Epidemiology of Viral Foodborne Disease

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ABSTRACT

Virus transmission via foods begins with fecal shedding of viruses by humans. Foodborne viruses infect perorally: These same agents have alternative fecal-oral routes, including person-to-person transmission and the water vehicle. No zoonotic viruses are transmitted via foods in North America. Viruses rank high among foodborne disease agents in the United States, even though observation, diagnosis, and reporting of foodborne viral disease are inefficient. Risk assessment in developed countries considers viral infection rates and personal hygiene of food handlers, as well as the opportunities for contamination of shellfish and other foods by untreated sewage. Licensing of a vaccine against hepatitis A that could be administered to food handlers in North America would provide an important means of preventing foodborne viral disease. However, the most general concern in preventing all foodborne viral disease is to keep all human fecal contamination out of food.

Viruses transmissible via foods seldom kill their host. Nevertheless, they can infect a single host for only a limited period before the infection is ended in some manner—typically an immune response by the host. This means that, like other infectious agents, these viruses must "con-tinue" to be transmitted to another host if they are to continue their existence. Furthermore, foodborne viruses are specific for humans; no zoonotic viruses are transmitted via foods in North America (6).

Fecal shedding

Foodborne viruses are enteric, which is to say that they are transmitted via a fecal-oral cycle in which foods sometimes serve as vehicles (4). Viruses transmitted in this way are most often passed from person to person by "contact," which occasionally includes coprophagy or anal-oral sexual contact, but usually is based on contamination via feces on fingers that touch another person's fingers, which then enter the recipient's mouth. Fomites such as toys may be involved in transmission at locations such as day care centers, but this is properly indirect transmission.

The period of transmissibility of an enteric virus is the period during which it is being shed in feces, with the minor exceptions that the Norwalk virus (and perhaps its close relatives) is sometimes shed in vomitus and that some enteroviruses (which are rarely foodborne) may infect the pharynx and be shed in limited quantities via the mouth.

Feces are, then, the medium by which enteric, foodborne viruses are shed by infected persons at significant levels for significant periods. Levels of these viruses are expressed in a great variety of units of measure, some based on infectivity (e.g., plaque-forming units, 50% tissue culture infectious doses, most probable number of cytopathic units, radioimmunofocus assay units, etc.), and others based on counts of viral particles with an electron microscope or on other physical measurements.

"Significant" levels of viruses in feces range from 10^6 to 10^{11} or more per gram (8), but the units of measurement are sometimes plaque-forming units or other infectious units and at other times physical particles. And, because one complete physical particle probably contains everything needed to infect a human, an "insignificant" level of fecal shedding of virus is probably just a level that is not readily detected by the method at hand. Of course, the longer the level of virus being shed in feces, the less virus is likely to be introduced into a food, and the less virus inactivation will be required to render the contaminated food safe.

Demonstrable fecal shedding of hepatitis A virus takes place during the last half of the incubation period (typically 10 to 14 days before onset of illness) and perhaps the first week or two after onset (1), with the higher levels probably occurring during incubation. The gastroenteritis viruses are shed during illness (24 to 48 h for the Norwalk virus and, probably, the other, Norwalk-like viruses; a few days for rotaviruses) and sometimes a few days further (1). Estimates are based both on laboratory measurements and on a copious epidemiologic record. It is noteworthy that quite high levels of virus may be shed during peak periods, but it is also important to note that chronic carrier states are not known to occur in persons infected with potentially foodborne viruses. Durations of carriage and fecal shedding apparently range from ca. 2 to 4 days for Norwalk virus and from 2 to 4 weeks for hepatitis A virus.

Peroral infectivity

Despite the statement above that a complete viral particle should contain everything needed to cause a human infection, the probability that one will be infected on ingesting a single particle is infinitessimal. One of the most important reasons for this is that RNA-dependent RNA
synthesis is extremely imprecise, so that the vast majority of progeny viral particles at the end of a replicative cycle are genetically atypical (7). Random genetic variation of this kind may have long-term persistence value for the "species," but it leads to production of only a small proportion of particles that are genetically competent to infect and to perpetuate the agent in its recognized form.

