Bacterial infections from aquatic species: potential for and prevention of contact zoonoses

O.L.M. Haenen (1)*, J.J. Evans (2) & F. Berthe (3)

(1) Central Veterinary Institute of Wageningen UR, Laboratory for Fish, Shellfish, and Crustacean Diseases, P.O. Box 65, 8200 AB, the Netherlands
(2) United States Department of Agriculture, Agricultural Research Service, Stoneville, MS, 38776, United States of America
(3) European Food Safety Authority, Animal Health and Welfare Panel, Largo N. Palli 5/A, Parma, I-43100, Italy
*Corresponding author: Olga.Haenen@wur.nl

Summary
As aquaculture production and the consumption of aquaculture products increase, the possibility of contracting zoonotic infections from either handling or ingesting these products also increases. The principal pathogens acquired topically from fish or shellfish through spine/pincer puncture or open wounds are *Aeromonas hydrophila*, *Edwardsiella tarda*, *Mycobacterium marinum*, *Streptococcus iniae*, *Vibrio vulnificus* and *V. damsela*. These pathogens, which are all indigenous to the aquatic environment, have also been associated with disease outbreaks in food fish. Outbreaks are often related to management factors, such as the quality and quantity of nutrients in the water and high stocking density, which can increase bacterial loads on the external surface of the fish. As a result, diseased fish are more likely to transmit infection to humans. This review provides an account of human cases of zoonoses throughout the world from the principal zoonotic pathogens of fish and shellfish.

Keywords
Aquaculture – Bacteria – Fish – Prevention – Zoonosis.

Introduction
‘Zoonosis’ refers to a disease that can be transferred from animals, whether wild or domesticated, to humans. With the global growth of aquaculture and the increasing volume of international trade in live aquatic animals and their products (37), zoonoses require special attention. The increasing interface between humans and aquatic animals which may harbour infectious agents is a potential public health concern. Despite an increased awareness of zoonotic disease agents, their diagnosis in humans by clinicians and medical practitioners is often hampered by a poor knowledge of the zoonotic potential of disease agents in aquatic species and the associated clinical signs (34).

Potential biological contamination of aquaculture products can occur from bacteria, viruses, parasites and biotoxins (46, 85). The location of the farm, the species being farmed, water temperature, husbandry systems, post-harvest processing, and habits in food preparation and consumption are among the main factors influencing the risk associated with aquatic animals and their products.

Zoonotic infections can be divided into:

a) topically acquired infections, caused by contact with aquatic animals or their products

b) foodborne infections, caused by the ingestion of raw or undercooked aquatic products.

Pathogens may be indigenous to the aquatic environment or occur as the result of environmental contamination, due to, for example, farms being located in polluted areas, the use of excreta as fertiliser and faecal effluents from human sewage, animal farms or wild animals (*Salmonella*, *Shigella*, pathogenic *Escherichia coli*, *Yersinia*, *Brucella*, *Edwardsiella*).

This paper presents an overview of the zoonotic potential of topically acquired (contact) bacterial infections caused by *Vibrio vulnificus*, *Edwardsiella tarda*, *Streptococcus iniae* and
**Mycobacterium marinum** from aquaculture species, and how to prevent them.

**Topically acquired (contact) bacterial infections**

The principal bacteria topically acquired by humans from fish, shellfish or crustaceans, through spine/pincer puncture or open wounds, are: *V. vulnificus*, *M. marinum*, *S. iniae*, *E. tarda* (48), *Aeromonas hydrophila* (59) and, less importantly, *Erysipelothrix rhusiopathiae* (13, 43). Although most fish-associated wound infections are self-limiting, more serious cases are associated with an underlying immune deficiency or incompetence in the patient, highly virulent strains, a large inoculum, deep penetration of the skin, or a combination of these factors. Patients develop mild-to-severe infections (7, 26, 82) which, as in the case of *V. vulnificus*, may prove lethal (5, 12, 52).

Groups most at risk of topically acquiring zoonotic bacteria from fish include aquaculture professionals; fish culturists, processors, and handlers; and commercial and recreational fishermen and fisherwomen. They routinely have direct skin contact with fish, often in humid indoor facilities and at temperatures close to the optimal growth conditions for bacteria. Individuals who are immunocompromised, and have open skin injuries and/or are pierced by fish spines, are at risk of developing a zoonotic infection. In 2012, Verner-Jeffreys et al. (83) found *V. vulnificus*, *V. cholerae* and *M. senegalense* in Garra rufa fish, used as pedicure fish for humans. It can be inferred that immunocompromised visitors to wellness centres are at risk from this practice.

