

Food Virology: Past, Present, and Future

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Food was first recognized as a vehicle for the transmission of viruses in 1914 when a raw milk-associated outbreak of poliomyelitis was reported (Jubb, 1915). Additional milk-borne outbreaks were recognized after this time, but with the development of a vaccine for poliovirus, no outbreaks were reported in the developed world after the early 1950s (Sattar and Tetro, 2001). However, in the mid-1950s, hepatitis A transmission by shellfish was first reported in Sweden (Roos, 1956) and then in the United States (Mason and McLean, 1962). Later, food-borne outbreaks of nonbacterial gastroenteritis were recognized, although a specific viral agent could not be isolated *in vitro*. For the next two decades, the study of food-borne viruses centered on virus transmission by shellfish and potential risks from the use of reclaimed wastewater for irrigation of food crops.

In the 1990s, molecular methods became available for the detection of difficult to cultivable or noncultivable viruses, which led to the realization that viruses are the leading cause of food-borne illness in the developed world (Bresee et al., 2002; Koopmans and Duizer, 2004). Although any virus capable of transmission by the fecal-oral route can be transmitted by foods, human caliciviruses (noroviruses and sapoviruses) are believed to be the major cause. Mead et al. (1999) estimated that 76 million cases of food-borne illness occur in the United States each year and that viruses cause an estimated 67% of these. They also estimated number of cases per year of calicivirus gastroenteritis at 23,000,000, or 40% of all cases (Mead et al., 1999). The number of documented food-borne virus outbreaks is believed to be on the increase worldwide (Koopmans et al., 2002). This trend will likely continue for a number of reasons as discussed in the next paragraph.

Persons that will experience more serious illness and greater chance of mortality from infectious disease are on the increase in the United States (Gerba et al., 1996). These include young children, pregnant individuals, older people, and immunocompromised individuals (cancer and organ transplant patients). This group currently represents almost 25% of the population in the United States and is expected to grow as the population ages. Persons in nursing homes are 100 times more likely to die of a rotavirus infection than the general population (Gerba et al., 1996). Enteric adenovirus 40 and 41, which appear to rarely cause disease in adults, can result in mortalities of 50% to 69% in immunosuppressed cancer and organ transplant patients (Hierholzer, 1992).

Increased consumption of foods traditionally eaten raw and globalization of international trade have increased the risks of viral contamination of

foods. Much of the produce consumed in the developed world now originates from less developed countries where sanitation and hygiene are not adequate. Recent outbreaks of hepatitis A and norovirus from foods imported to the United States and Europe demonstrate the importance of international trade in aiding the transmission of viral diseases (Dentinger et al., 2001). An increase in the reported number of produce-associated food-borne outbreaks corresponds with the increased consumption of fresh fruit and vegetables and the expanded geographical sources and distribution of these products during the past two decades (Sivapalasingam et al., 2004). Produce-associated outbreaks have increased from 0.7% of all outbreaks in the 1970s to more than 6% in the 1990s in the United States. From 1990 to 2002, produce was second only to seafood in the total number of outbreaks documented, and in the same period the number of cases of produce-associated illnesses was almost equal to those reported for all of beef, poultry, and seafood combined (Center for Science in the Public Interest, 2002). The development of molecular methods has shown us how important food is in the transmission of viruses. We are now able to detect viruses, which cannot be grown in cell culture and can track their origin with molecular fingerprinting.

Until recently, it was thought that food-borne enteric viruses could only originate from humans and hence their transmission was limited to contaminated food handlers, cross-contamination of food, and contamination by water. However, several recent outbreaks of hepatitis E virus have demonstrated that it is a zoonotic virus capable of transmission by consumption of raw or lightly cooked meat products (Mishiro, 2004; Tei et al., 2004). The close relationship between human norovirus and some animal caliciviruses, such as those found in calves, suggests that interspecies transmission to humans may be possible (Koopmans et al., 2002). In addition, there are several other animal viruses that have demonstrated an ability to cross species barriers and have the potential to become involved in human disease. These include coronavirus of severe acute respiratory syndrome (SARS), influenza virus, picornaviruses, toroviruses, parvoviruses, bornaviruses, and pestivirus.

The fundamental problem with regard to the detection of viruses in food is the presence of low numbers of highly infectious viruses, which requires sampling of large volumes of food to assess the risk of infection. Ingestion of even one virus particle has a significant probability of causing an infection. In contrast, bacteria require ingestion of thousands of cells to have the same probability of infection. In addition, viruses have to be extracted or removed from food before amplification in cell culture or detection by molecular methods. This is necessary to reduce the assay volume and remove substances that are toxic to cell cultures or interfere with detection by molecular methods. This limits the sensitivity of viral assays and makes it a more difficult and costly process as compared with the detection of food-borne bacteria. Fortunately, in the case of produce contamination, it is most likely to occur on the surface by contaminated irrigation water, improper handling, or cross-contamination. Uptake of human viruses by roots and into the

ingested part of produce seems an unlikely or rare event. However, in the case of shellfish, internal structures of the animal become contaminated creating additional difficulties in the recovery of the virus.

The application of polymerase chain reaction (PCR) assay has been a major advance in our ability to detect viruses in foods. However, removal of interfering substances, small assay volumes, and determination of infectivity are areas that still require much improvement before full advantage of this technology can be realized by food virologists. With the development of this technology comes the question: What do we do with it? We can use it to investigate outbreaks, demonstrate the virus in the implicated food(s), and track sources of contamination. In addition, we can test the effectiveness of the treatment processes or evaluate strategies to reduce exposure of foods to viral contamination. Beyond this, we may be limited by the sensitivity of the methods and what they can tell us about the safety of the food and the risk of viral illness.

Because low numbers of viruses are usually present in a food supply, we cannot sample large volumes of food like we have been able to do with water. Even with drinking water, the sampling of untreated water is done to estimate the risk of infection after treatment, because even low concentrations of virus (1 infectious virus in 100,000 L) are capable of causing a risk of infection of 1:10,000 per year if the water is consumed (Regli et al., 1991). This is where hazard analysis of critical control points (HACCP) comes into play. As our knowledge expands on viral contamination of foods, we need to identify how and where virus contamination of foods occur.

We obviously need a much greater understanding of viral contamination by water used in irrigation and processing. Controlling contamination by food handlers may be very difficult because of asymptomatic infections. It is currently unclear what proportion of food-borne infections can be attributed to workers in different parts of the food chain. It is important that HACCP systems be used to identify risks and help identify gaps in knowledge (Koopmans et al., 2002). Koopmans and Duizer (2004) noted that although infected food handlers at the end of the food chain are implicated in most outbreaks, contamination can occur anywhere (e.g., seasonal workers picking berries, sick individuals harvesting oysters, and recreational activities on lakes used for irrigation of crops, etc.).

Given the recent recognition of the significance of viruses in food-borne disease and the development of methods for virus detection, it appears that food virology as a field is poised to rapidly grow in the coming years.

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