Hosts have undoubtedly been evolving defenses against viruses since before the evolution of the human race. Specific immune responses, whether humoral or cell-mediated, are very effective—but slow. Interferons and other nonspecific responses are more rapidly mobilized by the body, but only after infection is established. Beyond this, there are hints that cells accessible to foodborne viruses in vivo are not exact counterparts of cells grown in vitro to support viral replication. This means that numbers of infectious units measured in laboratory cell cultures (when this can be done) may not relate closely to the numbers of peroral infectious doses in a viral suspension or a contaminated food (3). A great deal remains to be learned about how ingested viruses initiate infections via the digestive tract, which cells of the digestive tract have receptors to which viruses can attach productively, and whether "decoy" receptors that degrade viruses without allowing infection to occur exist in vivo as they do in vitro (10,11).

The targets of enteric viruses are essentially in the small intestine, with the occasional exception of enterovirus infections of the pharynx. Some enteric viruses infect as far cephalad as the duodenum, whereas others evidently parasitize the ileum. The esophagus, stomach, and colon are not known to be involved; and the hepatitis A virus is sometimes said to pass directly from the lumen of the digestive tract to the liver, without infecting the intestinal lining at all. Given the high attack rates in some recorded food-associated outbreaks of hepatitis A, it is difficult to imagine that such a seemingly inefficient process of infection would prevail; further studies are certainly needed.

**Food as a vehicle**

Vehicles (food and water) offer two potential advantages to an infectious agent, as compared to direct person-to-person transmission. First, the vehicle may transport the agent to new groups of potential hosts, who either lack preexisting immunity or are particularly susceptible in some other way. Second, the vehicle itself may facilitate transport of the ingested infectious agent to the susceptible area of the digestive tract. The first of these certainly applies to viruses; the second may or may not.

Because the source of viruses in the food vehicle is human feces, contamination may come from the unwashed hands of an infected person, from sewage, and sometimes perhaps from direct fecal deposition. Reports abound of outbreaks of foodborne viral disease in which food handlers were implicated (4). Approximately 1,000 of those reported to be infected with hepatitis A virus in the United States annually are food handlers by trade, but only one or two recorded outbreaks per year are traced to these people. Those who handle food professionally are often in a position to contaminate food eaten by more people, but those who handle food "incidentally"—to be eaten by family or guests—have also been the sources of contamination in significant outbreaks. Whether the source person was in the incubation phase, inapparently infected, or overtly ill, hepatitis A virus in a food got there because the infected person failed to wash all of the virus-containing feces off of his or her fingers. Although disposable gloves—properly used—may have some value, hands-on contamination of food can only be certainly prevented by proper hand washing, or by design of food handling tasks so that hands do not contact the food at all.

Sewage is another matter. Feces on fingers must comprise a small fraction of an infected person's total fecal output. The majority of virus-containing feces are typically disposed via water-carriage toilets and thus are present in sewage. Indeed, fecal indicators (bacteria) are typically the best available predictors of the presence of viruses where sewage contamination is suspected. Therefore, sewage at surfaces before treatment or is discharged without having been treated represents a major threat of transmitting viruses—directly or via food. The ability of sewage treatment and disinfection to eliminate viruses has been questioned from time to time; but it is clear that the greatest threat is from sewage that is discharged, accidentally or intentionally, without treatment.

**Primary contamination of foods occurs before harvest.** Shellfish that contain viruses from sewage contamination fall into this category (2). Secondary contamination occurs during processing, storage, distribution, or final preparation. Most hands-on contamination falls into this category, but there is a certain incidence of foodborne viral disease outbreaks involving fresh or frozen produce in which it is not certain whether contamination occurred before, during, or after harvest. Whether such contamination might derive from field workers who have neither toilet nor handwashing facilities remains to be seen, but the risk is clearly substantial.

**Outbreaks and secondary spread**

Unlike outbreaks, sporadic (single-case) viral illnesses are extremely difficult to attribute to transmission via food. Prospective studies of the association of hepatitis A with eating raw shellfish have probably yielded valid results, but most other food vehicles could not reasonably have been studied in the same way.

Prevailing wisdom is that most transmission of enteric viruses occurs by contact, directly from person to person. This has led to the proposition that even a small outbreak (or perhaps a single primary infection) of foodborne viral illness might lead to a fulminating outbreak of viral disease within a community. This might occur within communities that were so isolated that food afforded the only means by which a new virus could be introduced, but most introductions to isolated communities seem to have resulted from the arrival of an infected person who transmitted the virus by contact.