Data on the prevalence and incidence of topically acquired zoonotic infections from fish are scarce, as many are not reported or diagnosed. Apart from a few reviews (5, 25, 35, 59, 65), published reports often chronicle a single case. In addition, cases of human infection with these bacteria are not usually notifiable. *Vibrio vulnificus* infection in humans is notifiable in the United States (USA), and is currently being considered for possible notification in the Netherlands (O.L.M. Haenen, personal communication). A 2009 workshop held on zoonotic infections from fish and shellfish (41) identified the need to analyse the current literature and promote more systematic reviews of the available evidence.

*Vibrio vulnificus*, *V. parahaemolyticus*, *V. damsela* (28) and *V. cholerae* are the principal species of *Vibrio* involved in human infections (5), but there are at least 12 different species described which have zoonotic potential (1). Non-pathogenic strains of these species also exist. Most cases reported in Europe are the result of wound infections caused by seawater or seafood exposure, which can become systemic and even lethal in susceptible, immunocompromised people (31, 32, 44). Other zoonotic bacterial agents include *M. marinum*, which causes ‘fish tank granuloma’ in workers handling infected fish (46). It has been isolated from ornamental and food fish (27, 44, 79, 80), but there are no reports of illness associated with the consumption of farmed fish or crustaceans (85). *Erysipelothrix rhusiopathiae* and *S. iniae* are considered occupational hazards for people handling fish, affecting mainly immunocompromised individuals. *Edwardsiella tarda* causes gastroenteritis but can also cause generalised infections in humans, either from contact with or ingestion of fish which harbour the bacteria (35). Table I provides an overview, from the literature on human cases, of the four principal potential zoonotic bacteria topically acquired from aquaculture animals.

**The principal contact zoonotic bacteria from fish**

**Vibrio vulnificus**

*Vibrio vulnificus* is a microorganism that is frequently found in warm coastal waters (14). It has been isolated from seawater, sediments, plankton and shellfish (oysters, clams, crabs) in the Gulf of Mexico and off the Atlantic and Pacific coasts of the USA (75). The prevalence of pathogenic vibrios in waters depends on environmental factors, such as water temperature, salinity and phytoplankton concentration (32, 73). The presence of *Vibrio spp.* has also been reported in Europe, where levels are generally low, except in bivalves (9, 39, 64).

The species *vulnificus* has been subtyped into three biotypes, with serovars: biotype 1 in crustaceans and humans (74), biotype 2 in eels (10, 77), among others, and biotype 3 in tilapia (11). A polymerase chain reaction was developed (69) to subtype biotype 2 into potential zoonotic strains (serovar E). Biotyping is no longer considered accurate for subtyping. Current subtyping is based on sequence data, which showed that biotype 2 strains were polyphyletic (70). Biotype 2 was thought to be a pathovar, i.e. one of a set of strains of *V. vulnificus* with the pathogenic potential to infect fish and cause vibriosis (70).

In aquaculture and in the wild, *V. vulnificus* is known to cause disease and is a serious pathogen of Japanese eels (62) and European eels (10, 30). Affected eels show extensive haemorrhages and severe necrosis (24, 38). Clinical signs include haemorrhaging on the body surface, and in the gastrointestinal tract, gills, heart, liver and spleen (6). Since 1991, the bacterium has been isolated 23 times from indoor
cultured eels with deep ulcers and high mortality in the Netherlands (26, 42). *Vibrio vulnificus* is a zoonotic invasive pathogen (5). In low numbers, it causes primary wound infections when a skin injury comes into contact with infected seawater, fish or shellfish (23, 51, 55, 66), which may develop into fasciitis necroticans (26, 56, 68, 82) and even full sepsis and death (12). Immunocompromised patients (52) suffering from liver diseases are at risk (26). Mortality after wound infections may reach 25%. After sepsis, mortality may reach up to 55%, mostly within 48 h of the first appearance of clinical signs (19). Most human cases are from biotype 1; however, since 1993, biotype 2 has also been reported as a cause of human disease, with some severe cases of fasciitis necroticans and sepsis in patients (Fig. 1) (3, 19, 26, 61, 66, 71, 82). Biotype 3 is a rather new type which has caused wound infections after slaughtering tilapia in Israel (11).

