromonas* infections after water exposure in fresh and brackish water and to start the patient on an appropriate empiric antibiotic regimen immediately.

EDWARDSIELLA TARDA

Edwardsiella tarda is part of the Enterobacteriaceae family. It is a motile, facultative anaerobic gram-negative rod that can be found worldwide in pond water, mud, and the intestines of marine life and land animals (5). Risk factors for infection include water exposure, exposure to animals, raw fish ingestion, liver disease, iron overload states such as hemochromatosis, and immunocompromised hosts. Infection can lead to gastroenteritis, wound infections ranging from cellulitis to necrotizing fasciitis and myonecrosis, bacteremia and sepsis, meningitis, cholecystitis, abscesses, and osteomyelitis (4,5). Bacterial sepsis has a reported mortality rate approaching 50% (4).

Human infections are uncommon and may present with a constellation of non-specific symptoms. In managing infections caused by *Edwardsiella tarda*, it is important to first assess the clinical spectrum. The most frequent manifestation involves the gastrointestinal system but wound infections with abscess formation have been described following trauma (4). In the setting of soft tissue infection, debridement of nonviable necrotic tissue is sometimes necessary. The presence of invasive, necrotic deep tissue infections should indicate a high suspicion of underlying immunocompromise. *Edwardsiella tarda* is generally susceptible to most common antibiotics. Successful treatments have included ampicillin, ciprofloxacin, trimethoprim-sulfamethoxazole, and chloramphenicol (4,5).

ERYSIPELOTHRIX RHUSIOPATHIAE

Erysipelothrix rhusiopathiae is a nonspore forming, non-motile, gram-positive bacillus that causes erysipeloid, an infection commonly found in fishermen (4,6). Infections caused by this organism occur worldwide, most often in the summer months, in people with close animal contact or contact with animal products or feces. The organism has been found among swine, ducks, marine mammals, fish, and humans (7). Generally, the bacteria enter through disrupted skin and, to date, there have been no reports of infection occurring without open wound exposure or traumatic inoculation (6,7). Human disease has been described in 3 forms, a localized cutaneous infection, a generalized cutaneous infection, or a bacteremia with associated endocarditis (7). It is often a self-limiting but may cause localized pain at the site of inoculation. Lesions are characterized by dark red to purple circular areas with distinct borders (7). Biopsy of the lesion can be diagnostic. Treatment, although not always necessary due to the self-limited nature, includes penicillin, cephalexin, or ciprofloxacin (4,6,7).

VIBRIO VULNIFICUS

Vibrio vulnificus is a gram-negative bacillus encountered worldwide in warm, marine aquatic environments. In the US, it is most commonly found in coastal areas such as the Gulf Coast and Chesapeake Bay (8). The infection rate in coastal environments is seasonal with a peak incidence associated with increased water temperatures during summer months (4,9).

The spectrum of disease varies from gastrointestinal infections to necrotizing skin infections to severe, life threatening sepsis (8). Classically, severe sepsis presents in an immunocompromised or cirrhotic patient following the consumption of raw oysters (8,9). Soft tissue infection rates have continued to rise over recent decades. The most commonly associated risk factor is liver disease (8). There is also an increased risk of infection in patients with elevated iron levels, but the causal relationship remains unknown. Three biotypes of *Vibrio vulnificus* have been described with biotype 1 being the most common. Biotypes 1 and 3 are associated with soft tissue infections with fatality rates ranging from 8% to greater than 50% (8). Soft tissue infections associated with *Vibrio* tend to present as hemorrhagic bullous skin lesions with underlying erythema that can rapidly progress to necrotic ulcers along with a severe septic presentation (4,8,9). Inoculation can occur from traumatic wound entry, pre-existing wounds, or hematogenous spread following ingestion in a compromised host (8,9). Symptoms tend to occur within 1 to 2 weeks following initial exposure. Rapid identification by culture is paramount to a successful outcome.

Management of soft tissue infections will vary depending on the extent of infection, but typically includes the use of antibiotics such as cephalosporins, carbapenems, tetracyclines, aminoglycosides, and fluoroquinolones, among others (4,8). Surgical debridement is reserved for severe infections to remove necrotic tissue. In addition, some studies suggest the use of hyperbaric oxygen therapy as an adjunctive (8). Preventative measures to avoid *Vibrio* infections include avoiding consuming raw oysters and cross contaminated seafood especially during warmer months, wearing protective equipment when handling raw shellfish and avoiding exposure of open wounds to contaminated water or raw shellfish.

MYCOBACTERIUM MARINUM

Mycobacterium marinum is a waterborne organism that most commonly affects fish and amphibians but rarely can infect humans. When infection does occur, it is characterized by localized granulomatous skin lesions, usually following trauma to an extremity (10-12). It is commonly found in fresh, salt, and brackish water worldwide and is highly prevalent in aquariums. Prior to chlorination of pools, this infection was more commonly encountered and often misdiagnosed (11).

Localized skin infections following contact with contaminated water are characterized by purulent superficial and/or deep lesions that are granulomatous in nature and may be ulcerated, nodular, or verrucous (11). Infection can involve bursa, tendons, and bone in severe cases (4,10). In immunocompromised patients, infections can disseminate rapidly. Diagnosis is achieved via biopsy of the lesions along with histopathology and culture. Special mycobacterial culture techniques at cooler temperatures enhance recovery (4). The tuberculin skin test may be positive in these patients due to cross reactivity (11). Treatment of these infections is not standardized but often includes antibiotic therapy for 3-4 months (10,11). Antimicrobial options include doxycycline, clarithromycin or rifampicin, and ethambutol (10-12). Of note, the use of steroids may delay the diagnosis and treatment, obscuring the clinical picture (11). Surgical debridement is dependent on the extent of the soft tissue infection and may be warranted for necrotic tissue.

