REVIEW

Viruses of foodborne origin: a review

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Abstract: Enteric viruses are major contributors to foodborne disease, and include adenovirus, astrovirus, rotavirus, sapovirus, hepatitis A and E viruses, and norovirus. From a foodborne transmission perspective, norovirus is the most important; however, hepatitis A is associated with more serious illness. Foodborne viruses are transmitted through contaminated food, but also in combination with person-to-person contact or through environmental contamination. These viruses survive well in the environment, are excreted in abundance in feces, and have a low infectious dose, all of which facilitate spread within a community. Many colonized individuals experience mild gastroenteritis lasting a few days or are asymptomatic, although viral excretion may continue over days or weeks. Severe illness tends to be restricted to the very young and elderly, especially in closed communities such as schools and homes for the aged. In the USA, norovirus is considered to be responsible for two thirds of all foodborne illnesses occurring in a wide range of institutional settings, including schools, colleges, child care centers, cruise ships, prisons, and soldiers on campaign. Norovirus outbreaks also occur at one-time events, such as banquets, wedding receptions, birthday parties, and potluck meals, and are most often introduced by infected food workers producing, preparing, or serving food, or through self-service buffets. Often the infections are introduced from the community into institutions where they can infect the majority of residents unless quickly controlled. In countries where economic assessments have been completed, there is a high cost for prevention, control, and treatment of infections. Control measures are limited, but include proper clean-up and disinfection after vomiting or diarrhea, and prevention of food contact by infected individuals. As diagnostics improve, more foodborne illnesses relating to enteric viruses are expected to be identified, especially in developing countries where there are little data today.

Keywords: foodborne, enteric viruses, shellfish, food workers, prevention, control, ready-to-eat food

Introduction

Foodborne viruses are transmitted via contaminated food, but also in combination with person-to-person contact or via contamination of the environment, eg, water.[1] These viruses include human adenovirus (HAdV), human astrovirus (HAstV), norovirus (NoV), and human rotavirus (HRV), which infect parts of the intestinal tract, eg, the epithelial lining of the duodenum. Hepatitis A and E viruses (HAV and HEV) enter the bloodstream through the epithelium and from there to the liver hepatocytes and macrophages.[2,3] The pathology of sapovirus (SaV) and Middle East respiratory syndrome coronavirus (MERS-CoV) have not been well described. There are no known foodborne outbreaks from enteroviruses. From the limited available information, foodborne viruses have a low infectious dose and are dispersed in stool or emesis in

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high numbers (up to 10^{11} particles per gram of stool).[1] Food contaminated by fecal sources, such as shellfish harvested in polluted waters, fruits, and vegetables irrigated with water containing sewage or picked by infected workers, and ready-to-eat foods prepared by infected handlers are means of infection. Enteric viruses cannot multiply in food or water, but are generally very environmentally stable outside the host and are acid-resistant.[1] There has been limited success growing human enteric viruses in cell culture, mainly primate cells, but culturable surrogates for human viruses such as feline and murine caliciviruses for NoV and porcine enteric calicivirus for SaV are used for research. Enzyme-linked immunosorbent assay and reverse transcriptase polymerase chain reaction (RT-PCR) assays are used for routine detection in clinical specimens. International Organization for Standardization Technical Specification 15216:2013[4] describes a method for quantification of levels of HAV and NoV genogroup I (GI) and II (GII) RNA from test samples of foods, food surfaces, or food contact surfaces; target sequences within the viral RNA are amplified and detected by RT-PCR. This approach can be used for other human viruses after appropriate validation and using target-specific primer and probe sets. NoV and HAV are considered to be the main foodborne viruses of concern,[1] but as surveillance improves, other enteric viruses may be considered as emerging foodborne pathogens. The very young and elderly are more likely to be severely affected and have a high propensity for recurrent infectious intestinal illness.[5] The characteristics of viruses that have been implicated in foodborne disease are listed in Table 1.

Foodborne virus outbreaks

During the past century, most foodborne disease illnesses were attributed to bacterial pathogens; however, with better diagnostic technology and investigative epidemiology, it is now accepted that some enteric viruses are major contributors as well. However, some of these are only transmitted by food occasionally. For instance, Scallan et al[6] estimated that <1% of HAstV, HRV, and SaV cases are foodborne compared with 7% for HAV cases and 26% for NoV cases; only 41% of HAV and <1% of NoV are considered to be travel-related. Since the introduction of HRV vaccines, NoV has become the leading cause of medically attended acute gastroenteritis in US children, and is associated with nearly one million health care visits annually.[7] In Canada, NoV causes the greatest number of foodborne illnesses, accounting for 65% of the estimated 1.6 million cases reported for 30 known pathogens from 2000 to 2010.[8] Other enteric viruses represent relatively few

cases: SaV, 0.59%; HRV, 0.26%; adenovirus, 0.23%; HAstV, 0.12%; and HAV, 0.02%. These percentages are very similar to those of Scallan et al,[6] who estimated that there were 9.4 million foodborne illnesses caused by 31 pathogens in the USA, of which 58% were caused by NoV; other viruses were much lower (SaV, HRV, and AstV each at 0.16%, and HAV at 0.02%). These pathogen-specific results are similar to estimates of other countries (Australia, the Netherlands, New Zealand, and France) in that NoV is now considered to be the main contributor to the burden of foodborne diseases,[9–12] with the proportion foodborne for NoV ranging from around 11% in the UK[13] to 39% in New Zealand.[11]

Norovirus

NoV is the most frequently reported foodborne pathogen in many countries, although still underestimated.[10–14] The Centers for Disease Control and Prevention reports that 50% of foodborne outbreaks are attributed to NoV.[15] NoV causes an estimated one in 15 US residents to become ill annually as well as 56,000–71,000 hospitalizations and 570–800 deaths, predominantly among young children and the elderly. Studies in the UK and the Netherlands showed that NoV was responsible for 3.6%[13] and 15.6%[12] of foodborne illnesses, respectively. NoV-associated deaths are rare, with an incidence of 0.19–0.40 deaths per 10,000 population.[15] Although NoV is often spread through person-to-person contact, foodborne transmission can contribute to widespread exposures, resulting in large outbreaks. Foods commonly involved in NoV outbreaks are leafy greens (such as lettuce), fresh fruits, and shellfish. Most foodborne NoV outbreaks occur in food service settings like restaurants[15] and large catered events. Infected food workers can transmit NoV by touching ready-to-eat foods, such as raw fruits and vegetables, or foods that will not be cooked further, with their bare, inadequately washed hands. Unfortunately, it is not just workers with clinical symptoms who transmit NoV, since asymptomatic food handlers were found to be a major contributor to Danish outbreaks,[16] where contamination occurred with equal frequency during production, preparation, and serving, and at self-serve buffets. Some of the workers had been in contact with ill household members before handling the food and remained asymptomatic; others developed symptoms shortly after or were post-symptomatic. However, food may be contaminated by NoV at any point during production, shipping, handling, or preparation. NoV outbreaks can result from fecal contamination of foods at their source, eg, oysters harvested from contaminated water, environmental sources with leafy

greens, and raspberries spray-irrigated with contaminated water. Lettuce has been implicated in many NoV outbreaks,[17] eg, in Michigan in 2005 after a national submarine sandwich franchise restaurant catered four luncheons with a total of 88 ill.[18] In Denmark, eleven outbreaks with 260 cases were all linked to lettuce imported from France in 2010.[19] In Europe in 2012, 14% of reported foodborne outbreaks were attributed to viruses, predominantly NoV; mixed foods and buffet meals were the main foodborne vehicles, followed by shellfish, vegetables, juices, and bakery products.[20] Of particular note was a NoV outbreak in Germany associated with frozen Chinese strawberries mainly distributed through one large catering company, with 10,950 people, primarily school/kindergarten children, infected and 38 hospitalized.[21] The acid resistance of NoV and HAV might explain their association with outbreaks where acid fruits were implicated, eg, raspberries.[22] NoV outbreaks have also been caused by contaminated water from sewage in wells and in recreational water settings, eg, beaches, pools, and lakes.[15]

Over 90% of diarrheal disease outbreaks on cruise ships are caused by NoV, which is especially challenging to control on ships because of close living quarters, shared dining areas, and rapid turnover of passengers between cruises.[23] Before embarkation, NoV can be brought on board in contaminated food or water or by passengers who are already infected. Repeated outbreaks on consecutive cruises may result from infected crew or environmental contamination not sufficiently decontaminated since NoV can persist on surfaces and is resistant to many common disinfectants. Being aware of the risks, crews try to prevent infected persons from boarding using screening procedures, with limited effectiveness. Many cruise ships do not permit buffet self-service until 24–48 or more hours have elapsed after boarding in an attempt to prevent passenger-to-food transmission.