**Streptococcus iniae**

*Streptococcus iniae*, a Gram-positive bacterium, is a zoonotic pathogen in fresh water and marine fish, causing disease outbreaks in aquatic species (2) and invasive disease in humans (8). This pathogen causes significant economic losses, particularly in the tilapia and hybrid striped bass aquaculture industries in the USA, Japan, Israel, South Africa, Australia, the Philippines, Taiwan, Bahrain and other countries. Evans *et al.* (33) provide an overview of the epidemiological aspects of *S. iniae* in warm-water fish, including global distribution, fish host susceptibility, clinical signs of disease, sample collection, transport and storage for successful survival and isolation, identification by conventional, automated and molecular diagnostic techniques, antibiotic sensitivities, and vaccination and environmental influences on disease susceptibility.

**Edwardsiella tarda**

*Edwardsiella tarda* produces the disease commonly known as ‘fish gangrene’, ‘emphysematous putrefactive disease of catfish’ or ‘red disease of eels’ and referred to as *Edwardsiella* septicemia (ES), a systemic disease. The reader is referred to Evans *et al.* (35) for a review of all aspects of *Edwardsiella tarda* – in particular, the economic, environmental and social importance of the disease in fish and humans.

Topically acquired *S. iniae* infections have been reported from 26 patients in five countries: Canada (84), Hong Kong (58), Singapore (53, 54), Taiwan (72) and the USA (36). Most of the affected individuals were Asian (85%) and ranged in age from 40 to 88 years. Clinical signs included cellulitis, septicemia, endocarditis, arthritits, meningitis, osteomyelitis, fever and abdominal distension and pneumonia. Fifty-eight percent of the patients were known to have handled or been exposed to fresh fish. Underlying
conditions included chronic rheumatic heart disease, osteoarthritis, hypertrophic obstructive cardiomyopathy, duodenal ulcer and gallstones, diabetes mellitus, hepatitis C-related liver cirrhosis, alcoholism, hypertension, hypothyroidism and partial mastectomy; they were reported in 35% of those contracting *S. iniae* infections (34).

*Mycobacterium marinum* is an acid-fast rod-shaped bacterium that causes worldwide chronic and severe disease in many fish species in fresh water and brackish and marine waters (20, 34, 40, 60, 63, 81). At least 167 species from more than 40 families of fish are susceptible to *Mycobacterium* species (47).

In fish, *M. marinum* causes chronic systemic disease, with granulomas in multiple organs and tissues, loss of scales, slimeless skin, ulcers and eroded fins, followed by death (40). *Mycobacterium marinum* has an optimum growth temperature of 30°C, and does not grow well at 37°C.

In humans, *M. marinum* causes granulomatous inflammation and nodular or diffuse granulomas of the skin, subcutaneous tissues and tendon sheaths of fingers and hands, and is referred to as 'swimming pool granuloma', 'fish tank granuloma', 'fish handlers' fish fanciers' disease', or 'fish TB' (Fig. 2) (21). Invasive septic arthritis and osteomyelitis may occur in immunocompromised hosts (29, 45, 49, 50, 57, 59), causing chronic skin lesions, congestion of the whole finger and hand, and tenosynovitis. Between 1993 and 1996, 653 cases were confirmed in the USA, of which 49% were associated with aquarium exposure, 27% with injury by aquarium fish, and 9% with injury during bathing in seawater (34). In France, 63 cases were reported between 1996 and 1998, of which 84% were associated with fish tank exposure (4). Lahey (57) searched MEDLINE as far back as
1966 and discovered 35 invasive cases, occurring in patients at an average age of 43 years, who had been treated with immune impairment systemic steroids or chemotherapy, or had acquired immunodeficiency syndrome (AIDS). Sixty percent of these patients had tenosynovitis, 17% had septic arthritis and 37% had osteomyelitis, but it is unclear whether these conditions were attributable to infection. The source of infection was exposure to water or injury through fish spines or sharp edges on shellfish. The time until diagnosis for these cases was 17 months from the onset of symptoms, and the average duration of antibiotic therapy was 11.4 months, with surgery taking place in 69% of cases (34, 57). (In general, the average time to clinical diagnosis is 4.4 weeks.)