In conclusion, soft tissue infections following water exposure can lead to severe localized and systemic disease that can be limb and life threatening. The most commonly encountered organisms include *Aeromonas* species, *Edwardsiella tarda*, *Erysipelothrix rhusiopathiae*, *Vibrio vulnificus*, and *Mycobacterium marinum*. As these infections are relatively rare, it is important to have a high index of suspicion and inquire about open wounds, traumatic skin injury, and water exposure. Immunocompromised patients are at particular risk and must be addressed promptly. A detailed

physical examination is also critical to document extent and progression of infection. While standard empiric antibiotic coverage may be needed as skin flora remains the most common inoculated bacteria following trauma, if one of the water pathogens is suspected additional targeted therapy is warranted. Appropriate options could include a third or fourth generation cephalosporin and/or a quinolone such as levofloxacin. Surgical debridement of the skin and soft tissue may be needed depending on the extent of necrotic tissue.

REFERENCES

1. Chuang HC, Yu-Huai H, Chorng-Jang L, Lih-Shinn W, Yeong-Shu T, Chen-Chi T. Different clinical characteristics among *Aeromonas Hydrophila*, *Aeromonas Veronii* Biovar *Sobria* and *Aeromonas Caviae* Monomicrobial Bacteremia. *J Korean Med Sci J Korean Med Sci* 2011;26:1415.
2. Ko WC, Lee HC, Chuang YC, Liu CC, Wu JJ. Clinical features and therapeutic implications of 104 episodes of monomicrobial *Aeromonas* Bacteraemia. *J Infect* 2000;40:267-73.
3. Parker JL, Shaw JG. *Aeromonas* spp. *Clinical Microbiology and Disease*. *J Infect* 2011;62:109-18.
4. Noonburg GE. Management of extremity trauma and related infections occurring in the aquatic environment. *J Am Acad Orthop Surg* 2005;13:243-53.
5. Slaven EM, Lopez FA, Hart SM, Sanders CV. Myonecrosis caused by *Edwardsiella*: a case report and case series of extraintestinal *E. tarda* infections. *Clin Infect Dis* 2001;32:1430-3.
6. Wang Q, Chang BJ, Riley TV. *Erysipelothrix rhusiopathiae*. *J Vet Microbiol* 2010;140:405-17.
7. Brooke CJ, Riley TV. *Erysipelothrix rhusiopathiae*: bacteriology, epidemiology and clinical manifestations of an occupational pathogen. *J Med Microbiol* 1999;48:789-99.
8. Horseman MA, Salim S. A comprehensive review of *Vibrio vulnificus*: an important cause of severe sepsis and skin and soft-tissue infection. *Int J Infect Dis* 2011;15:e157-66.
9. Huang KC, Weng HH, Yang TY, Chang TS, et al. "Distribution of fatal *Vibrio Vulnificus* necrotizing skin and soft-tissue infections: a systematic review and meta-analysis. *Medicine (Baltimore)* 2016;95:1-8.
10. Johnson MG, Stout JE. Twenty-eight cases of *Mycobacterium marinum* infection: retrospective case series and literature review. *Infection* 2015;43:655-62.
11. Petrini B. *Mycobacterium marinum*: ubiquitous agent of waterborne granulomatous skin infections. *Eur J Clin Microbiol Infect Dis* 2006;25:609-13.
12. Ang P, Rattana-Apiromyakit N, Goh CL. Retrospective study of *Mycobacterium marinum* skin infections. *Int J Dermatol* 2000;39:343-7.

JUBLIA[®]
(efinaconazole)
Topical Solution 10%

SMASH ONYCHOMYCOSIS*

★ AT THE SITE OF INFECTION! ★

*For the treatment of onychomycosis of the toenail(s) due to *Trichophyton rubrum* and *Trichophyton mentagrophytes*.



JUBLIA allows some patients to have clearer toenails grow back. Individual results may vary.

INDICATION

JUBLIA (efinaconazole) topical solution, 10% is indicated for the topical treatment of onychomycosis (tinea unguium) of the toenail(s) due to *Trichophyton rubrum* and *Trichophyton mentagrophytes*.

IMPORTANT SAFETY INFORMATION

- JUBLIA is for topical use only and is not for oral, ophthalmic, or intravaginal use.
- Patients should be instructed to contact their health care professional if a reaction suggesting sensitivity or severe irritation occurs.
- The most common adverse reactions (incidence >1%) were (vs vehicle): ingrown toenail (2.3% vs 0.7%), application-site dermatitis (2.2% vs 0.2%), application-site vesicles (1.6% vs 0%), and application-site pain (1.1% vs 0.2%).
- JUBLIA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus, and should be used with caution in nursing women. The safety and effectiveness in pediatric patients have not been established.

Please see Brief Summary of full Prescribing Information on the adjacent page.

Reference: 1. JUBLIA [prescribing information]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC.

Find out more by visiting www.JubliaRx.com.



Jublia is a trademark of Valeant Pharmaceuticals International, Inc. or its affiliates.
©2016 Valeant Pharmaceuticals North America LLC. JUB.0146.USA.16 Printed in US