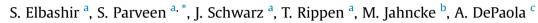
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## Seafood pathogens and information on antimicrobial resistance: A review



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### ABSTRACT

Seafood-borne diseases are a major public health hazard in the United States and worldwide. Per capita, seafood consumption has increased globally during recent decades. Seafood importation and domestic aquaculture farming has also increased. Moreover, several recent outbreaks of human gastroenteritis have been linked to the consumption of contaminated seafood. Investigation of seafood-borne illnesses caused by norovirus, and Vibrio, and other bacteria and viruses require a concrete knowledge about the pathogenicity and virulence properties of the etiologic agents. This review explores pathogens that have been associated with seafood and resulting outbreaks in the U.S. and other countries as well as the presence of antimicrobial resistance in the reviewed pathogens. The spectrum of such resistance is widening due to the overuse, misuse, and sub-therapeutic application of antimicrobials in humans and animals.

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#### 1. Global trends in seafood consumption

Most seafood is good source of proteins, long-chain omega-3 fatty acids, vitamin D, selenium and iodine. The consumption of seafood has significant health benefits, encompassing neural,

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visual, and cognitive development during gestation and infancy (Emmett et al., 2013) and minimizes the hazard of cardiovascular diseases (Zarrazquin et al., 2014). Food and Agriculture Organization (FAO) of the United Nations reported that world per capita supply increased from 9,9 kg in 1960s to 14,4 Kg in 1990s, 19.7 Kg in 2013 and over 20 kg in 2014 (FAO, 2016). Seafood consumption has also increased per country; China per capita has increased from 14.4 Kg in 1993 to 37.9 in 2013. Other East Asian countries per capita have also increased from 10.8 Kg to 39.2 Kg in 2013. Africa continental average increased to 10 Kg, North America including U.S. the average per capita increased to 21.4 Kg, Europe to 22.2 Kg, and Oceania to 24.8 Kg (FAO, 2016). Seafood consumption has increased in the United States (U.S.) over the last few decades with consumption growing on average from 3.5 Kg in 1980 to 5.6 Kg in 2006. In 2013 it declined to 4.9 Kg (USDA, 2015), which was still more than the average in 1980. Taking into consideration the population growth and increased per capita seafood consumption, the gross U.S. seafood supply has grown over 70% since 1980, to 2.2 billion Kg in 2009 (Wang et al., 2011). Seafood imports increased significantly from below 50% of the gross seafood consumption in 1980 to more than 91% in current years to meet the deficit in domestic production (NMFS, 2013). Recently, nearly 50% of the U.S. seafood imports are produced by aquaculture, and frozen seafood accounts for 75% of gross imports (Wang et al., 2011; NMFS, 2010). Fisheries and aquaculture farming provided a source of income for approximately 56.6 million people around the world in 2014 (FAO, 2016). Their engagement is either in part-time, small, intermediate, or large-scale production operations. Eighty four percent of such worldwide engaged populations are from Asia, 10% from Africa, 4% in Latin America and Caribbean, and the remaining 2% was distributed all over the world. They either work in wild capture or aquaculture farming. FAO introduced different codes to manage both wild capture and aquaculture farming (FAO, 2016).

Since the 1950s, antimicrobial resistance has been acknowledged as a public health hazard worldwide that has transported its way into the new millennium (CDC, 2010b). Approved antimicrobials (Table 2) are used for seafood species as therapeutics and prophylactics. As aquaculture farming is intensive, all antimicrobials are en masse. The residues of the unused antimicrobials precipitate and contaminate the aquatic environment and exert a detrimental effect on the microbiota and animal species over time (Marshall and Levy, 2011). Use of unsafe, or unapproved antimicrobials (e.g.; chloramphenicol, nitrofuran, etc.) can have a deleterious effect on human health. Some antimicrobials such as nitrofurans and fluroquinolones may result in antimicrobial resistance, while others such as gentian violet and nitrofurans may be carcinogenic. (FDA, 2015). The overuse and misuse of antibiotics in aquaculture can increase the prevalence of antibiotic-resistance, of zoonotic pathogens in an aquatic population (Cabello, 2006).