Misdiagnosis and delayed treatment of \textit{M. marinum} infection are common because of its diverse manifestations (18). The Centers for Disease Control and Prevention (CDC) in the USA included \textit{M. marinum} on their list of ‘Emerging infectious diseases’ from 2008. Additional topically acquired \textit{Mycobacterium} spp. with zoonotic potential include: \textit{M. chelonae}, \textit{M. fortuitum}, \textit{M. abscessus}, \textit{M. interjectum}, \textit{M. scrofulaceum}, \textit{M. szulgai}, \textit{M. similae} and \textit{M. triplex}.

**Prevention and treatment**

Zoonotic infections originating in aquatic animals are under-reported, making risk analysis difficult. Haenen \textit{et al}. (unpublished data, 2008) interviewed 18 fish farmers and processors. These farmers and processors usually worked without gloves, and did not know about zoonotic risks and prevention/hygiene. Most of those interviewed regularly injured their hands through puncture by fish (tilapia, catfish, barramundi) or by a knife, resulting in chronic hand infections. Clinicians failed to diagnose the causative agent. To reduce the risks of topically acquired infection, people should avoid direct contact with potentially contaminated fresh or salt water if they have open cuts, scrapes or sores on their skin.

People with compromised immune systems should avoid handling fish or cleaning fish tanks. They 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 (34, 41).

Bisharat \textit{et al}. (11) reported that, after human cases of infection with \textit{V. vulnificus} were reported in Israel in 1996 and 1997, related to exposure to tilapia and carp, a new policy was implemented. This policy prevented the selling of live fish and stated that fins, scales and intestines should be removed before marketing, the product must be cooled throughout processing, and people should be advised to purchase fish only from stores affiliated with the Fish Farmers’ Association. This reduced the number of human cases considerably.

**\textit{Vibrio vulnificus}**

Antibiotics are necessary to treat \textit{V. vulnificus} infections. Effective antibiotics include tetracycline, third-generation cephalosporins (e.g. ceftazidime), and imipenem, from the carbapenem class (these are typically restricted in use to avoid widespread bacterial resistance). In cases of wound infection, aggressive debridement is necessary to remove the necrotic tissue (26, 75).

**\textit{Edwardsiella tarda}**

\textit{Edwardsiella tarda} occurs sporadically in aquaculture animals and humans. Extra-intestinal infections caused by puncture wounds are susceptible to gentamycin, amoxicillin, trimethoprim-sulfamethoxazole, cephalosporins and oxyquinolones (59). As with other fish-derived zoonotic bacteria, culture at lower temperatures is required.

**\textit{Streptococcus iniae}**

The prevalence of \textit{S. iniae} can be underestimated, particularly in Asian populations. Constraints for diagnosis include the fact that the pathogen is often not identified by conventional microbiological identification systems. There is little surveillance of streptococci isolated from wounds and tissues, and clinicians often fail to discover the patient’s
history of fish exposure. Prevention consists of using protective equipment when cleaning and processing raw seafood, and ensuring good hygiene (34).

**Mycobacterium marinum**

There are many factors which can prevent the diagnosis of *M. marinum*:

- the link to fishery products is often not recognised or found
- the presentation of this disease in humans is insidious and non-specific
- there is generally a delay between the onset of symptoms and medical consultation (an average of five months)
- there is a delay in definitive diagnosis of, on average, 4.4 weeks
- the bacterium grows poorly at 37°C, so is often missed in hospital laboratories
- clinicians often fail to find or recognise a history of fish exposure (34).

Cheung et al. (18) reported that misdiagnosis often leads to the inappropriate use of antimicrobials, extension of the infection from the skin to the tenosynovium, and a poor prognosis. Clinicians should be aware of this type of infection, especially in subjects at risk (fishermen and aquarium hobbyists), and those with a history of trauma coupled with exposure to water or marine life. He advises a proactive diagnosis through histopathology and microbiology, with prompt antibiotic treatment with rifampicin, ethambutol and clarithromycin. Debridement is indicated in patients with deep-seated infections.