Overall, the burden of NoV illness is high. Recent estimates in the USA showed that NoV illness costs US $2.0–$3.7 billion annually, and has led to a loss of approximately 5,000 quality-adjusted life-years, making NoV one of the top five costly pathogens causing foodborne enteric illnesses.[24] The highest cost associated with 14 foodborne pathogens is also attributed to human NoV in the Netherlands, where foodborne NoV cases resulted in a burden of 275 undiscounted and 194 discounted disability-adjusted life-years in 2009.[25] NoV gastroenteritis outbreaks cost the English National Health Service US$184 million in one year (2002–2003).[26] This accumulation of evidence underlines the enormous impact of NoV on populations.

Outbreak example: wedding reception

In October 2012, the provincial public health directorate of Salzburg, Austria, reported a NoV outbreak associated with a mushroom dish among guests at a wedding reception.[27] Cases and kitchen workers tested positive for NoV GII.4 Sydney. No food safety training was documented for the employees and the kitchen staff's restroom lacked functioning facilities for hand hygiene. The mushroom dish was prepared on the morning of the wedding and reheated just before serving, with parsley added by hand prior to serving. One of the six NoV-positive kitchen workers was ill with diarrhea the day before and the day of the wedding. He cleaned flatware and dinnerware used for the dinner. The outbreak strain possibly entered the kitchen through this symptomatic kitchen worker and spread through hand contact to kitchen surfaces, dishes, and flatware. The epidemiologically associated dish could have been contaminated directly by the asymptomatic kitchen worker when adding the parsley. The mushrooms could also have been contaminated by contact with flatware or dishes, previously contaminated by the symptomatic kitchen worker during cleaning.

Hepatitis A

Globally, there are an estimated 1.4 million cases of HAV and 200 million asymptomatic carriers annually.[28] In developed countries, with good sanitary infrastructures, the infection rate is low, and many of these countries have instituted an immunization schedule for children and adults traveling to endemic regions.[29] HAV can be transmitted person-to-person, or through contaminated water and food, particularly fruit or ready-to-eat foods that have not been sufficiently heated to inactivate the virus. In non-endemic countries with a low incidence of disease and low vaccine coverage there is a large susceptible population, which regularly receives imported products from HAV-endemic regions. Since some of these products have a long shelf-life, especially if frozen or preserved, the potential is created for extended HAV outbreaks. Frequently when HAV infection has been identified in a food handler, the exposed public is notified and offered immunoglobulin.[29] Although the addition of sanitizers such as chlorine, peroxyacetic acid, and hydrogen peroxide achieve only a marginal reduction of viruses on fresh produce, they are useful to reduce the likelihood of cross-contamination between wash water and fresh produce. Depuration of bivalve molluscs does not necessarily remove infectious viral particles from the meat; HAV and HRV showed <2 log reduction after 4 days of depuration of experimentally

Table 1 Characteristics of the diseases caused by foodborne viruses

Virus, discovery date, classification	Structure and size	Transmission and infective dose	Survival	Incubation period and symptoms
NoV, 1968 (Norwalk virus); single-stranded RNA, non-enveloped viruses in the genus *Norovirus*, family Caliciviridae; five NoV genogroups (GI–GV) have been described, of which only GI and GII, and more rarely GIV, infect humans Nine genotypes have been proposed within GI and 22 within GII, with GII.4 (Lordsdale) being the most prevalent genotype worldwide in epidemics Several new genogroup variants can occur during epidemics	Single-stranded RNA genome of 7.3–7.6 kb, with a diameter of 28–35 nm	Fecal–oral; epithelial cells invaded; <100 viral particles	Survives on produce, ham, mussels, and food contact surfaces for several days; inactivated by ultraviolet light and high pressure processing; infective particles found when a NoV stool filtrate was subjected to a pH of 2.7 for 3 hours; 200 Gy reduced FCV by 1.6 log; a maximum of 1–2 log removal of viruses could be achieved by washing produce with water; NoV survives very well on doorknobs, cutting boards, and foods like lettuce and ham for over 15–30 minutes; however, there was a significant reduction in viral titer after 7 days for all samples at room temperature and 4°C. Norwalk virus and FCV were detected on stainless steel, formica, and ceramic coupons for up to 7 days post-inoculation; for FCV, there was an approximate 6–7 log drop in virus titer over the 7-day evaluation period. Transfer of both Norwalk virus and FCV from stainless steel surfaces to lettuce occurred with relative ease, especially if the lettuce was wet. 20 FCV dried onto glass coverslips and at 4°C had a 4.75 log reduction over 56 days. Survival was lower at room temperature, but still prolonged. These studies confirm lengthy NoV persistence on common food preparation surfaces and RTE foods.	0.5–3 days. Nausea, vomiting (often projectile), diarrhea, and abdominal pain, sometimes headache, myalgia, and low-grade fever; immunocompromised at greatest risk for severe infection; hospitalizations and deaths more likely in outbreaks associated with GII.4 viruses
HAV, 1973; genus *Hepatovirus*, family Picornaviridae; one serotype and seven different genetic groups (four humans and three simian); six human subtypes have been described (IA, IB, IIA, IIB, IIIA, IIIB); most human isolates are of genotype IA; Genotype III has been isolated from both humans and owl monkeys	Icosahedral, non-enveloped virus with a diameter of 27–32 nm	Fecal–oral; HAV enters the bloodstream through the epithelium of the oropharynx or intestine. The blood carries the virus to the liver, where it multiplies within hepatocytes and macrophages. Virions are secreted into the bile and released in stool. The infectious dose is 10–100 viral particles	HAV is resistant to pH 1 and survives for one hour at 60°C. HAV appears to be relatively resistant to free chlorine, especially when the virus is associated with organic matter; it persists in dried feces, the environment, produce, mussels, and on food contact surfaces for a month at room temperature. HAV on lettuce survives at 4°C for up to 12 days in ambient air and under various modified atmospheric conditions HAV is stable for 90 days on frozen raspberries, blueberries, strawberries, parsley, and basil	2–4 weeks (15–50 days) Acute, not chronic infection, characterized by sudden onset of fever, malaise, nausea, anorexia, fatigue, and abdominal discomfort, followed in several days by jaundice. Asymptomatic or mild infections frequent, but typically foodborne HAV is a much more severe and long-lasting illness than gastroenteritis; high mortality with fulminant hepatitis, especially in immunocompromised persons

