

COMMENTARY

Control strategies for vibrios: borrowing from the Japanese experience

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Vibrio species are ubiquitous in the aquatic environment. Most are not pathogenic for humans – and even within those species known to be pathogenic, only a subset of strains tend to carry the virulence factors necessary to cause disease. Strains of *Vibrio cholerae* which carry the gene for cholera toxin are responsible for the disease cholera [1]; the most dreaded of the *Vibrio*-associated illnesses, cholera remains a major global cause of morbidity and mortality. In 2012, 245 393 cases and 3034 deaths were reported to the World Health Organization by 48 countries [2]. Actual numbers are probably substantially higher, due to underreporting. However, cholera transmission, and cholera epidemics, tend to occur in settings where water is not safe and sanitation poor, as seen in association with natural and humanitarian disasters. A second *Vibrio* species, *Vibrio parahaemolyticus*, is also a well-recognized global pathogen [3]. While lacking the virulence of *V. cholerae*, it is probably the leading cause of seafood-associated foodborne illness in the world, with global spread of recently recognized clonal groups highlighting its pandemic potential [4, 5]. And a third, *Vibrio vulnificus*, while causing fewer cases than *V. parahaemolyticus*, is the leading cause of seafood-associated deaths in the United States, with cases closely linked with eating raw oysters [6, 7].

V. parahaemolyticus was first described in 1950 in Japan, where it was isolated from clinical samples from patients with diarrhoea, and from ‘shirasu’ (dried sardines). In early studies of the microorganism,

it was found that illness was caused almost exclusively by strains that produced a haemolytic reaction on a modified blood agar, known as Wagatsuma agar (named after the region in Japan where the reaction was first described) [6, 8]; in the current molecular age, this reaction (and virulence) has been linked with carriage of the gene for the *V. parahaemolyticus* thermostable direct haemolysin (*Vp-tdh*), or related haemolysin genes (*trh* and *trh* variants) [9, 10]. Infection with a pathogenic strain of *V. parahaemolyticus* results in mild to moderate diarrhoea; in some patients, particularly those who are immunosuppressed, serious wound infections and sepsis can also occur [11]. Epidemiologically, illness is linked almost exclusively with consumption of seafood – as *V. parahaemolyticus* is a normal part of the aquatic microbiota, seafood (and seawater) from ‘pristine’ areas with no evidence of human faecal contamination can carry the microorganism.

V. parahaemolyticus has consistently ranked as the most common or one of the most common causes of foodborne illness in Japan. In recent data from coastal areas of China, it again heads the list of foodborne pathogens [12]. In the United States, it is the most common bacterial infection associated with seafood. While the number of reported US cases remains fairly small (334 cases reported in 2011, the most recent year for which data are available [6]), the number of cases there continues to increase; numbers for 2012 were further inflated by the occurrence of a *V. parahaemolyticus* outbreak involving at least 29 persons after consuming shellfish from Oyster Bay Harbor in New York, and, in 2013, 104 illnesses were reported in association with an outbreak involving Atlantic Coast shellfish. *V. parahaemolyticus*, as with other *Vibrio* species, is very sensitive to water temperatures,

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with numbers increasing rapidly when water temperatures rise; as such, there are data suggesting that increasing incidence is linked with global warming [13], with the potential for even further increases in numbers of cases as mean surface water temperatures rise across the next decades.

As outlined in the paper by Hara-Kudo & Kumagai [14] in this journal, Japanese public health authorities responded to increasing numbers of *V. parahaemolyticus* cases in Japan in 1997–1998 by implementing an aggressive regulatory system for control of the microorganism. This included the following key elements:

- Seafood handlers were advised to use disinfected or artificial seawater, or potable water to wash and process shellfish and finfish.
- The temperature for seafood during distribution and storage was set at $\leq 10^{\circ}\text{C}$.
- Microbial standards for *V. parahaemolyticus* in seafood were set at ≤ 100 most probable number (MPN)/g, with non-detectable levels per 25 g required for raw consumption and ready-to-eat boiled seafood, respectively.
- Consumers were advised to consume seafood within 2 h of removal from the refrigerator. Restaurants were advised to serve seafood to consumers immediately after taking the seafood out of the refrigerator.

Between 1998 and 2012, the number of cases and outbreaks of *V. parahaemolyticus* infection in Japan decreased 99-fold and 93-fold, respectively. Did this decline result from decreases in overall *V. parahaemolyticus* contamination rates in seafood – and/or a decrease in percentage of total *V. parahaemolyticus* that carried the *tdh* or *trh* virulence-associated genes? As outlined in the Hara-Kudo & Kumagai paper [14], the answer to both questions is ‘no’ – levels of contamination of seafood with pathogenic *V. parahaemolyticus* remained roughly the same across the time period under study, while case numbers plummeted, strongly suggesting that implementation of the new regulatory framework was the critical factor.

How does this compare with the situation in the United States? In 1997, the U.S. Food and Drug Administration put in place regulations requiring companies that harvest and handle seafood to develop and implement a hazard analysis critical control point (HACCP) plan (‘Seafood HACCP’). HACCP plans are intended to cover a range of potential public

health hazards associated with seafood (including *V. parahaemolyticus* and *V. vulnificus* infection), and involve a series of steps, including identification of potential hazards, characterization of critical control points in the harvest/processing system where these hazards can be controlled, and implementation of systems for taking corrective action when systems go ‘out of control’ at these points. Common to most Seafood HACCP plans are water/sanitation and temperature controls. In contrast to the more focused Japanese system, such plans generally do not include microbial ‘performance standards’ that limit counts of specific microorganisms to certain levels.

