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Viruses Associated With Foodborne Infections

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Introduction

In recent years, there has been increasing awareness regarding food safety in terms of food poisoning that results in viral gastroenteritis i.e., stomach flu. It is important to clearly define these terms, for the purpose of this article, prior to focusing on the smaller group of diverse viruses associated with food borne illness.

Food safety encompasses the handling, preparation, and storage of food to prevent food-borne illness.

Food poisoning (also referred to as foodborne illness) is caused by eating contaminated food. Infectious organisms, which include bacteria, viruses and parasites (or their toxins), are the most common causes of food poisoning.

Infectious organisms or their toxins can contaminate food at any point of processing or production. Contamination can also occur in the home and eateries, if food is incorrectly handled, stored, or cooked.

Viral gastroenteritis (also known as stomach flu) is an intestinal infection with symptoms including watery (usually non-bloody) diarrhea, abdominal cramps, pain, nausea or vomiting, or both, and sometimes headaches, muscle aches and fever.

The most common way to develop viral gastroenteritis (stomach flu) is through contact with an infected person or by ingesting contaminated food, water and water products such as ice.

There is a huge annual cost of illness, disease burden and quality-adjusted life year (QALY) loss globally, caused by food-borne pathogens, which has been reported on by many investigators (Scallan *et al.*, 2011). In the Western world, the viruses frequently reported as having the highest total cost-of-illness, to date, are norovirus and rotavirus. These viruses will be discussed first. This profile could change, however, as new virus threats are constantly emerging.

A variety of different foods and different agents are implicated in foodborne illnesses, and we will elaborate on these in the following sections.

Foodborne Illness and the Response of the Host

Many agents cause gastroenteritis, the most common outcome being diarrhea. This can range from mild, self-limiting illness to fatal infection. Diarrheal disease is the major cause of illness and death in children in developing countries, while in the developed world it is usually mild, except in the very young, the elderly and the immunocompromised.

Gastroenteritis (acute gastroenteritis, AGE) is caused by a variety of different pathogens, including parasites, bacteria and viruses (**Table 1**).

Defense Mechanisms

Every day we swallow large numbers of microorganisms in our food and beverages, and from contact with our environment e.g., from fingers. Our body's defense mechanisms, [innate (non-specific) and adaptive (specific) defense systems] are very efficient, and the microorganisms rarely succeed in surviving passage to the intestine in sufficient numbers to cause infection. The body's innate (non-specific) defense is the first line of protection and does not distinguish between infectious agents. It includes physical (e.g., skin and mucous membranes) and chemical barriers (e.g., sweat, gastric juices), cellular (e.g., natural killer cells and phagocytosis) and modular defenses (e.g., interferon) and bodily responses (e.g., inflammation and fever).

With regard to protection against potential enteric pathogens, the intestinal tract has an abundant microbiota that competes with invading pathogens for space and nutrients. The peristaltic action of the digestive tract encourages movement through the system, deterring colonisation by invading pathogens, with vomiting and diarrhea flushing harmful microbes and their chemical products from the digestive tract. The extremely acidic stomach environment discourages pathogen replication. However, these fortifications are not impenetrable e.g., the enteric virus Hepatitis A has the ability to survive and penetrate the body through the gastrointestinal tract (Campbell *et al.*, 1999).

In addition, the epithelial barrier of the intestine is embedded with mucous-producing goblet cells. These simple columnar cells secrete gel-forming glycoproteins (mucins), to produce a transparent, impervious barrier (Johansson and Hannsson, 2013) on the luminal surface. The prevailing mucin of the intestinal tract is MUC2 (Mucin 2), which is a major structural component of intestinal mucus layer. Goblet cells emerge during foetal development at 9–10 weeks of gestation (Kim and Khan, 2013) and are continuously secreted, migrating from the intestinal glands; crypts of Lieberkühn to the lumen of the intestinal tract via the apex of the digestive villi.