Duration and therapy	Shedding	Prevention and control	Detection methods	Outbreaks and food implicated	References
2–3 days (2 weeks); Typically mild, self-limiting	Shed in stools and vomitus, lasting 10 or more (28) days; 30 million virus particles can be expelled in a single vomiting incident; the shedding of virus in stools begins before onset of symptoms (prodromal stage), typically peaks (at about 10^{10} viral particles per gram of stool) on day 4 following exposure, and may persist for many weeks in the general population, or for months in immunocompromised individuals and very young children; in children, NoV gastroenteritis tends to be less severe than HRV gastroenteritis	Good hygienic practices; prevent infected workers from preparing food; RTE foods, eg, hors d'oeuvres with much handling at greatest risk; avoid or thoroughly cook shellfish	ELISA, RT-PCR	Often the infections are introduced from the community into various settings, especially during winter when outbreaks are common leading to temporary closures of hospitals and nursing homes. In the USA, >60% of all NoV outbreaks occur in long-term care facilities. This contrasts with the settings reported in Europe, Japan, and other high-income settings, where outbreaks in acute-care hospitals are common and roughly equal in number to outbreaks in long-term care facilities; however, what proportion of these outbreaks are foodborne is unknown. Person-to-person transmission most frequent but many foodborne and waterborne outbreaks reported, mostly in foodservice settings like restaurants and large catered events, and institutional settings, eg, schools, universities, child care centers, sporting events, prisons and troops overseas, banquet halls, wedding receptions, and family social events like birthday parties and potluck meals, where people eat food prepared by others. Many outbreaks reported from oysters harvested from polluted waters	3,10,14–16, 20,22,47, 94–99
Two (6) months. No specific antiviral drug treatment	Peak shedding 2 weeks before onset of jaundice, but HAV can be excreted up to 5 months post infection. Infections most likely in winter and spring months; HAV is excreted in large quantities, eg, 10^6–10^8 per gram, approximately 11 days prior to appearance of symptoms and 36 days after recovery; many virions excreted in stools of asymptomatic persons as well	Hepatitis A can be prevented by vaccination, good hygiene and sanitation, and avoidance of shellfish from polluted waters; bacterial indicator testing of harvest areas and depuration of shellfish are of limited value for detected or removing enteric viruses. Immunoglobulin given to contacts of an infected food worker. Proper hand hygiene essential; separate vaccines for children and adults; lasts 20 years	Detection of IgM antibody to capsid proteins 5–10 days before onset of symptoms and persist for 6 months ELISA	RTE foods and bivalve molluscs, associated with foodborne disease outbreaks, some large; strawberries, tomatoes, lettuce, cole slaw, green onions, sushi, oysters, crab, grapes, cake, burritos, deli meat, salsa, French fries, milkshake, ice, unspecified sandwiches and salads	2,3,22,29, 47,69,95, 100–104

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Table I (*Continued*)

Virus, discovery date, classification	Structure and size	Transmission and infective dose	Survival	Incubation period and symptoms
			Inactivated by heating to >85°C for one minute, (however, since it is more common to heat bivalves until the shells are opened, which in clams is obtained at 70°C after 47±5 seconds, HAV and other enteric viruses probably survive); ultraviolet radiation, formalin, ozone, iodine, or concentrated chlorine, and high pressure processing are effective, but modified atmosphere packaging does not inhibit HAV; 3 kGy was needed to achieve a 1 log reduction of HAV on lettuce and strawberries; a maximum of 1–2 log removal of viruses could be achieved by washing produce with water. HAV survives freezing	Hepatitis A represents about one third of all cases of viral hepatitis. Unlike hepatitis B and C, hepatitis A infection does not cause chronic liver disease and is rarely fatal, but it can cause debilitating symptoms and fulminant hepatitis (acute liver failure), which is associated with high mortality
HEV, 1983; HEV is the only member of the genus *Hepevirus*, family Hepeviridae HEV has four genotypes: genotype 1 is regularly found in HEV-endemic areas such as Africa and Asia; genotype 2 in Mexico and West Africa; genotype 3 in the USA, Europe, and Japan; and genotype 4 in Asia. Genotypes 1 and 2 are mainly transmitted by water, while 3 and 4 are zoonotic genotypes associated with consumption of meat from infected animals	Single-stranded positive-sense RNA genome of 7.2 kb; spherical viral particle 27–30 nm in size	Fecal–oral from water and food, person-to-person transmission uncommon. Unlike HAV found in domestic and wild animals, eg, pigs, rodents, chickens, dogs, cows, sheep, and goats, HEV has also been identified in pets; exposure of pet owners may account for sporadic cases of HEV infection. Foodborne transmission of HEV has occurred via ingestion of contaminated deer, boar, and pig meat. Replication of viral particles occurs in intestinal mucosal cells, but starts in the cytoplasm of hepatocytes; virions are transported with bile from liver tissue to the intestines. The highest infection risk is associated with travel to endemic countries, overcrowded refugee camps, people with chronic liver disease, handling non-human primates, pigs, cows, sheep, and goats; likely some animal cross-species transmission. The infectious dose is unknown	HEV is stable in alkaline and acidic environments, when frozen for more than 10 years, and remains infectious at up to 60°C, suggesting that raw, rare-cooked, or slightly steamed contaminated seafood may transmit HEV to consumers	2 weeks to 2 months. Influenza-like symptoms, abdominal pain, tenderness, nausea, vomiting, and fever in the first phase of 1–10 days. The second phase (15–40 days) with concurrent jaundice, anorexia, hepatomegaly, myalgia, and dark urine is followed by viremia, liver enzyme elevations, antibody seroconversion, and clearing of the virus; typically, disease self-limiting without progression to chronic illness; however, 60% cases of HEV infection in immunocompromised patients after solid organ transplantation develop chronic hepatitis without antiviral treatment

Duration and therapy	Shedding	Prevention and control	Detection methods	Outbreaks and food implicated	References
	Risk factors include travel to endemic areas, sharing a household with a 3–10-year-old child; contact with an HAV-infected person, consumption of bivalve molluscs, and untreated water	There are two vaccines: one containing inactivated HAV, and another containing a live but attenuated virus to protect against HAV in more than 95% of cases for longer than 25 years. IgG administered intramuscularly is used for the prevention of HAV infection. HAV can be eliminated on surfaces by using a solution of 1:100 dilution of household bleach in tap water; foods must be heated to temperatures >85°C for at least one minute to inactivate the virus			
Higher mortality in pregnant women than healthy non-pregnant adults	Humans and other animals excrete a considerable amount of virus early in the acute phase of HEV infection and contribute to maintain the cycle of endemicity	Control of animal waste, run-off, and decontaminated sewage limits spread of HEV to coastal and surface waters/shellfish. Vaccine available in the People's Republic of China	RT-PCR and real-time RT-PCR; EIA, no cell culture	Disease typically transmitted through fecally contaminated water and foods. Genotypes 1 and 2 are mainly transmitted by water, while 3 and 4 are zoonotic genotypes and associated with the consumption of meat from infected animals. Food animals may contain HEV, and high risk foods include undercooked liver or meat from domestic pigs, wild boars, deer, and hare; shellfish in polluted waters	3,36–38, 105,106

(Continued)

Table I (*Continued*)

