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**Introduction**

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**History of Virology**

The invention of the microscope, and many subsequent improvements, afforded a window into the microcosm. Over time, bacteria (good and bad) and many other classes of microbes were discovered, but viruses were too small to be seen even with the most efficient light microscopes. Filters were devised that would retain bacteria and other microbes, but under some circumstances the filtrates were found capable of causing disease. This led to the term *filterable virus*; ‘virus’ came from classic Latin for a cause of disease (implicitly more a poison than an infectious agent) – it had no plural and no explicit definition, since causes of disease were poorly understood until recently. The first viruses described were the ones that caused mosaic disease of tobacco and another that caused foot-and-mouth disease in animals. Inevitably, viruses of human disease were also detected; but because they could not be cultivated in the laboratory, their incrimination as pathogens required indirect investigations.

**Environmental Virology**

It was eventually demonstrated that viruses causing human disease might be transmitted directly from an infected person to a susceptible person or indirectly by means of a vector, fomes, or vehicle. Vectors are living things, often insects: If they propagate the virus, they are biological vectors; if they simply carry the virus from place to place, they are mechanical vectors. A fomes (plural, fomites) is an inanimate object, such as a shared towel. Vehicles are water or food. Environmental virology first focused on insects, fomites, and water. However, some early reports indicated that viruses could also be transmitted by foods.

**Food Virology**

Early outbreaks, which were reasonably well documented for their time, implicated raw milk as a vehicle for poliomyelitis, which was then called infantile paralysis. We now know that polioviruses do not infect cattle, so the milk was probably contaminated from milkers’ hands soiled with their feces. The poliovirus would have been inactivated if the milk had been pasteurized, but machine milking affords a relatively certain means of preventing poliovirus contamination of the milk, whereby this particular foodborne virus risk is now negligible in developed countries. A seminal outbreak report from Sweden showed that oysters subject to human fecal contamination could transmit hepatitis. Much has since been learned regarding the ability of bivalve mollusks to concentrate virus selectively from environmental water as they feed by filtration, retain the virus, and infect people who eat the shellfish raw. Although any food mishandled by an infected person may serve as a vehicle for virus, shellfish are the only vehicle that can selectively concentrate virus.

**Viruses Transmitted via Food and the Environment**

The threat of poliovirus transmission via food and water has been largely obviated by the use of vaccines to eradicate the polioviruses in developed countries; poliovirus transmission in poorer countries has multiple routes. Hepatitis A continues as a significant foodborne virus, even though effective vaccines have been available for over a decade; these await full implementation. Some outbreaks previously attributed to hepatitis A virus (HAV) are now known to have been caused by hepatitis E virus (HEV). However, the great gap in foodborne disease recording in developed countries, where such instances are investigated, has long been ‘gastroenteritis of unknown etiology.’ A possible case in point occurred at an international...
Gastroenteritis Viruses

The gastroenteritis viruses most often transmitted via food and water are the noroviruses (see also Chapters Viruses: Foodborne Viruses and Viruses: Norovirus). They are members of the family Caliciviridae, as are the somewhat larger sapoviruses. Both genera comprise single-stranded, plus-sense RNA coated with protein.

Another important genus is the rotaviruses, which comprise segmented, double-stranded RNA with multiple protein coats. The rotaviruses are important causes of infant diarrhea worldwide, but are not necessarily transmitted via food and water. Other gastroenteritis viruses are transmitted less frequently via food.

Hepatitis Viruses

Of the several viruses that cause hepatitis in humans, HAV and HEV are the ones transmitted by a fecal–oral route and therefore sometimes via contaminated food and water (see also Chapters Viruses: Hepatitis Viruses Transmitted by Food, Water, and Environment and Viruses: Foodborne Viruses). In each instance, there is only one serotype worldwide, but genetic groupings can be demonstrated by sequencing. Both comprise single-stranded, plus-sense RNA coated with protein. HAV is in the family Picornaviridae, whereas HEV is in a family of its own (Hepeviridae), having been ruled out of the Caliciviridae family for differences in genomic organization. HAV is human–specific, so its transmission via food or water results from human fecal contamination. HEV may also be transmitted from person–to–person by the fecal oral route, but several HEV strains infect animals such as swine, and some of these are transmissible to humans as zoonotic infections.