Table 1 Agents of acute gastroenteritis (AGE)

Agent of age	*Examples*
Parasites	*Protozoa;* *Giardia lamblia*, *Cryptosporidium parvum*, *Entamoeba histolytica* *Helminths (worms);* *Ascaris lumbricoides* (Ascariasis), *Ancylostoma duodenale* (hookworm), *Necator americanus* (hookworm), *Strongyloides stercoralis* (Strongyloidiasis), *Taenia saginata* (tapeworm), *Enterobius vermicularis* (pinworm), *Trichuris trichiura* (whipworm), *Fasciola hepatica* (fluke)
Bacteria	*Escherichia coli*, *Salmonella enteriditis* serovars, *Campylobacter spp.*, *Vibrio cholerae*, *Shigella spp.*, *Clostridium perfringens, Bacillus cereus*, *Vibrio parahaemolyticus*, *Yersinia enterocolitica*
Viruses	Noroviruses (NoV, SRSV, NLVs), Rotavirus (RV) in particular rotavirus A (RVA), Hepatitis A virus (HAV), Hepatitis E virus (HAE), Adenovirus, Astroviruses, Coronaviruses (including Severe acute respiratory syndrome or SARS-Cov), Nipah virus (NiV) and H5N1 avian influenza viruses. Many other virus families associated with enteritis including the *Picornaviridae* (enterovirus, HAV, parechovirus and others), reoviridae (rotavirus), *Astroviridae*, *Picobirnavirus*

The primary function of the mucus layer is to provide a physical barrier between invading pathogens and the epithelium lining of the tract, while allowing for nutrient transport and absorption.

Additionally, antimicrobial peptides (α-defensins and cathelicidins) are secreted from Paneth cells, originating from the intestinal crypt cells into the mucus, which can inhibit the activity of invading pathogens. Defensins, acting as natural antimicrobials, eliminate pathogens by disrupting the structure of the cell wall, or by inhibiting growth using other mechanisms. Also present are enzymes such as lysozyme (muramidase) and phospholipase A. Lysozyme cleaves the peptidoglycan of bacterial cell walls by hydrolyzing the β1–4 glycosidic bond between N-acetylmuramic acid and N-acetylglucosamine.

Cellular protection is delivered by phagocytic cells, namely neutrophils and macrophages, which represent between 50%–70% of all leukocytes (white blood cells). Neutrophils are continuously being produced in the bone marrow. Neutrophils circulate within blood, and migrate towards microbe damaged cells following the release of chemical signals (chemotaxis). Following detection of the invading pathogen and using cytoplasmic extensions, the neutrophil engulfs and destroys invaders within the neutrophil vacuole (phagocytosis). While neutrophils respond rapidly, they have a short-life span (1–2 days) and are unable to perform phagocytosis repeatedly. Following pathogen extermination, neutrophils self-destruct in a natural process referred to as apoptosis.

Macrophages (15–30 μm), on the other hand, are long-lived phagocytes that develop from blood monocytes. While also eliminating pathogens by phagocytosis (intracellular killing), they eradicate defunct neutrophil debris and are capable of multiple phagocytic episodes. Although macrophages respond more slowly to an infection site, they arrive in larger numbers.

Neutrophils and macrophages are too small to engulf larger parasites such as worms (helminths). One mechanism to eradicate larger pathogens is via eosinophils (leukocytes) and natural killer (NK) cells, which eliminate invading pathogens by secretory extracellular killing techniques. Eosinophils secrete cytotoxic proteins to defend against parasitic worm infections with NK cells releasing biologically toxic molecules targeting virus-infected and tumor cells, causing the formation of pores in the membrane of the attacking pathogen, instigating lysis or penetrating the cell causing apoptosis due to the destruction of nuclear DNA. (Coico and Sunshine, 2015). Additionally, NK cells produce cytokines; IFNγ (interferon-gamma) and TNFα (tumor necrosis factor-alpha), which initiate an enhanced immune response from macrophages and dendritic cells (see "Relevant Websites section"). Damaged/diseased tissue cells release substances called alarmins that activate immunity and inflammation (Chan *et al.*, 2012). Other defensive cells are mast cells and basophils, which release histamine, triggering the responses of inflammation and fever.

The body's defensive inflammatory process is characterised by the presence of pain, redness, swelling, heat and loss of function of the affected tissue. The purpose of this response is increased blood flow and capillary permeability (vasodilation) to assist with the migration of leukocytes to the site of infection and then, to neutralise, confine and prevent the systemic spread of the pathogen, followed by tissue repair and regeneration.

The role of dendritic cells is to initiate the body's adaptive immune response, facilitated by their antigen-presenting cell (APC) properties. The dendritic cells ingest the pathogen from the site of infection in the intestinal lumen, the antigen is degraded into peptide pieces and transported to lymphoid tissue to activate the process. Also, essential are major histocompatibility complex (MHC) proteins (cell surface proteins), to assist with cell recognition from antigen-specific T lymphocytes (T-cells), displaying the corresponding T-cell receptor (TCR). This stimulates antigen-specific B lymphocytes (B-cells), producing and secreting specific antibodies which then migrate to the site of infection and play a role in binding to and neutralizing invading viruses. This response usually occurs 4–7 days following commencement of the innate defense system. Cytotoxic T lymphocytes are also important in destroying e.g., virus infected cells ('altered self'), via recognition of foreign antigens displayed on the surface of infected cells, with the MHC proteins. Following successful elimination of the invading pathogen, the adaptive immune system instigates a regulatory response to discontinue to process, while retaining the specific immunologic response (memory) that was employed.