Virus, discovery date, classification	Structure and size	Transmission and infective dose	Survival	Incubation period and symptoms
HRV, 1973; in the family Reoviridae, seven RV groups (A–G); Group A causes most human disease	Non-enveloped, double-stranded RNA surrounded by a three-layered icosahedral protein capsid; viral particles are up to 76.5 nm in diameter	Fecal–oral, possible aerosol; 1–10 (100) virions needed to infect enterocytes of small intestine	Lasts many weeks in the environment; HRV reduced by 1 log on blueberries and basil after 2 days in frozen storage; HRV inactivated at a pH of 2 at 37°C with a half-life of less than one minute, but not in fruit juice (pH 3.01) stored at 4°C for 3 days HRV SA-11 survived on lettuce, radishes, and carrots for up to 30, 30, and 25 days, respectively, at refrigeration temperature after direct inoculation; however, at room temperature, the survival periods were 25, 4, and 15 days, respectively.	2 (1–4) days; HRV infection characterized by abrupt onset of fever and vomiting followed by watery diarrhea, abdominal cramps, dehydration; more severe for malnourished and immunocompromised; neonatal infections are often asymptomatic, but infant deaths occur, mainly in developing countries; less severe for adults and subsequent infections
HAstV, 1975; genus *Astrovirus*, family Astroviridae; seven established genotypes, correspond with seven serotypes	Non-enveloped, single-stranded, positive-sense RNA which contains three open reading frames; spherical, capsid of about 35 nm with icosahedral protein	HAstV, can infect the epithelium of the duodenum; although initially detected in children's stool, HAstV have been found in the feces of a wide variety of animals, eg, cats, dogs, cattle, deer, pigs, sheep, bats, rats, and poultry	At 4°C, HAstV persists for 60 days desiccated on china and 90 days on paper, shorter time at higher temperatures; survives in fresh water and seawater for many days, but chlorination reduces viability	3–5 days. Vomiting (not as much as with HRV or NoV), abdominal cramps, watery diarrhea, headache, fever, malaise, anorexia; asymptomatic infections occur in children and adults; hospitalization rare; serological studies indicate that most children are infected with HAstV and develop antibodies to the virus early in life, perhaps protecting against later infections; immunocompromised and elderly are at high risk for infections
SaV, 1976; genus Sapovirus, family Caliciviridae; SaV are divided into seven genogroups, four of which (genogroups I, II, IV, and V) contain viruses that infect humans, while GIII, GVI, and GVII infect porcines	Non-enveloped, small single-stranded positive-sense RNA viruses, genome contains two major open reading frames, 30–38 nm in diameter	Fecal–oral route. SaV can be transmitted from person to person via contact with SaV-positive feces, vomitus, or SaV-contaminated materials/surfaces or via contaminated food and drinking water; SaV may enter the food supply at any point along the farm-to-fork continuum, eg, sewage-contaminated waters used for growing or irrigating products consumed raw, such as shellfish and fresh produce; although, like other enteric viruses, most foods are thought to be contaminated by an infected food handler. Likely a low infectious dose similar to that of NoV	Porcine SaV is stable at pH 3.0–8.0 at room temperature for one hour, sensitive to ethanol treatment (60% and 70%) at room temperature for 30 seconds, inactivated by 200 mg/L sodium hypochlorite at room temperature for 30 minutes, inactivated by heating at 56°C for 2 hours, but survives on lettuce for a week at 4°C	0.5–2 days. Diarrhea and vomiting often accompanied with fever, nausea, and abdominal cramps

Duration and therapy	Shedding	Prevention and control	Detection methods	Outbreaks and food implicated	References
3–8 (up to 22) days; self-limiting, therapy focused on replacement of fluids and electrolytes, given that no antiviral agents are currently available. Probiotics decrease diarrheal duration	10^{11} particles/stool. Virus typically shed in feces for 4 days although excretion for >30 days has been reported in immunocompromised patients	Good hygiene not enough; Oral vaccine for infants	ELISA, RT-PCR, rarely cell culture	Outbreaks of HRV Group A diarrhea are common among hospitalized infants, young children in child care centers, and elderly people in nursing homes; foodborne and waterborne outbreaks rare: RTE food contaminated by food preparers: sandwiches (chicken, tuna, turkey), salads (chicken, tuna), conch, deli meat, multiple foods	22,43,47, 69,107–110
2–3 (9) days; recurrence possible 7–10 days later	Volunteer studies showed that many are asymptomatic but with diarrhea profuse shedding of HAstV can occur	Hands, fomites, and contaminated water are among the principal vehicles for the transmission of enteric viral diseases and this would apply to HAstV; good hand hygiene, decontamination of food contact surfaces, and avoidance of shellfish from polluted waters reduce the risk of HAstV foodborne and waterborne infections	RT-PCR. ELISA, cell culture, eg, Vero cells	Common source and person-to-person transmission. Fecally contaminated fomites have been implicated in outbreaks in institutions, eg, child care centers, hospitals, nurseries, schools and military facilities; foodborne infections rare, fecally contaminated salad items; indirect evidence of HAstV causing waterborne gastroenteritis	45,47,69, 111,112
2–6 days. Self-limiting; therapy for dehydration and electrolyte imbalances; no vaccines	10^{5}–10^{11} viral copies per gram stool. Virus typically shed in stool for up to 2 weeks after illness onset, although some infected individuals may shed high volumes of virus ($\geq 10^{5}$ viral copies per gram stool for as long as 4 weeks)	Shellfish should be adequately cooked and fresh produce washed thoroughly before consumption, proper hand hygiene, and disinfect potentially contaminated environmental surfaces with a chlorine bleach solution with a concentration of 1,000–5,000 ppm for other approved disinfectants	RT-PCR, ELISA	SaV outbreaks occur throughout the year in all age groups in various settings, such as child care centers, kindergartens, schools, colleges, hospitals, nursing homes, restaurants, hotels, wedding halls, and ships; occasional foodborne outbreaks; boxed lunches, meat balls, ham; SaV at 10^{4} copies per gram of digestive tissue in oysters, cockles, clams; up to 10^{5} copies per liter in wastewater treatment plant influent; 10^{9} copies per liter in untreated wastewater	52,53, 69,113

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Table 1 (*Continued*)

Virus, discovery date, classification	Structure and size	Transmission and infective dose	Survival	Incubation period and symptoms
AiV, 1989; genus *Kobuvirus*, family Picornaviridae	Single-stranded positive-sense RNA molecule with 8,251 bases excluding a poly(A) tail; it contains a large open reading frame with 7,302 nucleotides; similar structure to HAstV	Fecal–oral route. Attachment of the virus to host receptors mediates endocytosis of the virus into the host cell; the capsid then undergoes a conformational change and possibly opens a pore in the host endosomal membrane and the viral genomic RNA penetrates into the host cell cytoplasm	Survives in the environment but inactivated by ultraviolet light; may survive high pressure processing at 600 MPa for 5 minutes	0.5–2.5 days. Diarrhea, vomiting and abdominal cramps; children may be hospitalized
MERS-CoV, 2012; Arabian Peninsula, lineage C of *Betacoronavirus*, family Coronavirinae	Enveloped virus with a positive sense single-stranded RNA genome and a nucleocapsid of helical symmetry; genome contains 30 kb nucleotides and 10+ plus open reading frames	Aerosols most frequently, but possibly through consumption of dromedary camel products	Coronoviruses are stable in feces and urine at room temperature for at least 1–2 days; heat and disinfectants destroy them	2–14 days. Fever, cough, shortness of breath, evidence of pulmonary parenchymal disease (eg, pneumonia or acute respiratory distress syndrome); mortality rate of 30%
HAdV, 1953; genus *Mastadenovirus,* family Adenoviridae; 51 HAdV serotypes, further subdivided into six species or subgroups A–F; subgroup F HAstV types 40 and 41 responsible for gastroenteritis; there are also non-human AdV	Non-enveloped viruses with a diameter of 70–100 nm, double-stranded, linear DNA displaying genome sizes of 34–37 kb surrounded by a icosahedron with fiber-like projections	Aerosol into either the respiratory or gastrointestinal tracts (infects the mucosa of the duodenum), the oropharynx or conjunctiva; fecal–oral spread, including contact with recreational freshwater or tap water, infected tissue, airflow filters, fomites, or environmental surfaces; decontamination with 85%–95% ethanol for at least 2 minutes or with NaOH for 10 minutes	Stable after several weeks in moisture-free environments, and resistant to many disinfectants	5–9 (2–14) days; acute febrile respiratory disease, gastroenteritis, infantile diarrhea, hepatitis, keratoconjunctivitis, meningoencephalitis, cystitis, upper and lower respiratory tract infections, and myocarditis; immunocompromised at greater risk from serious illness
Enteroviruses, most known for many years. RNA viruses of the Picornaviridae family, are ubiquitous pathogens which include more than 70 different serotypes of polioviruses, Coxsackievirus group A and group B viruses, and echoviruses group; poliovirus is the virus on main concern but is almost eradicated today	Morphologically all enteroviruses are alike: small, ether insensitive viruses, single-stranded RNA genome, and the nucleocapsid has an icosahedral symmetry, and is naked	Humans are the only known natural hosts and fecal–oral is the most common route of transmission; viruses replicate in the lymph nodes of the respiratory or gastrointestinal system; an initial minor viremia results in spread to secondary sites, eg, heart, liver, and skin, central nervous system; as antibodies develop, viremia ends and the clinical recovery begins	Poliovirus, echovirus, and Coxsackievirus remained infectious for 2 to >12 days on painted wood, glass, and cotton fabric, with greater survival being observed if the inoculum also contained coliform bacteria, protein, fat, and dust particles; enteroviruses can survive in soil, sludge, vegetables, and freshwater sources for prolonged periods of time; poliovirus titer was reduced by 3 log after 28 days in seawater; 0–1 log decline on lettuce, green onions, white cabbage, strawberries and raspberries at 4°C over 15 days; polio survived in crabs and oysters for many days	Fever, vomiting, diarrhea, and malaise; manifestations associated with specific viral agents include hemorrhagic conjunctivitis, pharyngitis, pleurodynia, herpangina, hand-foot-and-mouth disease, paralysis, hepatitis, myocarditis, pericarditis, encephalitis, aseptic meningitis, and multi-organ failure