In addition, we need to better educate diagnosticians on the clinical signs of these diseases in both fish and humans, as well as on their culture conditions, prevention, hygiene and therapy. It would also be wise to require zoonotic bacteria to be notifiable to the appropriate international bodies, such as the World Health Organization and the World Organisation for Animal Health.

Further research is needed into issues of antibiotic resistance, disinfection studies and risk assessment for these infections.

**Conclusions**

Topically acquired zoonoses from fish are not numerous, but individual cases may be severe.

Topically acquired zoonoses are vastly under-reported worldwide. This is partly the result of not recognising that fish can be the source of zoonotic infection, and partly because zoonotic agents derived from fish are still non-notifiable in most countries.

Most of the topically acquired zoonoses in aquaculture are caused by *V. vulnificus*, *M. marinum* and *S. iniae*. There is a considerable lack of knowledge of the zoonotic risks from fish among those at risk, either through their occupation or by having a compromised immune system, and also among diagnosticians. Anamneses and culture methods have not been adapted to identify aquatic zoonotic agents and should include lower incubation temperatures. In all, more international research and much-improved communication are needed to prevent topically acquired zoonoses from fish.

**General recommendations**

The control of topically acquired infections from aquatic animals requires much improvement in communication and medical diagnostics. It is of paramount importance to develop and distribute zoonosis fact sheets to fish culturists and fish processors, veterinarians, doctors, hospitals and Veterinary Services.
Infections bactériennes d’origine aquatique : risques d’exposition zoonotique par contact et prévention

O.L.M. Haenen, J.J. Evans & F. Berthe

Résumé
Au fur et à mesure que le secteur de l’aquaculture produit davantage et fournit un nombre croissant de consommateurs, on assiste à un risque accru d’exposition à des infections zoonotiques lors de la manipulation ou de l’ingestion de ces produits. Les principaux agents pathogènes pouvant être transmis à l’homme par contact direct de plaies cutanées avec des poissons ou des crustacés infectés, ou suite à une coupure par des arêtes ou des pinces, sont *Aeromonas hydrophila*, *Edwardsiella tarda*, *Mycobacterium marinum*, *Streptococcus iniae*, *Vibrio vulnificus* et *V. damsela*. Ces agents propres au milieu aquatique ont tous été retrouvés lors de foyers d’infections bactériennes survenus chez des espèces de poissons destinées à l’alimentation humaine. Ces foyers ont souvent été imputés à des facteurs relevant de la gestion des élevages, par exemple une qualité ou quantité inappropriées de substances nutritives dans l’eau ou une densité trop élevée des populations, facteurs susceptibles d’accroître la charge bactérienne sur la surface externe des poissons. De ce fait, les poissons infectés sont davantage à même de transmettre l’infection à l’homme. Les auteurs font le point sur la situation mondiale des infections humaines par les principaux agents pathogènes zoonotiques présents chez les poissons et les crustacés.

Mots-clés

Infecciones bacterianas procedentes de especies acuáticas: probabilidad y prevención de las zoonosis por contacto

O.L.M. Haenen, J.J. Evans & F. Berthe

Resumen
A medida que se intensifican la producción acuícola y el consumo de los productos de la acuicultura, también aumenta la probabilidad de contraer infecciones zoonóticas al manipular o al ingerir esos alimentos. Los principales patógenos que el hombre contrae por vía tópica a partir de peces o crustáceos, ya sea al lesionarse con espinas o pinzas o a través de una herida abierta, son *Aeromonas hydrophila*, *Edwardsiella tarda*, *Mycobacterium marinum*, *Streptococcus iniae*, *Vibrio vulnificus* y *V. damsela*. Todos estos patógenos propios del medio acuático también han sido vinculados con brotes infecciosos en peces destinados al consumo humano. A menudo los brotes guardan relación con factores zootécnicos como la calidad y cantidad de nutrientes presentes en el agua o una elevada densidad de población, que pueden elevar la carga bacteriana en la superficie
externa de los peces. Una consecuencia de ello es la mayor probabilidad de que los peces enfermos transmitan la infección al ser humano. Los autores exponen una serie de casos descritos en distintas partes del mundo de zoonosis humanas causadas por los principales patógenos zoonóticos de peces y crustáceos.

**Palabras clave**

---

**References**