The immunologic memory facilitates rapid recognition and response to previously encountered pathogens. Consequently, the immune system has the ability to respond to successive exposures more efficiently (memory). Vaccination uses this biologic system as a means for the artificial introduction of a pathogen to induce a response to aid immunity.

Viral Diarrhea

Non-bacterial gastroenteritis and diarrhea is usually caused by viruses. Acute viral gastroenteritis (AGE) is seen in all parts of the world, especially in infants and young children. AGE ranges from mild and self-limiting to severe, debilitating diarrhea, occasionally resulting in mortality. These illnesses have a huge impact, particularly in parts of Asia, Africa and Latin America, with over 3 million fatalities recorded per annum. AGE also has major effects on nutritional status and growth.

Viruses appear to be the commonest causes of gastroenteritis in infants and young children but are not distinguishable clinically from other types of gastroenteritis. Some of these viruses are specific for humans, while others are implicated in zoonotic disease. In most instances, infection follows the general rules for faecal-oral transmission. Enteric viruses are transmissible by food and water and enter the body through the gastrointestinal tract, thus the viruses are commonly acquired after ingestion of sewage contaminated food or water or from poor hygiene when preparing food. The viruses are shed in high concentrations in faeces and vomit and can remain infectious in the environment for several months. Many viruses are difficult or impossible to cultivate in vitro, and tests are unreliable or not developed, thus many cases of non-bacterial acute gastroenteritis viruses are under reported.

Viruses in Food

Well established viral pathogens will be discussed in this section. Later in the article, emerging viral pathogens associated with food poisoning/foodborne illness/foodborne infections will also be discussed.

Established Viral Pathogens

There are several different viruses involved in foodborne outbreaks. Some of these are human viruses that infect and cause illness following ingestion. Virus particles are shed in the faeces. To date, the most notable examples in this category are Noroviruses and Hepatitis A virus. These viruses are different, belonging to different families (**Table 2**): Noroviruses (formerly called Small Round Structured Viruses or SRSVs) belong to the family *Caliciviridae* and are small, non-segmented, positive sense, single stranded non-enveloped, icosahedral RNA viruses. Hepatitis A virus is also a small, non-segmented, positive sense, single stranded non-enveloped icosahedral RNA virus, but belonging to the family *Picornaviridae*. Hepatitis A virus is slightly smaller and contains a linear genome.

Norovirus

Is one the five pathogens (namely, *Salmonella*, *Campylobacter*, *Listeria*, Toxoplasma, and norovirus) responsible for causing roughly 90% of mean loss due to foodborne illness in the United States (Hoffman *et al.*, 2012; Scallan *et al.*, 2011).

Classification and Biophysical Properties

As outlined above, noroviruses are small, non-enveloped, positive sense RNA viruses, within the family Caliciviridae. Noroviruses have been classified into seven genogroups (GI-GVII) and over 30 genotypes. GII.4 has long been established as a predominant variant, but new variants are continually emerging (Lennon *et al.*, 2014).

Transmission, Implicated Foods, Disease Symptoms and Clinical Picture

Transmission of the virus may occur through sewage contamination early in the food chain or lack of personal hygiene later in the food chain, particularly when 'ready-to-eat' (RTE) food-items are involved. Transmission can also occur via by person-to-person contact, environmental contamination, as well as via food- and water-borne transmission. Typically, Noroviruses cause problems in individuals who have consumed contaminated raw oysters. Other implicated foods are fruit and vegetables that have, for example, been irrigated with contaminated water.

Outbreaks frequently occur in hospitals, nursing homes, restaurants, cruise ships, schools, summer camps, and even at family dinners. In these cases, large numbers of people often eat food handled or prepared by others.

The symptoms of Norovirus infection vary, but may include nausea, vomiting, abdominal pain or cramps, watery or loose diarrhea, malaise, low-grade fever, muscle pain. Signs and symptoms usually begin 12–48 h after first exposure to the virus and last one to three days. Shedding of virus can continue for up to two weeks post recovery. Some people with norovirus infection may show no signs or symptoms but are still contagious and can spread the virus.