Abbreviations: NoV, norovirus; Ig, immunoglobulin; FCV, feline calcicivirus; RTE, ready-to-eat; HRV, human rotavirus; ELISA, enzyme-linked immunosorbent assay; AiV, Aichi virus; SaV, sapovirus; EIA, enzyme-linked immunosorbent assay; HAdV, human adenovirus; HAstV, human astrovirus; HAV, hepatitis A virus; HEV, hepatitis E virus; MERS-CoV, Middle East respiratory syndrome coronavirus; RT-PCR; reverse transcriptase polymerase chain reaction; RQ-PCR, real time quantitative polymerase chain reaction.

Duration and therapy	Shedding	Prevention and control	Detection methods	Outbreaks and food implicated	References
Duration unknown but longer than one day; self-limiting	10^2–10^{12} RNA copies per gram stool	Presumably good hygiene and avoiding uncooked oysters	RT-PCR, cell culture in Vero cells	Widespread in environment, particularly wastewaters; outbreaks from oysters in Japan, and France; outbreak of unknown origin occurred in Germany	55,98,114
Anti-viral drugs have some effect	Patients can shed the virus after resolution of symptoms, but the duration of infectivity is unknown. Patients are not contagious during the incubation period; asymptomatic cases might not be contagious	General hygiene, face masks when working with camels; cooking or avoiding consuming camel products. No vaccines	RT-PCR of sputum, feces, and urine	Camels and camel products, eg, milk and possibly meat; limited person-to-person transmission	61,115,65
1–2 weeks; usually self-limiting but antiretroviral therapy can be used	From <10^6 virus copies per gram stool (low risk of adenoviremia) to 10^6–10^{11} virus copies per gram (high risk of viremia and disseminated disease); 10^2–10^4 viral copies per mL blood	Chlorinate swimming pools; good hygiene practices; live oral vaccine against two types	RT-PCR, RQ-PCR, immunofluorescence staining for antigen detection and viral culture, eg, human lung	Child care centers and in households with young children (infantile diarrhea), summer camps, schools, swimming pools, armed forces bases, nosocomial transmission, occasionally foods: ice, sausage	69,116–118
Antiviral drug treatments; intravenous immunoglobulin may be of benefit for immunodeficient patients with persistent enterovirus infection	Up to 60 days in stool	Avoidance of drinking polluted water. Oral poliovirus vaccine	Viral culture, PCR, and serologic diagnosis	Hand, foot, and mouth disease, conjunctivitis, respiratory illness (Coxsackievirus and enterovirus), viral meningitis (echoviruses); historic waterborne outbreaks from polio virus	47,68,119

contaminated mussels, while HAdV and poliovirus were reduced by at least 3 log.[22] Because shellfish can be held in depuration tanks for only a relatively short period, relaying in pristine waters for weeks could be a good alternative for heavily polluted shellfish.[22,30]

Outbreak examples

Clams

The largest viral foodborne disease outbreak ever documented occurred in Shanghai, People's Republic of China, in 1988, with almost 300,000 cases associated with consumption of clams harvested from newly discovered clam beds in sewage-polluted waters.[31] A risk assessment applied to two HAV outbreaks in Valencia, Spain, associated with frozen coquina clams imported from Peru in 1999 (184 cases) and 2008 (100 cases) showed the likelihood of infection.[32] Both outbreaks lasted several months, with clams from different shipments being consumed. These bivalve molluscs complied with European Union standards, based on the numbers of *Escherichia coli* in shellfish meat, but *E. coli* is not necessarily a reliable indication of enteric viruses in molluscan shellfish or their waters. Very similar HAV sequences were detected in clinical and bivalve samples from both outbreaks. The authors estimated that from the 1999 outbreak, there were 1–10 infectious units per gram after light cooking of clams with attack rates of 0.12–0.57, assuming a single serving of 60 g of shellfish. A risk assessment showed that, as to be expected, the attack rates decreased the more the clams were cooked, eg, for the 1.2×10^5 genome copies in a May 2008 shipment these were 0.91 (raw), 0.43 (lightly cooked), and 0.21 (well cooked). Based on national epidemic data, HAV cases were also likely associated with these clams in Peru.

Green onions

The most widespread HAV outbreak in the USA affected at least 640 people with four deaths in north-eastern Ohio and south-western Pennsylvania in late 2003 arising from green onions served in salsa at a restaurant in Monaca, Pennsylvania; the onions were likely contaminated at source in Mexico.[33]

Semidried tomatoes

In 2010, 59 cases of non-travel-associated illness with genotype I, subtype B (IB) strains of HAV in France were linked with most cases consuming semidried tomatoes from one of three different sandwich shop chains, traced back to a supplier in France that imported frozen semid-

ried tomatoes from Turkey.[34] Three other HAV outbreaks caused by highly similar IB strains were associated with eating semidried tomatoes in Australia in 2009 and in the Netherlands in 2010. The investigation showed that a foreign supplier was likely, and that the diffuse pattern of distribution of cases pointed to a contamination source further back in the food production chain; contaminated water could have been used during cultivation of the tomatoes, as described for a green onion outbreak.[33] It is possible then that all four outbreaks could have originated from a Turkish farm operation.

Pomegranate arils

An outbreak of HAV genotype I subtype B infection in 165 individuals occurred in ten US states in 2013 associated with pomegranate arils imported from Turkey where this genotype is common.[35] Sixty-nine individuals were hospitalized, two had fulminant hepatitis, and one required a liver transplant.

Frozen berries

In June 2013, frozen berry mix containing fruit from the USA, Argentina, Chile, and Turkey purchased by approximately 240,000 people in the USA was subject to recall after at least 158 people were infected with HAV, 69 of whom were hospitalized;[2] the isolated HAV strain is known to circulate in North Africa and the Middle East but rarely in the USA.

Hepatitis E virus

The World Health Organization reports over 20 million HEV infections annually with 56,600 related deaths, mainly associated with contaminated water, with the highest prevalence in East and South Asia.[28,36] In industrialized regions, although the incidence of clinical HEV in humans is low, the seroprevalence of antibodies against HEV is relatively high, indicating a high proportion of subclinical disease and/or underdiagnoses.[37] Although some exposure may arise from travel to endemic regions, HEV can be acquired domestically. Detection of HEV in pork liver sold in retail locations has been reported in Japan, the USA, and the Netherlands.[37] Foodborne HEV outbreaks have been reported, usually from the consumption of raw or undercooked meat. Locally acquired HEV infections have increased in the UK since 2010. A case-control study investigated the association between consumption of pork products, eg, pies, ham, and sausages, and HEV infection; cooking practices for processed pork may be inadequate, eg, <70°C for 20 minutes to prevent HEV transmission.[38] The following outbreaks

demonstrate how HEV is transmitted through a variety of contaminated foods.

