

Edwardsiellosis, an Emerging Zoonosis of Aquatic Animals

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Abstract

Zoonotic diseases from aquatic animals have not received much attention even though contact between humans and aquatic animals and their pathogens have increased significantly in the last several decades. Currently, *Edwardsiella tarda*, the causative agent of Edwardsiellosis in humans, is considered an emerging gastrointestinal zoonotic pathogen, which is acquired from aquatic animals. However, there is little information about *E. tarda* pathogenesis in mammals. In contrast, significant progress has been made regarding to *E. tarda* fish pathogenesis. Undoubtedly, research about *E. tarda* pathogenesis in mammals is urgent, not only to evaluate the safety of current *E. tarda* live attenuated vaccines for the aquaculture industry but also to prevent emerging *E. tarda* human infections.

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Human food and health are inextricably linked to animal production. This link between humans and animals is particularly close in developing regions of the world where animals provide transportation, clothing, and food (meat, eggs and dairy). In both developing and industrialized countries, this proximity with farm animals can lead to a serious risk to public health with severe economic consequences. A number of diseases are transmitted from animals to humans (zoonotic diseases). According to the World Health Organization (WHO), about 75% of the new infectious diseases affecting humans during the past 10 years have been caused by pathogens originating from animals and derivative products. Every year millions of people get sick due to food borne zoonoses diseases caused by *Salmonella*, *Campylobacter*, *Brucella*, *Escherichia coli*, *Leptospira*, *Yersinia*, *Shigella* and *Francisella* bacteria infecting cattle, swine, poultry and wild animals.

Zoonotic diseases from aquatic animals have not received much attention even though contact between humans and aquatic animals and their pathogens has increased significantly in the last several decades. The worldwide decline of ocean fishery stocks has provided impetus for rapid growth of fish, crustacean, and shellfish aquaculture. Currently, the aquaculture industry is one of the most important sources of human food and is also the fastest growing animal-producing food sector [1-3]. This growth has led to an increase in contact between humans and aquatic animal pathogens. At this time, only a few zoonotic pathogens from aquatic animals have been identified, which are commonly encountered while working with fish. There are no viral or fungal zoonoses and only a few parasitic zoonoses could be acquired from fish through the oral-gastric route. Bacteria are the primary pathogens with zoonotic potential acquired through handling or eating aquatic animals [4]. Most of the zoonotic bacterial pathogens of fish are Gram-negative, although there are some important Gram-positive pathogens affecting fish and humans. Currently, *Edwardsiella tarda*, the causative agent of Edwardsiellosis in humans, is considered an emerging gastrointestinal zoonotic pathogen, which is acquired from aquatic animals [5,6]. The genus *Edwardsiella* is one of the most primitive within the Enterobacteriaceae family [7]. This genus is composed of three species, *E. ictaluri*, *E. hoshinae* and *E. tarda*. *E. ictaluri* appears to be a host-restricted pathogen of channel catfish (*Ictalurus punctatus*). This is in contrast to *E. hoshinae* and *E. tarda*, which have a wide host range. *E. hoshinae* forms part of the bacterial flora of reptiles and infectious diseases caused by this species have never been reported in humans. *E. tarda* is considered a common inhabitant of the intestinal flora of aquatic animals, however under certain unknown circumstances causes intestinal and extra-intestinal infectious diseases in reptiles, amphibians, birds, and mammals including humans [8-19]. In addition, isolation of *E. tarda* has been reported in invertebrates [20], cattle, swine, dogs, Weddell seals [21-23] and Antarctic animals [16]. These reports suggest that *E. tarda* has a wide geographic distribution in addition to a wide host range. Today, with the increasing contact between aquatic animals and humans, *E. tarda* is becoming an important pathogen in terms of global public health. First described by Ewing et al. in 1965 [22], *E. tarda* seems an uncommon pathogen of humans, but clinical cases have continuously been increasing during the last several decades. The most common manifestation of Edwardsiellosis infection in humans is gastroenteritis, which occurs more commonly in tropical and subtropical climates [24-26]. *E. tarda* extra-intestinal symptoms, which usually occur in patients with hepatobiliary, diabetes, malignancy, immune suppression, and iron overload syndromes [27], including soft tissue infections [28], meningitis [29], peritonitis, vertebral osteomyelitis [30], and endocarditis [31,32]. Although rare, *E. tarda* neonatal infections have also been reported [33-37]. These extra-intestinal manifestations, when associated with bacteremia, could carry up to 50% mortality [24,27,38].

In the aquaculture industry, *E. tarda* infections have been reported worldwide in economically important marine and fresh water fish species

including, Japanese eel (*Anguilla japonica*) [39], barramundi (*Lates calcarifer*) [40], channel catfish [41], largemouth bass (*Micropterus salmoides*) [40], mullet (*Mugil cephalus*) [42], crimson sea bream (*Evynnis japonica*) [43], tilapia (*Tilapia nilotica*) [44], chinook salmon (*Oncorhynchus tshawytscha*) [45], red sea bream [46], yellow tail [46], flounder [47], carp (*Cyprinus carpio*) [48], sea bass (*Dicentrarchus labrax*) [49], turbot [50], Asian catfish (*Claris batrachus*) [51], brook trout (*Salvelinus fontinalis*) [52], Indian carp (*Catla catla*) [51], rohu (*Labeo rohita*) [51], European eel (*Anguilla anguilla*) [53] and Far Eastern catfish (*Silurus asotus*) [54].

Certainly, the broad host aspects of *E. tarda* pathogenesis and the development of prevention methods against this emerging enteric zoonotic pathogen require attention. Currently there are no commercial vaccines against *E. tarda* infections either for humans or farm fish, although several live attenuated *E. tarda* vaccines have been proposed for the aquaculture industry. The genetic design of these vaccines goes from random mutagenesis [55] to precise in-frame deletions of genes that encode for virulence factors [56]. With these improvements in fish vaccinology come additional concerns about the use of this zoonotic pathogen as a live attenuated vaccine for aquatic animals for human consumption. How do these *E. tarda* vaccines for fish affect mammals? For instance, is it environmentally safe to use an emerging aquatic human pathogen as a parent for live attenuated vaccine? How much do we know about *E. tarda* pathogenesis in mammals? There is no question about the advantages of an immersion live attenuated bacterial vaccine for the aquaculture industry when compared to traditional injectable vaccines. Immersion live attenuated vaccines are easy to use, trigger mucosal and humoral immune responses, and are much less expensive than traditional injectable vaccines. However, there is little information about *E. tarda* pathogenesis in mammals. In contrast, significant progress has been made in understanding *E. tarda* pathogenesis [5]. Undoubtedly, research about *E. tarda* pathogenesis in mammals is urgent, not only to evaluate the safety of current *E. tarda* live attenuated vaccines for the aquaculture industry but also to prevent emerging *E. tarda* human infections.

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