Risk Reduction, Prevention and Control

There are several recommendations concerning food preparation, disinfection and decontamination, outlined on e.g., the Centres for Disease Control and Prevention (CDC) website (see "Relevant Websites section"). These measures involve practicing good

Table 2 Virus families associated with gastroenteritis in humans

Common name	*Adenovirus*	*Astrovirus*	*Norovirus*	*Rotavirus*	*SARS*	*Nipah*	*Influenza*	*Hepatitis A*	*Hepatitis E*
Family	Adeno-viridae	Astro-viridae	Calici-viridae	Reo-viridae	Corona-viridae	Paramyxo-viridae	Paramyxo-viridae	Picorna-viridae	Calici-viridae
Dimensions (nm)	80–110	27–30	27–32	60–80	120–160	150–300	150–300	27–30	35–40
Nucleic acid	dsDNA	ssRNA	ssRNA	dsRNA	ssRNA	neg ssRNA	neg ssRNA	ssRNA	ssRNA
Envelope	No	No	No	No	Yes	Yes	Yes	No	No
Virus associated with gastroenteritis in humans	Adenoviridae 40 and 41	Astroviruses	Norovirus (NoV, SRSV, NLVs), Sapovirus	especially RVA (RVB, RVC)	SARS-CoV	Nipah	Influenza (H5N1)	HAV	HEV

hand hygiene, washing fruit and vegetables and cooking seafood, especially shellfish e.g., oysters, thoroughly, individuals who are ill avoiding contact with others, also food preparation, for at least 48 h after symptoms abate, and decontamination using suitable disinfectants and detergents. Some people are particularly vulnerable and should take measure to avoid norovirus infection, especially infants, older adults and people with underlying disease where vomiting and diarrhea can be severely dehydrating and require medical attention. Preventative measures e.g., avoiding raw shellfish should be taken in these instances.

Rotavirus

For many years, rotavirus (RV) has been recognized as a major cause of gastroenteritis in the young of many animal species, including humans (Bishop *et al.*, 1973; Estes and Kapikian, 2007; Flewett *et al.*, 1975). In humans, RV associated disease typically occurs in children less than 5 years of age but rotavirus can infect all ages, including adults (Anderson *et al.*, 2012; Collins *et al.*, 2015; Gunn *et al.*, 2012). In 2008, an estimated 453,000 deaths worldwide were attributed to rotavirus infection, with most deaths occurring in resource-poor countries (O'Shea *et al.*, 2016; Tate *et al.*, 2012).

Classification and Biophysical Properties

Rotavirus belong to the family *Reoviridae* and are medium sized, segmented, double stranded non-enveloped, icosahedral RNA viruses. The 11 segments encode six virion proteins (VP1–4, 6–7) and six non-structural proteins (NSP1–6). Rotaviruses are classified into 8 antigenically distinct groups and one proposed group (A–I) (Mihalov-Kovács *et al.*, 2015), using immunological and phylogenetic analysis of the VP6 gene. Rotavirus groups A, B, C, H and I have been identified in mammals, including humans, while rotavirus D–G to date have only been identified in non-human mammal and avian species. A tenth novel rotavirus species has been identified in Schreiber's bats *(Miniopterus schreibersii)*, provisionally known as *Rotavirus J* (Bányai *et al.*, 2018). Within the RVA group, the viruses are classified antigenically and genetically, based on the main antigenic determinants, the outer capsid proteins, VP7 and VP4, which specify the G and P serotypes/genotypes, respectively. A whole genome classification system has been adopted for classification of all 11 segments of the rotavirus genome, applying nucleotide homology cutoff values to distinguish genotypes.

Transmission, Implicated Foods, Disease Symptoms and Clinical Picture

Transmission of rotavirus is predominantly faecal-oral. In humans, rotaviruses are ubiquitous, with 95% of children worldwide being infected by three to five years of age. In infants, prior to the introduction of rotavirus vaccines, RVAs could be detected in up to 50%–60% of all childhood hospitalisations due to acute gastroenteritis each year, were estimated to cause 138 million cases of gastroenteritis annually, and 527,000 deaths in children <5 years of age living in developing countries. In other animals, rotavirus disease also occurs in the young of the species and in farm animals, leads to significant economic losses.