Outbreak examples

Sausage

In 2007, in Corsica, France, seven of 13 individuals who ate raw figatellu, a traditional sausage made with pig liver and commonly eaten raw, were identified with acute or recent HEV infection. Genotype 3 HEV sequences were recovered from seven sausages purchased from supermarkets in southeastern France and were genetically linked with patients who ate raw figatellu.[39]

Venison

An HEV outbreak was reported from Japan in 2003 associated with consumption of undercooked deer meat 6–7 weeks before symptom onset. The HEV nucleotide sequences in the remaining meat matched those from patients and also wild boar meat in a separate study. Family members who did not eat the meat, or ate very little, did not become infected.[40,41]

Shellfish

Four vacationers reported acute HEV infection upon returning from a world cruise to the UK in 2008. Investigation revealed 195 of 789 persons were seropositive for HEV and 33 had immunoglobulin M levels, indicating recent acute infection (eleven were symptomatic). Analysis showed significant association between acute HEV infection and being male, drinking alcohol, and consuming shellfish while on board, demonstrating this was likely a common source foodborne outbreak.[42] The type of shellfish could not be specified, but could have arisen from European shipments contaminated by polluted waters and brought aboard at Southampton.

Rotavirus

HRV is among the leading causes of diarrhea and dehydration in children worldwide, particularly group A.[3] Group B rotavirus, also known as adult diarrhea rotavirus has caused major epidemics of severe diarrhea affecting thousands of persons of all ages in the People's Republic of China. Group C rotavirus has been associated with rare and sporadic cases of diarrhea in children in many countries; however, the first outbreaks were reported in Japan and England. In the USA, the occurrence of rotavirus disease has dropped considerably since introduction of a vaccine in 2006.[3] It is difficult to distinguish illness caused by HRV or other enteric viruses, although HRV may cause more severe diarrhea and is more frequently associated with fever and vomiting than acute diarrhea caused by other agents. HRV can spread rapidly in child care centers, where children may be asymptomatic. Rotaviruses are rapidly inactivated at a pH of 2 at 37°C, with half-lives of less than one minute. These acidic conditions represent the environment encountered in the stomach; this could account for the fact that HRV disease occurs in children younger than 3 years as the stomach in this age group is characterized by a higher pH.[22] The Centers for Disease Control and Prevention reports over 3 million cases of HRV illness annually in the USA, with an estimate of 15,433 cases that are identified as foodborne.[43]

Outbreak example: campus sandwiches

A HRV outbreak occurred on a Washington DC university campus in 2000, with 108 cases associated with eating tuna or chicken salad sandwiches from a campus dining hall. The investigation reported that 40/44 case patients and 27/40 controls consumed at least one deli sandwich from the dining hall during the outbreak period. It was also noted that six employees reported illness. Group A HRV was recovered from 9/27 stool specimens. The outbreak began as foodborne, but spread by person-to-person contact during the second week.[44]

Human astrovirus

HAstVs are widespread globally.[45] Several large foodborne HAstV outbreaks have been reported.[46,47] Similar to NoV, foods may become contaminated with HAstV at the preharvest stage, as with bivalve molluscs grown in polluted waters or fresh produce, eg, lettuce, green onions, raspberries, and strawberries irrigated with contaminated water. These products usually undergo little if any processing before consumption and act as vehicles for human enteric virus transmission. Serving and chopping utensils or other food contact surfaces play an important role in the institutional spread of HAstV infections, as these viruses can persist on surfaces in high numbers. HAstV is stable in drinking water, fresh surface water, and seawater, indicating another means of transmission. This is demonstrated by an outbreak of gastroenteritis among children and adults who bathed in a Helsinki outdoor wading pool contaminated with NoV and HAstV.[48] Kobuvirus, SaV, and HAstV were detected in stools of cases and food handlers (six, three, and one, respectively) during eleven oyster-related outbreaks between 2002 and 2006 in Japan.[49] In a more recent study, 286 fecal specimens from 88 oyster-associated gastroenteritis outbreaks were examined for the presence of ten human enteric viruses using antigenic or genetic detection methods to determine the prevalence of

these infections.[50] Most were caused by NoV, but in five of these outbreaks, HAstV was the major pathogen. For all these outbreaks, the authors hypothesized that the enteric viruses could have been circulating within a given population and been transmitted through the oysters. The following outbreak gives details of one of the earlier HAstV outbreaks.

Outbreak example: school lunches

HAstV can be an important agent of epidemic acute non-bacterial gastroenteritis in school-aged children and adults in Japan. HAstV was first detected in 1978 among children and staff during an outbreak of gastroenteritis at a Sendai kindergarten. In June 1991, a large outbreak of acute nonbacterial gastroenteritis occurred among students and teachers at ten primary and four junior high schools in Katano City, Osaka, Japan.[51] The outbreak affected more than 4,700 people, lasted 5 days, and was believed to be associated with contaminated food from a common supplier. The 14 school cafeterias had separate water supplies, but received lunches from a common supplier delivering the food prepared in three central kitchens.

Sapovirus

SaV is an important pathogen causing acute gastroenteritis in humans globally, especially in infants and young children; SaV outbreaks have become more frequent recently, especially in Japan.[52,53] Although these examples are Japanese, the causative strains have global links, indicating SaV are widespread and surveillance may not identify these viruses as agents causing outbreaks elsewhere.

Outbreak example: box lunches

In January 2010, the largest Japanese foodborne outbreak of SaV occurred in the Aichi, Gifu, and Mie Prefectures. Illness was strongly associated with eating a delivered box lunch prepared by one catering company in Aichi Prefecture. Gastrointestinal symptoms were reported by 655/3,827 (17.1%) individuals.[54] Symptoms included diarrhea (92.8%), abdominal pain (62.7%), nausea (59.8%), chills (39.2%), vomiting (37.1%), malaise (35.4%), fever (32.5%), and headache (20.2%). Of the 655 cases, 350 (53.4%) developed gastrointestinal symptoms 24–48 hours after eating the lunch. SaV genotype I.2 was detected in seven of nine people who became ill and in seven of 52 catering company food workers; all were negative for NoV and enteropathogenic bacteria. These SaV outbreak strains showed 99.5% nucleotide sequences identical to the strain detected in two simultaneous gastroenteritis outbreaks in school children

in Hokkaido, Japan. SaV GI.2 has been frequently detected from outbreak cases in Taiwan, the Netherlands, Sweden, Slovenia, and Hungary during 2007–2009. This suggests worldwide circulation of SaV GI.2, although its main source remains unclear.