How well has Seafood HACCP worked in controlling pathogens such as *Vibrio* species? Since the late 1990s, when Seafood HACCP was implemented, the number of *Vibrio* infections in the United States, as determined by the U.S. FoodNet sentinel surveillance system, would appear to have more than doubled, with a 32% increase in incidence between 2010–2012 and 2013 [15]. The U.S. FDA has put in place ‘mid-course corrections’ for Seafood HACCP, which have had uncertain public health impacts, and in 2009 there was a proposal for imposition of post-harvest processing requirements for oysters; however, this latter proposal does not appear to have progressed, at least in part due to industry opposition. States have stepped into this gap: most notably, in April 2003, California put in place regulations prohibiting the sale of raw oysters from the Gulf of Mexico between 1 April and 31 October unless they had undergone post-processing treatment to reduce counts of *V. vulnificus* to <30 MPN/g (technically, ‘undetectable’ levels). These regulations were focused specifically on reducing the risk of *V. vulnificus* infection, and have been highly successful: in the years since these regulations were implemented, number of oyster-associated *V. vulnificus* infections in California has dropped from an average of 5.5 cases/year to none, a highly significant difference [16]. In 2010, the U.S. FDA, in collaboration with the Interstate Shellfish Sanitation Commission, also encouraged the implementation of temperature requirements for shellfish. While Florida, Texas, and Louisiana have such regulations in place, there have been no evaluations to assess their effectiveness [17].

The paper by Hara-Kudo & Kumagai [14] demonstrates that focused, science- and risk-based regulatory controls, when implemented in an appropriate regulatory environment, can have a profound public health impact. In the United States, we have a

complex regulatory framework [Seafood HACCP (implemented by companies), and a patchwork of state regulations], but, aside from the California regulations, their public health impact is unclear. For the United States (and the rest of the world, including the EU), it will be interesting to see what the future holds: can cost-effective regulatory systems with measurable public health impact be crafted to deal with the burgeoning global problem of rising infection rates due to *V. parahaemolyticus* and other *Vibrio* species such as *V. vulnificus*? And perhaps of even greater importance, is there the political will to put such systems in place?

DECLARATION OF INTEREST

None.

REFERENCES

1. **Morris JG.** Cholera: a modern pandemic disease of ancient lineage. *Emerging Infectious Diseases* 2011; **17**: 2099–2104.
2. **WHO.** Cholera 2012. *Weekly Epidemiological Record* 2013; **88**: 321–336.
3. **Joseph SW, Colwell RR, Kaper JB.** *Vibrio parahaemolyticus* and related halophilic vibrios. *Critical Reviews in Microbiology* 1982; **10**: 77–124.
4. **Nair GB, et al.** Global dissemination of *Vibrio parahaemolyticus* serotype O3:K6 and its serovariants. *Clinical Microbiology Reviews* 2007; **20**: 39–48.
5. **Chowdhury NR, et al.** Assessment of evolution of pandemic *Vibrio parahaemolyticus* by multilocus sequence typing. *Journal of Clinical Microbiology* 2004; **42**: 1280–1282.
6. **CDC.** (<http://www.cdc.gov/ncezid/dfwed/PDFs/covis-annual-report-2011-508c.pdf>).
7. **Morris JG.** Cholera and other vibrioses: a story of human pandemics and oysters on the half shell. *Clinical Infectious Diseases* 2003; **37**: 272–280.
8. **Miyamoto Y, et al.** In vitro hemolytic characteristic of *Vibrio parahaemolyticus*: its close correlation with human pathogenicity. *Journal of Bacteriology* 1969; **100**: 117–119.
9. **Nishibuchi M, Kaper JB.** Thermostable direct hemolysin gene of *Vibrio parahaemolyticus*: a virulence gene acquired by a marine bacterium. *Infection and Immunity* 1995; **63**: 2093–2099.
10. **Shirai H, et al.** Molecular epidemiologic evidence for association of thermostable direct hemolysin (TDH) and TDH-related hemolysin of *Vibrio parahaemolyticus* with gastroenteritis. *Infection and Immunity* 1990; **58**: 3568–3573.
11. **Daniels NA, et al.** *Vibrio parahaemolyticus* infections in the United States, 1971–1998. *Journal of Infectious Diseases* 2000; **181**: 1661–1666.
12. **Li Y, et al.** *Vibrio parahaemolyticus*, southern coastal region of China, 2007–12. *Emerging Infectious Diseases* 2014; **20**: 685–688.
13. **McLaughlin JB, et al.** Outbreak of *Vibrio parahaemolyticus* gastroenteritis associated with Alaskan oysters. *New England Journal of Medicine* 2005; **353**: 1463–1470.
14. **Hara-Kudo Y, Kumagai S.** Impact of seafood regulations for *Vibrio parahaemolyticus* infection and verification by analyses of seafood contamination and infection. *Epidemiology & Infection*. doi:10.1017/S0950268814001897.
15. **CDC.** Incidence and trends of infection with pathogens transmitted commonly through food—Foodborne diseases active surveillance network, 10 U.S. sites, 2006–2013. *Morbidity and Mortality Weekly Report* 2014; **65**: 328–332.
16. **Vugia DJ, et al.** Impact of 2003 state regulation on raw oyster associated *Vibrio vulnificus* illnesses and deaths, California, USA. *Emerging Infectious Diseases* 2013; **19**: 1276–1280.
17. **U.S. Government Accountability Office.** Food safety: FDA needs to reassess its approach to reducing an illness caused by eating raw oysters (<http://www.gao.gov/assets/520/511457.pdf>). September 2011.