The symptoms are usually characterised by watery dehydrating diarrhea and vomiting, often accompanied by abdominal cramps and low-grade fever, lasting 6–10 days. Subsequent reinfections are associated with mild or subclinical presentations (Bishop *et al.*, 1973; Velázquez *et al.*, 1996); however, such reinfections are important in boosting immunity and maintaining long-term protection from rotavirus disease.

Risk Reduction, Prevention and Control

Due, in part, to the segmented nature of the genome, accumulation of point mutations (genetic drift) and re-assortment (genetic shift) are responsible for the huge genetic heterogeneity of rotaviruses. These mechanisms, in combination with the potential for interspecies (zoonotic and anthroponotic) transmission, can also lead to the emergence of "novel" strains in a given species, with a potential for epidemic or epizootic spread (Martella *et al.*, 2010; Matthijnssens *et al.*, 2008). The zoonotic potential of RVA has been documented on several occasions (Martella *et al.*, 2010). Uncommon human RVA genotypes include G5, G6, G8, G10 and G11, in combination with P[3], P[9], P[10], P[11] and P[14] P types, and are generally considered to be animal to human re-assortment variants. However, certain animal-like genotypes have become established in human circulation, particularly in developing countries.

Since its discovery, many attempts have been made to produce effective rotavirus vaccines, with an emphasis on those directed to the prevention of human disease. Today, two oral live attenuated vaccines are being used in rotavirus immunisation programmes globally; RotaTeq™, which is a pentavalent human-bovine reassortment containing human RVA derived G1 to G4 and P [8] types within the backbone of the WC3 bovine strain, and Rotarix™, a monovalent human G1P[8] live attenuated vaccine. Both vaccines are efficacious and endorsed by the WHO, which recommends the implementation of these vaccines in national immunisation programs (WHO, 2009).

The introduction of universal mass vaccination (UMV) has resulted in a significant decrease in childhood rotavirus infection morbidity and mortality (Curns *et al.*, 2010; Pendleton *et al.*, 2013; Tate *et al.*, 2012; Usonis *et al.*, 2012; Zeller *et al.*, 2010).

Food-Borne Viral Hepatitis

Hepatitis or inflammation of the liver can have a number of causes, including medications, toxins, alcohol use and viral infection. There are 5 hepatitis viruses, A–E, but only A and E are transmitted by the oro-faecal route. Both viruses are major causes of infectious disease with associated socio-economic consequences caused by morbidity and, in vulnerable groups, mortality.

Hepatitis A

Classification and Biophysical Properties

Hepatitis A Virus (HAV), also known as Hepatovirus A, belongs to the order *Picornavirales* in the family *Picornaviridae* and is the type species of the genus *Hepatovirus*. It is an icosahedral, non-enveloped virus with a monopartite, positive, single-stranded RNA genome. Humans and vertebrates serve as natural hosts. There is a single serotype of HAV but several genotypes: IA, IB, IIA, IIB, IIIA, IIIB primarily in humans and IV–VI, primarily found in non-human primates (Cristina and Costa-Mattioli, 2007). The virus infects hepatocytes and Kupffer cells (liver macrophages).

Transmission, Implicated Foods, Disease Symptoms and Clinical Picture

Transmission: HAV is spread in food, in the water system, by touching contaminated surfaces or by direct contact with an infected person. Contamination of food can occur at any stage from farm to fork. According to the WHO, approximately 1.5 million people are infected each year, although the true infection rate is probably much higher due to the asymptomatic nature of many infections (Hepatitis A fact sheet. In: World Health Organisation: media centre). Due to the prolonged infection times, the economic consequences of an outbreak through absenteeism from work can be significant. In developing countries where sanitation is poor, most children are infected while young and are asymptomatic. This gives them immunity and, as such, they cannot become re-infected as adults. In such areas, epidemics of the virus are uncommon but unvaccinated adult visitors from areas where HAV is not commonplace are vulnerable. In economically developed countries, epidemics are rare, because good hygiene practices will prevent person-to-person spread. However, in transitional economies, the introduction of improved sanitation may mean that the population is not exposed as children. As such, the introduction of the virus to these susceptible populations of adults can result in significant outbreaks (Lemon *et al.*, 2018).

The symptoms: The virus is normally mild without permanent repercussions and is typified by fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain, dark urine, clay-coloured stools, joint pain and jaundice (yellowing of the skin and eyes). The development of fulminant hepatitis is rare (less than 0.5% of cases) and can lead to more serious illness, including liver failure and death. Severe illness is more common in older people, while in children around 70% are asymptomatic and in those with clinical manifestations the symptoms are generally mild. Infected persons may shed infectious virus for several weeks before they show symptoms. In those individuals where symptoms occur, they usually start appearing 4 weeks after exposure, but can occur as early as 2 and as late as 7 weeks following exposure. Symptoms usually develop over a period of several days and last less than 2 months, although some people (10%–15%) with hepatitis A can have symptoms for as long as 6 months (Jeong and Lee, 2010).