Antimicrobials are introduced in aquaculture through feed or water immersion as treatment or for prophylaxis (Heuer et al., 2009). Antimicrobials (e.g.:  $\beta$ -lactams, streptomycins, and aminoglycosides) in bacteria found naturally in soil are potential sources of aquatic environment contamination. Sewage and sediments containing antimicrobials are probable sources of contamination in sea, river, and aquaculture water (Kümmerer, 2009).

There are different methods of resistance transfer for certain drug-bacteria combinations; plasmid mediated transmission is the leading mode of acquired resistance (FDA, 2009). Tetracycline resistance (Tet) determinants (A – E classes) were detected in *Aeromonas hydrophila* isolates recovered from catfish aquafarms pond sediments, the intestines of the farm-raised catfish, and retail catfish. Such Tet determinants induced resistance to tetracycline and its family members (e.g., oxytetracycline) (Depaola et al., 1988). Another study revealed the presence of the Tet D determinant in

Gram-negative isolates *Citrobacter freundii, Klebsiella pneumoniae, Plesiomonas shigelloides* and *Enterobacter agglomerans*, while the Tet E determinant was present only in *Aeromonas hydrophila* (DePaola and Roberts, 1995). All these isolates were recovered from catfish intestines, aquaculture pond water and sediments.

Horizontal spread of resistance genes to human pathogens, direct transfer of antimicrobial resistance gene, or horizontal spread from aquaculture to the food chain and to the human digestive system were reported by Heuer et al. (2009) Resistance to antimicrobials classified as critically important for humans reduces their therapeutic abilities (WHO, 2007, 2005).

Transmission through zoonotic bacteria (e.g. *Salmonella* and *Vibrio* species), which have the ability to induce disease in both aquatic species and humans, is classified as direct transmission Direct transmission of antimicrobial resistance may be introduced through ingestion of contaminated seafood or water containing zoonotic bacterial pathogens. The bacterium itself harbors the antimicrobial gene (Heinitz et al., 2000). . Transmission of antimicrobial resistance from aquatic pathogens to human pathogens through horizontal gene transfer is classified as indirect transmission (Heuer et al., 2009). The incidence of indirect transmission increases among the closely related bacterial genera, multidrug-resistant plasmids are easily transferred to *E. coli* from *Aeromonas salmonicida* (a fish pathogen) (Kruse et al., 1995).

As a result of the widespread and at times inappropriate use of antimicrobial drugs and the development of subsequent resistance to those drugs, the number and severity of infections are increasing as well as is the frequency of treatment failure. Patients are at risk and may suffer from complications of increased frequencies of illness, aggravated severity of disease, (bacteremia and/or septicemia), and death due to antimicrobial resistant bacteria (Kruse and Sørum, 1994).

#### 2. Pathogens associated with seafood consumption

Despite that the use of Hazard Analysis Critical Control Point (HACCP) reduced the incidence of seafood illnesses in the U.S. (CDC, 2002); the Centers for Science in the Public Interest-CSPI (2009) stated that the continuous growth of U.S. consumption and importation of seafood over the last few decades increases concerns about seafood safety. Significantly, seafood has been a major product incriminated in foodborne outbreaks in the U.S. The Centers for Science in Public Interest-CSPI (2009) also reported that 838 seafood-related outbreaks with 7298 illnesses occurred between 1998 and 2007. Among them, finfish and molluscan shellfish were associated with 60% and 15%, respectively. Finfish was responsible for the highest number of foodborne-disease outbreaks in 2007, which was more than poultry and beef. The seafood outbreaks were more linked to intoxication illnesses than infection (CDC, 2010a). In a recent epidemiological study, the Centers for Disease Control and Prevention (CDC) investigated seafoodassociated outbreaks associated with pathogens between 1973 and 2006. They identified 188 outbreaks of which (76.1%) were bacterial, 21.3% were viral, and 2.6% were parasitic (Iwamoto et al., 2010).

Contamination of water (e.g.: seawater) and sediments is due to the presence of naturally occurring pathogens (e.g. *Vibrio* spp., some species of *Aeromonas*, spores of *C. botulinum* type F) or enteric bacteria (e.g.: non-typhi *Salmonella*, and *Campylobacter*). Such contaminated environments can result in unsafe seafood. Cross contamination of seafood and seafood products may take place during harvesting, handling, preparation, processing, transportation, and storage. In addition, inter-cross contamination between operations may occur (Lee and Rangdale, 2008).

Based on their prevalence, etiologic agents are categorized as

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