Aichi viruses

Aichi viruses (AiV) have been proposed as causative agents of human gastroenteritis potentially transmitted by fecal–oral routes through contaminated food or water.[55] AiV was first isolated in 1989 in Japan from stool specimens collected from 12 of 15 subjects in three outbreaks of oyster-associated nonbacterial acute gastroenteritis in Aichi Prefecture.[56] The authors conceded that shellfish may be contaminated by several types of prevalent human enteric viruses, and whether or not the AiV isolates were significant etiologic agents of gastroenteritis remained to be clearly established. However, AiV was subsequently detected in feces of patients with gastroenteritis worldwide. For instance, AiV was isolated in Vero cells from six (12.3%) of 47 patients in five gastroenteritis outbreaks, five (0.7%) of 722 Japanese travelers returning from tours to Southeast Asian countries and complaining of gastrointestinal symptoms at the quarantine station of Nagoya International Airport in Japan, and five (2.3%) of 222 Pakistani children with gastroenteritis.[57] Several AiV studies demonstrated a high prevalence of AiV antibodies in adults (80%–99%), indicating widespread exposure to AiV, but a low incidence of AiV infection in patients with either sporadic or epidemic gastroenteritis. AiV is frequently found in wastewater and river water.[58]

Outbreak example: shellfish

Following a flooding event close to a shellfish production lagoon, 205 cases of gastroenteritis were linked to oyster consumption.[59] Analysis of stool samples collected from 12 individuals showed eight were positive for multiple enteric viruses; one had seven different enteric viruses. Analysis of shellfish implicated in the outbreak demonstrated the same diversity of enteric viruses, with some viral genomic sequences identical to case samples. Shellfish were contaminated by as many as five different enteric viruses; this was the first time AiV was identified in European oysters. Over 3 weeks following the outbreak, there was a progressive reduction in virus contamination in shellfish samples; although the actual etiology of the outbreak was inconclusive, it likely included AiV. Although the authors concluded this was the first documentation of AiV transmission by food in Europe, it is uncertain what role AiV played in these infections. The role

of AiV as a human pathogen has been strengthened since then; 457 stool specimens from children hospitalized with acute diarrhea and 566 stool specimens from adults and children involved in 110 gastroenteritis outbreaks were screened for AiV by RT-PCR amplification of the genomic region of the 3C and 3D nonstructural proteins.[55] The results show a low incidence of AiV in pediatric samples and mixed infections with other microbiological agents in some cases. From the outbreak survey, it appears that the presence of AiV is an indicator of mixed infections causing gastroenteritis outbreaks and AiV could be involved in half of the oyster-associated outbreaks; however, in two fecal samples from hospitalized children, AiV was the only microbiological agent detected among all of the known agents, such as HRV, AstV, adenovirus, SaV, NoV, and bacteria. Since children typically do not consume oysters, there may be other vehicles for AiV transmission. This was confirmed in an outbreak of gastroenteritis in Germany where AiV was the only pathogen found excreted at concentrations as high as 10^{12} RNA copies per gram stool; no obvious food source was identified.[60]

Middle East respiratory syndrome coronavirus

MERS-CoV is a newly recognized virus occurring mainly in the Middle East.[61] As of June 2014, 683 cases, including 204 deaths, have been reported to the World Health Organization from Iran, Jordan, Kuwait, Lebanon, Oman, Saudi Arabia, Qatar, United Arab Emirates, and Yemen. Human-to-human transmission seems limited to family and health care settings, but a recent study raises concerns that MERS-CoV could be transmitted by camel milk and its products.[62] Dromedary camels in the Middle East and Africa are now thought to be the intermediate hosts for transmission of MERS-CoV from bats to humans because MERS-CoV-specific antibodies and RNA fragments are widespread in camels from Saudi Arabia, Egypt, Tunisia, Nigeria, and Kenya. From studies in Kenya and Saudi Arabia, MERS-CoV has been circulating in dromedary camels for at least 20 years, and young dromedary camels have lower seroprevalences and are more likely to carry infectious virus.[63] Swabs from milking camels and milk from two locations in Qatar tested positive for MERS-CoV RNA using real-time RT-PCR testing. Analysis of an outbreak of MERS-CoV infection in humans associated with a barn in Qatar in October 2013 found dromedaries and humans were infected with nearly identical strains of MERS-CoV.[62,64] Samples were obtained from 14 camels on October 17, 2013. MERS-CoV was detected in nose swabs from three camels by three independent RT-PCRs and sequencing.

The nucleotide sequence of an ORF1a fragment (940 nucleotides) and a 4.2 kb concatenated fragment were very similar to the MERS-CoV from two human cases on the same farm and from another human isolate (differed by one nucleotide sequence). Eight additional camel nose swabs were positive on one or more RT-PCRs, but could not be confirmed by sequencing. All camels had MERS-CoV spike-binding antibodies that correlated well with the presence of neutralizing antibodies to MERS-CoV.[65] Another study in Saudi Arabia found extensive circulation of different genetic variants of MERS-CoV in camels and antibodies to MERS-CoV in samples from as early as the 1990s.[62] Local camel milking customs do not include cleaning the udders before milking, allowing possible transfer of contamination from udders to milk. Milk could be contaminated by nasal secretions or feces from the camel, saliva of the calves allowed to suckle prior to milking to initiate the milk flow, or dirt from the bowl or hands of the milker.[62] Raw milk is a potential source of infection from MERS-CoV; boiling milk before consumption could prevent transmission. A powdered camel milk product from the United Arab Emirates is now sold in Europe; such processing is likely to destroy any virus present. Antibodies to MERS-CoV were detected in serum and milk collected according to local customs from 33 camels in Qatar, April 2014. At one location, evidence of active virus shedding in nasal secretions and/or feces was observed for seven of 12 camels; viral RNA was detected in the milk of five of these seven camels.[62] The presence of MERS-CoV RNA in the milk of camels actively shedding the virus warrants measures to prevent putative foodborne transmission of MERS-CoV.

Severe acute respiratory syndrome (SARS) is an enteric as well as a respiratory disease.[66] SARS-CoV entered the human population through the preparation and consumption of food of animal origin, particularly civet cats, which contracted the infection from a bat reservoir.[67] Some in Malaysia, Indonesia, and the People's Republic of China consider eating bat meat a delicacy or a cure for asthma, kidney ailments, and general malaise, and even bat feces are used in traditional Chinese medicine.[67] Thus, coronaviruses may represent potential foodborne disease agents.

Other viruses rarely transmitted through food
Enteroviruses

Enteroviruses (polioviruses, Coxsackievirus, and echoviruses) as a group have not been associated with foodborne illness,[68] but polio virus has historically been linked to waterborne illness, and probably still is in endemic Pakistan.

Adenoviruses

Adenoviruses are commonly associated with severe gastroenteritis in closed communities, but links to a foodborne source are infrequent. In Kansas in 2007, 64 cases reported eating sausages at a restaurant;[69] although HAdV and NoV were isolated, no food vehicle was confirmed.

Infectious H5N1 avian influenza virus

Infectious H5N1 avian influenza virus has been cultured from duck meat, and the consumption of duck blood and direct contact with poultry has resulted in human infection. Those who had intestinal infection with H5N1 reported diarrhea as the sole first symptom of illness and other patients reported consumption of raw duck blood as their only possible exposure to poultry.[70,71] Other studies have identified the infectious virus in stool samples, indicating the possibility of viral replication in the human digestive tract.[72–74]

Nipah virus

NiV may be transmitted through consumption of fruits contaminated with the saliva of fruit bats.[75] NiV infection was first recognized in a large outbreak of 276 reported cases in peninsular Malaysia and Singapore in 1998–1999.[76] Most patients had contact with sick pigs. Patients presented primarily with encephalitis and 39% died. The growth of large intensively managed commercial pig farms in Malaysia with fruit trees on the farm created an environment where bats could drop partially eaten fruit contaminated with NiV-laden bat saliva into pig stalls. The pigs could eat the fruit, become infected with NiV, and efficiently transmit virus to other pigs because of the dense pig population on the farms and frequent respiratory shedding of the virus among infected pigs. Farmers were infected directly from the sick pigs. In Bangladesh, NiV is transmitted from bats to people by ingestion of fresh date palm sap. *Pteropus giganteus* bats frequently visit date palm sap trees and lick the sap during collection; NiV can survive for days on sugar-rich solutions such as fruit pulp. In the 2005 Nipah outbreak in Bangladesh, the only exposure significantly associated with illness was drinking raw date palm sap. In outbreak investigations, villagers, especially children, commonly report consuming fruit that has been partially eaten by bats.[76]