Risk Reduction, Prevention and Control

HEA can survive outside a host cell for several weeks in groundwater and it has been shown to retain infectivity after 92 days at 25°C in seawater. The virus is tolerant of desiccation and freezing and will survive on vegetables throughout the production process until consumption (A critical review of the effect of heat, pH and water activity on the survival of Hepatitis A and E viruses – A Report to the United Kingdom Food Standards Agency July 2014). HEA is more resistant to heat than other picornaviruses and The Centre for Disease Control states that temperatures of 85°C for a least 1 min are required for inactivation. Hep A is vaccine preventable (Ott *et al.*, 2012). Monovalent formalin killed vaccines are available worldwide and live attenuated versions are available in a number of countries. A double dose of vaccine can provide long-term protection and single dose immunisation strategies have been shown to be effective at least in the short and medium term. As well as for active immunisation, the vaccine can be used prophylactically in the first few weeks of infection. Human immunoglobulins can also be used for both preventative and post-exposure prophylactic treatment (Liu *et al.*, 2009). Post-exposure prophylaxis provides high levels of protection (80%–90%) if provided in the first 2 weeks of exposure. Otherwise standard methods for the prevention of food-borne infections apply: ensuring good sanitation and a clean water supply, hand washing and food safety.

Hepatitis E

Classification and biophysical properties

Hepatitis E Virus (HEV) is a small non-enveloped icosahedral virus, 27–34 nm in size, with a single-stranded positive sense RNA genome. The virus belongs to the family *Hepeviridae*, genus *Orthohepevirus*. There are four species in this genus, and the viruses that infect humans belong to the species *Orthohepevirus A*. Currently, eight genotypes of *Orthohepevirus A* have been identified. HEV1

and HEV2 infect humans only, HEV3 has a range of known host animals including humans and swine, HEV4 infects humans and swine, HEV5 and HEV6 have been detected in wild boar and HEV7 has been detected in camels (Sridhar *et al.*, 2017).

Transmission, Implicated Foods, Disease Symptoms and Clinical Picture

Transmission: Hepatitis E virus (HEV) is the most common cause of acute viral hepatitis worldwide (Sridhar *et al.*, 2015). The virus is responsible for endemics and epidemic outbreaks and the WHO estimate there are 20 million infections and 3.3 million symptomatic cases worldwide per year; in 2015 these led to 44,000 deaths (World Health Organization, 2017). HEV is primarily transmitted through the faecal-oral route via shedding in the faces of infected individuals and subsequent contamination of drinking water. Other routes of transmission are consuming raw or undercooked foods from infected animals or shellfish, blood transfusions or vertical transmission from pregnant women to the foetus (Wulffen *et al.*, 2018). The virus has a worldwide distribution but is most prevalent in South and East Asia and is associated with areas where sanitation is poor and contaminated faeces can enter the water system. In regions where the virus is endemic, outbreaks are common, usually associated with contaminated drinking water, recurring at intervals of years and may involve thousands of people. Such infections are predominantly genotype 1 or 2 (Melgaço *et al.*, 2018). In non-endemic regions, infections were previously associated with international travel, but now the majority of cases are zoonotic genotype 3 or 4 infections from swine or deer. Handling of swine and manure of porcine origin is now a public health concern and infectious HEV has been isolated from meat products (Yugo and Meng, 2013).

The symptoms: While HEV is primarily a disease of the liver, it has also been associated with non-hepatic diseases such as subacute and monophasic neurological disorders of the peripheral nervous system, acute pancreatitis, glomerulonephritis, mixed cryoglobulinemia, severe thrombocytopenia and haemolytic anaemia (Pischke *et al.*, 2017). The hepatic symptoms of HEV are indistinguishable from other forms of acute hepatitis and laboratory diagnosis is required for a definitive diagnosis. The incubation period is approximately 2–6 weeks. HEV is characterised by fever, reduced appetite, nausea and vomiting, abdominal pain, and a slightly enlarged, tender liver (hepatomegaly) (Kamar *et al.*, 2017). In rare cases, acute hepatitis E can be severe, resulting in liver failure and death. Pregnant women and immunosuppressed people are at high risk of these severe symptoms. In pregnant women mortality rates of 30% have been recorded (Perez-Gracia *et al.*, 2017). Like HAV, infection of young children is often mild or asymptomatic.