Other Viruses

With few exceptions, other viruses potentially transmissible via food or water are enteric agents, transmitted by a fecal–oral cycle. Viruses belonging to the Picornaviridae family (i.e., polioviruses, coxsackieviruses, echoviruses, and other enteroviruses) have had the longest and most intensive scrutiny. There is no doubt that vehicular transmission of these occurs on occasion, but much less frequently than the noroviruses. Other enteric virus groups that may occasionally be transmitted via food and water are the astroviruses, parvoviruses, adenosviruses 40 and 41, and reoviruses.

Nonenteric viruses may sometimes be transmitted via foods. Tickborne encephalitis viruses may infect dairy animals as a result of tick bites and be shed in milk, causing human infections if the milk is not pasteurized. Coronavirus have occasionally been transmitted via food, and the infamous SARS (severe acute respiratory syndrome) virus was alleged to be transmissible via vehicles as well.

Assessment of Risk from Viruses

Diagnostic procedures for some viral infections are relatively new, whereas others have been in place for decades. However, in the United States and some other developed countries, diagnosis of viral gastroenteritis and hepatitis is far from routine; poorer countries are even less likely to perform laboratory diagnoses. This means that estimates of the impact of these viral infections, whether or not they are foodborne, are likely to be inaccurate.

Relative Incidence

Although most norovirus infections are not acquired from food, the U.S. Centers for Disease Control and Prevention (CDC) estimate that noroviruses cause almost 5.5 million foodborne illnesses in the United States annually, which is 54% of the total for domestically acquired illnesses from the leading 31 foodborne agents. Other viruses said to cause substantially smaller numbers of U.S. foodborne illnesses are astroviruses, HAV, rotaviruses, and sapoviruses. With the exception of HAV, all are primarily causes of gastroenteritis. Comparable estimates or data from other countries are extremely difficult to obtain. (see also Chapters Food Poisoning Outbreaks and Viruses: Foodborne Viruses).

Severity

CDC estimates that foodborne norovirus infections lead to over 14 000 hospitalizations and about 149 deaths annually. The other foodborne viruses are said to have far less impact. Although the noroviruses usually cause only transient (≤2 days’ duration) gastroenteritis, studies in The Netherlands indicate that they can cause chronic or prolonged infections and illness in some very young and elderly patients and occasional death in those with immune impairments. HAV infections in young children may be mild but produce lifelong immunity, whereas HAV infections later in life often produce debilitating disease that may last for weeks. HEV infections (rare in the United States) are similar, except that they most often affect young and middle-aged adults and can cause death in 20% of women infected during the third trimester of pregnancy.

Cost

Estimates of the costs of these foodborne diseases are rare and largely unreliable. Most of the illnesses are not treated and so incur no medical costs, but both gastroenteritis and viral hepatitis result in periods of missed work or study. Food
workers in particular should not work while shedding virus, but HAV is shed for 10–14 days before onset of symptoms, and norovirus is shed in feces for variable periods up to several weeks after diarrhea is in remission, so excluding these people is difficult. An alternative approach to assessing the impact of a disease agent is disability adjusted life years (DALYs), which the World Health Organization defines as “The sum of years of potential life lost due to premature mortality and the years of productive life lost due to disability”; this obviates differences in income levels or disability in persons who have no income and is applicable to mental as well as physical disabilities. These kinds of data for foodborne viral illnesses would be welcome and could be used in risk assessments.

Fecal–Oral Transmission of Viruses and Public Health

As stated earlier, most foodborne viruses are transmitted by a fecal–oral cycle and may pass from person to person or via water and food. In addition, norovirus infections often cause periods of projectile vomiting that lead to infection of those exposed by an aerosol route. Because most of these viruses are human specific, human feces are the principal concern.

Disposal of Human Feces: Technology

Casual fecal disposal still occurs in some areas, due either to indifference or to lack of alternatives. The water-carriage toilet is the norm in most developed areas, even in poorer countries; what becomes of the wastewater varies. In rural settings, on-site wastewater treatment is the ideal, and the manner of treatment determines the potential of the effluent to contaminate groundwater or surface water. In urban settings, wastewater is ideally transported to a central treatment facility where it is treated and disinfected before discharge. Feces from facilities aboard public conveyances (buses, trains, ships, airplanes), as well as portable facilities provided for field workers, are ideally conveyed to a treatment facility rather than being discharged directly to the environment. Less-than-ideal waste treatment occurs in many parts of the world, either for lack of economic resources or lack of the collective will to control this hazard.