On the other hand, it is noteworthy that secondary (contact-transmitted) cases are typically few during a recognized outbreak of foodborne viral disease, so that such outbreaks tend to be self-limiting (4). This is not to say that no one with a primary (food-acquired) illness ever trans-
mits their infection to someone else by contact. It simply suggests that general standards of sanitation and personal hygiene in developed countries are adequate to limit secondary transmission of previously foodborne viruses; whereas, contact transmission of virus in a day care center is likely to continue because feces of infected infants tend to be disseminated more freely than food-handler feces. Secondary transmission of hepatitis A during food-associated outbreaks has been aggressively investigated—both in situations where immune serum globulin was administered to contacts of those with food-associated infection and where no such precaution was taken; and secondary infections have been found to be equally rare in either situation.

**Risk assessment**

**Numerical** risk assessment is an approach that starts with a mathematical formula and inserts specific values—gleaned from selected, published research—for the independent variables (9). The intent is to provide decision-makers with information of the following type: "If you do this (or fail to do that), the result will be this number of human illnesses that would otherwise not have occurred." I understand and accept the rationale, but my reservations regarding the applicability of present research data to virus transmission via food lead me to consider numerical risk assessment beyond the scope of this paper.

Instead, let us consider a situation in which a quantity of food is already at risk, or a decision must be made on the basis of local circumstances. A recurrent inquiry is: What precautions are appropriate when a U.S.-based food company expands its operations into the “developing world”—particularly the least affluent countries? In such instances, it is known that—for the time being—those who survive to the age of 5 years are probably immune to hepatitis A (5) and are probably no more likely than food handlers in developed countries to harbor other potentially foodborne viruses. Key concerns are not with viruses, but with general hygienic measures to prevent introduction of parasites and bacteria into food that is offered for sale both to local residents and to tourists coming from more affluent nations.

Alternately, a potential source (infected person or persons, sewage, etc.—in the United States) of viral contamination of food is identified, and a regulatory agency or food company must do an ad hoc risk assessment, imposing generalizations sparingly onto the present set of observations. Where an infected worker is involved, one starts with the nature of the worker’s duties and the potential period of virus shedding, relative to days worked handling food. Judgments may also be required regarding the quality and reliability of the worker’s personal hygiene—supervisors and coworkers may have different impressions than those voiced by the worker (12). The fate (sale, reprocessing, destruction, etc.) of a large quantity of detained food may rest on this style of risk assessment. Unfortunately, contamination by infected, professional food handlers does not account for the majority of outbreaks of foodborne viral disease; risks from an infected amateur food handler are usually recognized only after an outbreak of disease among the family that attended a reunion or patrons of a benefit food sale. At the most banal level, the risk of virus contamination by an infected food handler may depend on the availability and likelihood of use of basic-hand washing facilities.

**Risk management—prevention**

Clearly, the risk of virus transmission via foods is best minimized by keeping human feces, at any level, out of food. However, immunization to eradicate some potentially foodborne viruses is also a possibility. The most devastating of foodborne viral diseases is hepatitis A. Once vaccines against hepatitis A that are licensed in Europe become available in North America, food companies would probably do well to have all workers immunized against the virus at company expense (13). This alone will not prevent all transmission of hepatitis A via foods, but it will preclude some such transmission and may prevent the needless destruction of foods at risk of having been contaminated by an infected handler. Vaccines against rotaviruses, but perhaps not against the Norwalk-like viruses, may also be of some value.

Beyond this, all workers who handle food, pre- or postharvest, need to have access to proper toilet and handwashing facilities and to be supervised in such a way as to ensure that the facilities are used. Conditions under which foods are harvested are the concern of all who subsequently deal with the food, not just those who supervise the field work. Sick leave—paid absence from work during illness—is another important safety measure for the food industry. And, amateurs must be apprised that, even though they are not paid for their food-handling services, hygienic lapses on their part can readily make people, including their own friends and family, sick.

Feces properly disposed via a water-carriage toilet must not be allowed to contaminate food, nor water other than the sewage itself. This requires proper transport and treatment of the wastewater before discharge, regardless of whether a private or public treatment facility is used. The antiviral efficiency of sewage treatment is questioned from time to time, but fully treated effluents have not yet been shown to have contributed to foodborne or waterborne viral disease. Alternatives to water-carriage toilets are available for feces disposal, but all require diligence to ensure that infectious agents such as viruses are not transmitted as a result of careless discharge.

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**REFERENCES**