Risk Reduction, Prevention and Control

HEV is self-limiting and most cases do not require treatment. For those with acute symptoms or for high risk individuals, hospitalisation is required. The antiviral drug ribavirin may be given, although in pregnant women this must be carefully considered, due to the teratogenic nature of this antiviral compound (Krzowska-Firych *et al.*, 2017). A recombinant subunit vaccine to prevent hepatitis E virus infection exists in China but is not licenced elsewhere (Nan *et al.*, 2018).

Adenovirus

Classification and Biophysical Properties

The family *Adenoviridae* contains 5 genera; *Atadenovirus* (8 species) infecting birds, lizards and mammals; *Aviadenovirus* (14 species) infecting birds; *Ichtadenovirus* (1 species) isolated from sturgeon; *Mastadenovirus* (45 species) infecting mammals only, including humans and; *Siadenovirus* (6 species), mostly infecting birds and 1 frog species. Virions are non-enveloped, 70–90 nm in diameter with a double-stranded DNA genome and an icosahedral capsid. There are 7 human species of human adenoviruses, A–G (Lennon *et al.*, 2007). Within these species there are at least 79 subtypes distinguished either by serological differences of by genotypic classification (Chen and Tian, 2018).

Transmission, Implicated Foods, Disease Symptoms and Clinical Picture

Transmission: Adenovirus-associated gastroenteritis often occurs in clusters in schools, hospitals or military camps. Adenoviruses are spread person-person contact, by coughing and sneezing, by touching contaminated surfaces or by the faecal-oral route (Eckardt and Baumgart, 2011). Adenoviruses infections are not associated with contaminated food, but transmission can occur in water, through public water systems or in swimming pools; the latter are predominately associated with conjunctivitis (Rodríguez-Lázaro *et al.*, 2012).

Symptoms: Adenoviruses in humans cause respiratory infections, gastrointestinal disease and conjunctivitis with hemorrhagic cystitis, hepatitis, hemorrhagic colitis, pancreatitis, nephritis, or encephalitis (Lynch and Kajon, 2016). Adenoviruses infections are often asymptomatic or mild and self-limiting. However, they can be associated with severe morbidity or mortality, with immunocompromised and the young being more susceptible. However, novel or emerging strains have been found to cause mortality in people of all ages such as Ad14, which was responsible for fatal respiratory illness in the USA (Centres for Disease Control, 2007). A number of human adenovirus subtypes can cause gastrointestinal symptoms, but subtypes 40 and 41 from species F are the most commonly associated with AGE and have been reported to be responsible for 5%–20% of acute gastroenteritis in children

(Ziros *et al.*, 2015). Adenovirus-associated gastroenteritis is most common in children under 2 years old and is uncommon in adults, accounting for 1.5%–5.4% of cases (Eckardt and Baumgart, 2011). The incubation period is around 8–10 days after which diarrhea develops and, in some cases, mild vomiting. Fever lasting 2–3 days may develop; severe dehydration is rare (Wood, 1988).

Risk Reduction, Prevention and Control

Currently vaccines against human adenovirus 4 and 7 are being used by the US military, but no vaccines are available for general use (Chen and Tian, 2018). As the virus is usually self-limiting in most cases, treatment of adenoviral gastroenteritis is not required. In severe cases, hospitalisation and rehydration may be needed. Prevention of adenovirus infection is by standard antiviral hygiene methods; avoiding sharing of eating and drinking utensils, hand washing and avoiding contact with sick individuals, especially in at risk environments such as hospitals. Adenoviruses are susceptible to chemical disinfectants but can be resistant to UV irradiation (Rodríguez-Lázaro *et al.*, 2012); in swimming pools, chlorine levels must be adequate.

Astrovirus

Classification and Biophysical Properties

The family *Astroviridae* consists of 2 genera; *Avastrovirus* and *Mamastrovirus* infecting birds and mammals, respectively. Virions are non-enveloped, approximately 28–40 nm in diameter with a single-stranded positive sense genome and an icosahedral capsid. The International Committee for the Taxonomy of Viruses (ICTV) currently identifies 19 species in the genus *Mamastrovirus* infecting felines, canines, cattle, cervids, rodents, swine, sheep, mink, bats, rabbits, sea lions and dolphins. The viruses that infect humans (referred to as classical HAstVs) have traditionally been classified into 8 serotypes, but recently a number of viruses have been detected in humans that are more similar to those from other animals, suggesting cross species transmission (Bosch *et al.*, 2014).