Viral Contamination of Food

Human enteric viruses occur in foods as a result of direct or indirect human fecal contamination, with the already-stated exception of norovirus in human vomitus. Direct contamination generally stems from contact of fecally contaminated, unwashed hands with food; this may occur at any point from handling of produce in the field to final serving. Although skin disinfectants vary in antiviral effectiveness, washing with soap and water seems to remove viruses effectively from skin. Ideally, food workers – especially those engaged in final preparation and serving – should be immunized against hepatitis A, and they should not handle food while ill. However, hepatitis A immunization seems to be rare in food workers, and there are often disincentives to staying home while ill. Viruses may also occur in the feces of persons who are not overtly ill, either due to inapparent infection or during the incubation or convalescent periods. This means that hand-washing is critical for preventing food contamination at all times.

Indirect fecal contamination of food may result from use of human feces as a soil amendment, but this is relatively rare because nightsoil fertilization is now done in very few locations. Water containing human feces is a much more common source of food contamination. As stated above, water used for feces disposal may not be treated or disinfected before discharge. Such water may be used for irrigation, washing produce at harvest, and as a diluent in pesticide application, among other possibilities. Some of the poorer countries are obliged to use whatever water is available for food production, without the option of treatment beforehand. Discharges to saline water may not be treated because the water will not be made potable, but edible shellfish in such waters often collect/concentrate viruses selectively from their environmental water and convey them to consumers.

Economic Demands and Rewards

A risk-free food supply is the ideal, but the competitive nature of the food business necessitates some compromises. For example, water used for irrigation and other field operations should ideally meet drinking-water standards of purity, but this is seldom feasible in affluent nations, and poorer countries are often obliged to use water that is highly contaminated. Quantitative risk assessment is finding application in the field of food virology and may eventually enable determination of return on investment, in terms of illness prevented by specific risk-management interventions. Costly, incremental gains in food safety must be applied with caution in that increased food costs may lead to increased hunger, to the net detriment of public health. Evaluating costs of foodborne viral disease in terms of DALYs seems unlikely to provide needed cost–benefit data, but such information may be better than none.

Control

Control of foodborne illness ought to take place before an outbreak occurs; but this does not always happen. Effective control measures are sometimes ignored; but in the case of foodborne viruses, useful interventions are still largely in development. Progress has been slowed by the need to develop appropriate laboratory techniques. The fact that viruses cannot multiply in foods is of some help.

Monitoring

The greatest progress in food virology to date has been in the area of molecular detection methods (see also Chapter Virology: Detection). These methods began as adaptations of clinical diagnostic methods, with enhanced sensitivity and adaptation for matrix effects of food and water samples. Application of detection methods to enhance food safety entails applying them either in surveys to determine the general prevalence of human enteric viruses in specific foods or in monitoring foods to determine their virologic safety. Monitoring presents important problems in that samples are seldom truly representative of the batch from which they are derived, and only a very small
quantity of sample is actually tested by a molecular method. Since viruses cannot be enriched from food samples, concentration methods have been developed; these do not increase the quantity of virus obtained from the original sample. Neither do most methods distinguish infectious from inactivated virus. All this means is that it is not productive to apply these methods in a test-and-hold program in which batches of food are detained until cleared by laboratory testing.

Development of monitoring methods has addressed indicators, given the problems of testing for human enteric viruses in food. An indicator, in this context, might be any agent (or even substance) whose presence in food samples is easily demonstrated and is correlated with viral contamination. The rationale is that enteric viruses are present only if fecal contamination has occurred, so any indicator of fecal contamination may suggest the presence of viruses. Easiest to detect are fecal pigments or fecal bacteria, but these have very low specific correlation with viruses. Coliphages (viruses that infect enteric bacteria) have what might be a closer ecologic relationship to enteric viruses but have not shown good correlation. Human enteric viruses that can express themselves in cell culture (vaccine polioviruses, adenoviruses, etc.) offer some attractions, but they are likely only to be present in food that has been contaminated with community fecal material, rather than by an individual food worker. Although indicators continue to be studied, none has yet shown itself to be a valid substitute for direct testing of viruses in food or water. Thus, monitoring for them does not appear likely to improve food safety.

**Prevention**

Preventing transmission of virus A via food B ideally involves conduct of a proper risk assessment/hazard analysis, followed by identification of a valid risk management intervention (critical control point – CCP). In its original application in the U.S. space program, a CCP would either prevent or eliminate the hazard in question, with prevention the preferred option. In the case of human enteric viruses, prevention depends ultimately on keeping human feces, in any quantity or dilution, out of food. This would also prevent a great many other foodborne diseases, but human behavior still occasionally results in direct or indirect fecal contamination, so the quest for a valid CCP is likely to lead to efforts to eliminate the contaminant. Physical removal of viral contaminants from shellfish is one of the objectives of depuration and re-laying; the effectiveness of these techniques in removing viruses is still being evaluated. Thus, if viral contamination is assumed and the contaminant cannot be removed in most instances, the alternative is inactivating the virus in the food, to prevent consumer infections.