Control

Because the burden of viral foodborne illness, particularly NoV, is high, prevention and control strategies require serious consideration. One major cause of viral outbreaks is the infected food worker.[16,75,77] The following measures are primarily aimed at foodborne NoV but apply equally to other enteric viral pathogens.[10,21,35,78–85]

- Clean and disinfect common environmental surfaces touched by many people.
- Emphasize thorough hand washing with approved hand disinfectants placed next to sinks.
- Reinforce strict personal hygiene for all individuals because asymptomatic colonized employees can transmit pathogens as well as those who are symptomatic.
- Display clearly visible signs for employees to wash their hands after toilet visits and before food consumption accompanied by frequent verbal and written reminders.
- Educate employees that if they feel gastrointestinal symptoms beginning, they must stop working immediately, and only resume work at least 2 days following remission of symptoms.
- Ensure certified kitchen managers supervise employees who handle food.
- Manufacturers, distributers, and retailers must have effect systems in place for timely recalls and improved trace back systems for suspected contaminated food.
- Develop specific interventions for reduction of the frequency of foodborne NoV outbreaks by focusing on food workers, produce, and shellfish.
- Improve viral diagnostics, including sequence analysis of predominant NoV genotypes, to identify chains of infection.
- Develop specific viral vaccines, antiviral drugs, and sanitizers effective against NoV.
- Develop an efficient cell culture system, a robust animal model, and rapid and sensitive viral detection methods.

Conclusion

Nine viruses are described in association with foodborne illness (NoV, HAV, HEV, HRV, HAstV, SaV, AiV HAdV), with NoV causing most outbreaks, while food is not a major means of transmission for most other viruses. Poliomyelitis, once the scourge of any society that allowed their population to be in contact with sewage waters, is practically eliminated worldwide; at present, enteroviruses are not considered to be foodborne. MERS-CoV and other coronaviruses have zoonotic links but are not proven to cause foodborne outbreaks. Infectious H5N1 avian influenza virus has been responsible for illness relating to consumption of duck blood, and NiV was certainly linked to illness directly through consumption of fruit and palm tree sap in contact with bats and probably through bats themselves. However, both H5N1 and NiV have been transmitted more extensively through contact with food

animals, eg, poultry and pigs. Recognition of enteric viruses as possible foodborne pathogens has been delayed since many of these viruses produce mild and often uninvestigated infections, are still not culturable and difficult to isolate, have symptoms similar to those caused by bacterial pathogens, and there are limited surveillance systems globally to detect viral pathogens. Thus, new foodborne viral diseases are likely to emerge in the future as diagnostic and surveillance methods improve. We should expect viruses to be foodborne if they have very low infectious doses, are excreted in high concentrations in stools or emesis of infected persons, and are found in food animals, including bush meat. Such viruses easily spread via the fecal–oral route, from person-to-person or to food and food contact surfaces, eg, one individual can trigger an outbreak by touching food or by simultaneously infecting coworkers in a restaurant. Workers in the harvesting, production, preparation, and serving of food, especially food requiring much handling, have been frequent transmitters of NoV and other viral infections;[10,16,75,77] examples of such food are sandwiches, raw vegetables (especially leafy greens), berry fruits, sushi, hors d'oeuvres, layer cakes, and cake frosting. Treated sewage contains 10^2–10^4 NoV PCR detectable unit (pdu)/L and if discharged into surface water may reach areas where shellfish are harvested,[86] and it is not surprising that molluscan shellfish, particularly oysters, have been implicated in outbreaks. The mechanism of virus entrapment in oysters may be more bound electrostatically to shellfish mucus or through attachment to zooplankton than straight filtering, as the viruses are too small to be filtered out by the gill filaments; more research is required to determine the actual mechanisms(s), and how they avoid being purged, digested, or otherwise destroyed by shellfish digestive processes.[87] NoV contributes the largest number of foodborne disease cases in countries where surveillance is sufficiently sophisticated to identify viruses, but there are many developing countries where there is no public health awareness of this pathogen. Since NoV and other enteric viruses are globally distributed, more foodborne viral illnesses arising from outbreaks are expected to be identified in more countries in the future. As the genetic types become better understood and diagnosed on a regular basis, we may see patterns among the outbreaks that indicate regional, host, food, or environmental vehicle preferences.

Adequate hand hygiene is the most effective prevention measure given that both ill and asymptomatic persons can transmit the viruses. Control and clean-up of contamination is achieved using chlorine-based compounds.[88] Unfortunately, alcohol-based hand rubs have limited effectiveness against NoV and some other non-enveloped viruses, and are not permitted to be used in food settings by the US Food and Drug Administration.[89] Although vaccines are available for HRV, and have reduced gastroenteritis in children,[7] none as yet exist against NoV. The burden of NoV infection justifies continued efforts toward vaccine development and identification of specific groups for such interventions, eg, young children, the elderly, and possibly health care workers, travelers, and military personnel.[90] For those viruses transmitted through contact with animals, eg, camels, poultry, pigs, bats, and bush game, care must be taken not to have direct contact without suitable precautions to avoid respiratory inhalation or oral ingestion of viral particles, and to cook meat thoroughly.

It is difficult to determine the significance of some viruses that may cause foodborne disease. The frequency of DNA sequencing in recent years has led to identification of new human and animal viruses, eg, MERS-CoV. While the pathogenicity of some newly characterized human viruses has been demonstrated, it remains unknown or controversial for other viruses, which may be commensal or pathogenic in only a very small fraction of infections.[91] Multiple viruses may be isolated from diarrhea in persons with gastroenteritis. Genetic characterization of previously unknown viruses allows rapid design of the nucleic acid tests needed to determine their association with different medical conditions, their presence in different populations, and the design of antibody tests for determining seroprevalence. AiVs have been associated with gastroenteritis, often in mixed infections with other enteric viruses, and a high seroprevalence has been reported. Kobuviruses have been detected worldwide in both pigs and cows and were also associated with diarrhea. Detection of stool AiVs (sometimes called saliviruses) in many countries shows that these viruses are very widely disseminated.[91] The large degree of genetic diversity among some saliviruses based on partial three-dimensional sequencing may reflect the presence of multiple species and genotypes, which may exhibit different biological properties and antibody neutralization profiles. The association between salivirus shedding and diarrhea indicates that such infections may account for a significant fraction of the unexplained cases of diarrhea occurring worldwide. Research is needed to evaluate the efficacy of manure and water treatments to establish viral inactivation since water and treated manure can come into contact with shellfish and fresh produce. In this way, effective measures to prevent viral contamination at the primary level can be introduced rather than depending solely on preservation methods to establish a viral decline on foods.[22]

Another challenge is the determination of infectious doses of enteric viruses, including those that are foodborne, as a means of determining risk of infection and developing prevention and control measures. A paucity of existing information indicates these are very low, but more research is required to produce precise estimates. This may differentiate known pathogenic viruses such as NoV and HAV from the low infectious species, which may include HAstV and AiV, and identify which enteric viruses we should be most concerned about. The impact of new viral foodborne pathogens on susceptible populations, such as immunocompromised persons, the very young, very old, and those with comorbidities as opposed to the healthy adult population should also be determined. As Pintó et al have demonstrated for HAV,[32] once doses and the amount of viral particles likely to be transferred to food by infected food handlers are known, it will become possible to determine the risk of illness from specific food items such as shellfish or berries more precisely. Once these viruses have become established in a community, elimination is difficult. There is a trend for peak exposure during the cooler and drier seasons in both temperate and tropical countries, at least for HRV,[92] but the impact of seasonality needs to be explored for other enteric viruses.

Perhaps, the biggest concern is not widespread foodborne transmission, but the fact that this mode of transmission may favor cross-species infections that are not evident otherwise, with the potential for adaptation of viruses to humans, especially with the increasing pressure on the environment from population growth, allowing more contacts between humans and animals in biotopes that were previously non-existent or rare.[93]

Disclosure

The authors report no conflicts of interest in this work.

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