**Inactivation**

The viral particle (virion) of a human enteric virus comprises just nucleic acid (most often a single strand of RNA) coated with protein. The nucleic acid contains all the information needed for the virion to enter a susceptible host cell and direct production of progeny virus by the cell. The coat protein (capsid) protects the viral nucleic acid while out in the environment and combines specifically with a receptor on the host cell to induce engulfment of the virion by the cell and initiation of the infectious cycle. The capsid is also the antigen to which hosts respond by producing antibody; although this property has no known function in the viral infectious cycle, antibody evoked by infection or immunization will often limit or prevent infection by the target virus. Replication (especially RNA-dependent RNA replication) is highly error-prone, so that many progeny virions are probably noninfectious by reason of defects in the information the nucleic acid contains. The majority of progeny virions are probably infectious, but they have very little functional redundancy, so that almost any change in any part of the virus is likely to result in inactivation (loss of infectivity). The durability of enteric viruses, which enables their transmission via the environment, resides principally in the capsid – similar respiratory viruses often have nearly identical nucleic acid organization but much more labile capsids. A generic property of enteric viruses seems to be resistance to acid pH. Furthermore, these viruses remain infectious for days to weeks at room temperature, weeks to months in the refrigerator, and years in the freezer. Some also withstand drying on surfaces.

Effective agents of viral inactivation include heat, strong oxidizing agents, alkali, and UV. Biodegradation also inactivates virus, but at a slower pace. Compared to many other viruses, enteric viruses are relatively heat resistant: HAV levels in raw milk were reduced as little as one log by standard pasteurization. However, none of the enteric viruses will withstand boiling, and lesser temperatures are effective over appropriate periods of time. Chemicals and UV are effective against viruses in water or on exposed surfaces, but not in the interior of a food. This means that true CCPs are likely to be based on cooking or thermal processing, which is sometimes precluded by gastronomic considerations. For these reasons, consumption of uncooked foods must always entail some virus risk, unless it can be absolutely proven that fecal contamination has been prevented. On the other hand, thermal processes for most foods (at home or in commerce) that will guarantee inactivation of any virus that may yet be present are still awaiting validation. The fact that the noroviruses and hepatitis viruses do not infect laboratory host systems places a great premium on development of other methods to test these viruses and show whether they have lost infectivity. Some modes of inactivation (e.g., UV) that cause breaks or cross-links in the viral nucleic acid may yield negative tests by molecular methods, but only if the disruption occurs in the segment that is targeted for amplification by the selected primers.

**Immunization**

Another way of preventing viral contamination of food and water is to immunize people so that they do not shed virus in their feces. HAV is the only major foodborne virus for which there are licensed vaccines. Efforts are being made to develop other vaccines but are hindered by inability to propagate the viruses within in-vitro systems and – in the case of the noroviruses – questions as to the durability of immunity even after natural infection. However, during norovirus epidemics, a transient herd immunity seems to occur.

Where sanitation is generally good, susceptibility to HAV continues into the age groups for whom infection produces significant illness. This suggests that the vaccine would best be administered in childhood, to minimize later risks; unfortunately, universal
childhood immunizations may be difficult to implement. Immunization might also be required for food workers; problems include the high cost of the vaccine (relative to what food workers are paid) and the need to administer two injections at an interval of at least 6 months (food workers may change jobs during that time).

Summary

The difficulties of studying viruses in the laboratory has delayed the recognition that they are the leading cause of foodborne illnesses in developed countries, and perhaps worldwide. Human enteric viruses may be transmitted directly from person to person or via water, as well as food. The principal syndromes caused are gastroenteritis or hepatitis, but other systemic or chronic effects occur at times. Some strains of HEV have animal reservoirs, but the majority of viruses transmitted to humans via food are human specific. Although the viruses cannot multiply in food or water, they are relatively durable and continue to present a health threat for considerable periods of time.

Preventing fecal contamination of food and water will effectively prevent viral transmission via these vehicles (note that noroviruses are also shed in vomitus), but human lapses lead to fecal contamination on occasion. Detection of viruses in foods by molecular methods has reached a high state of development, and advances continue to be made. However, these methods cannot inherently distinguish between infectious and inactivated virus, so they require further modification to enable their use in studying the antiviral effectiveness of food processes. Overall, a great deal of research remains to be done.

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Further Reading

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