Transmission, Implicated Foods, Disease Symptoms and Clinical Picture

Transmission: HAstVs are predominantly transmitted through the faecal–oral route as well as through drinking water and in sewage. Recreational activities in sewage contaminated water bodies is a risk of infection. HAstVs are considered to be food-borne viruses with molluscs grown in, or fruits or vegetables irrigated with contaminated water, representing the biggest threat (Vu *et al.*, 2017). As would be expected, poor food hygiene practices may play a role in outbreaks, particularly as asymptomatic carriers are more likely to contribute to infection in the food industry than symptomatic workers. Contaminated fomites and surfaces can represent a threat in institutions such as schools and hospitals (Abad *et al.*, 2001). As we are now aware that inter-species infections with astroviruses can occur, and, as such, the zoonotic route should be considered as a potential source of astrovirus infection (Bosch *et al.*, 2014).

The symptoms: Classical human astroviruses are known to cause mild gastrointestinal disease in children, but symptoms and prevalence are serotype dependant. Immunocompromised and elderly patients are also susceptible. Serotype 1 is the most common, with a reported level of seropositivity of 90%–100% having been reported in children by 5 years of age (Koopmans *et al.*, 1998). The symptoms are usually watery diarrhea, vomiting, fever, abdominal pain, anorexia, and headache but these are usually mild in nature and self-limiting, typically lasting for 2–4 days (Vu *et al.*, 2016). However, HAstVs do cause asymptomatic infections (Méndez-Toss *et al.*, 2004) and the association of these viruses with disease is not fully understood. While the symptoms are mild, HAstVs do contribute to a large proportion of outbreaks of diarrhea, 0.5%–15% of all cases, and often occur as co-infections with other viruses such as noroviruses and rotavirus (de Benedictis *et al.*, 2011). Rarer astroviruses have been reported as being responsible for fatal cases of central nervous system infection (Fremond *et al.*, 2015).

Risk Reduction, Prevention and Control

As with most gastrointestinal infections control of HAstVs is by prevention of contamination of food and water and prevention of person to person, or fomite to person spread through hygiene and handwashing. While survival of astroviruses in drinking water is known to be high, chlorination has been shown to be effective in reducing astrovirus viability by alteration of the capsid, resulting in non-infectious virions (Abad *et al.*, 1997) and 90% alcohol has been shown to be effective for decontamination of surfaces and hands (Kurtz *et al.*, 1980). No vaccines are available for HAstVs. As infections are usually mild and self-limiting, no treatment is normally required. However, those with severe gastroenteritis may require oral or intravenous rehydration.

Emerging Viral Pathogens Associated With Food Poisoning

Recent emerging epidemic and pandemic virus infections that cause severe disease in humans and that are associated with food production, preparation and food contamination include the coronavirus, severe acute respiratory syndrome (SARS-CoV), Nipah

virus, Ebola virus and some of the highly pathogenic influenza virus strains, such as the H5N1 subtype. Transmission may be by a variety of routes, but often the emergent epidemic is started by contamination of a food source by saliva, urine or faeces from a wild reservoir species or use of a wild animal (bush meat) as the food source and infection through the capture and butchering process (e.g., HIV is thought to have entered the human population by this route). These infections have a low probability of occurring, but a very high impact if they establish infection in domestic animals and humans.

SARS-CoV

Classification and Biophysical Properties

The *Coronaviridae* belong to the order *Nidovirales* of single stranded, positive sense RNA viruses. Within the *Coronaviridae* there are 2 sub-families, of which the *Coronavirinae* contain 4 genera. Phylogenetically, SARS-CoV is within the *betacoronavirus* genus (ICTV, 2017). In older literature, SARS-like CoVs were assigned to group 2b coronaviruses (Lau *et al.*, 2005). The viruses are roughly spherical (120–140 nm diameter), with an envelope that contains many surface glycoproteins that form a corona (crown) under electron microscopy (Masters and Perlman, 2013). Although enveloped, the virus is relatively stable especially in faeces and urine for 1–2 days (or longer) at room temperature, and up to 4 days if stool is from diarrhea patients (the pH is higher) (see "Relevant Websites section"). However, they are sensitive to heat, lipid solvents, oxidizing agents and non-ionic detergents (Markey *et al.*, 2013a). Many coronaviruses are associated with respiratory and intestinal disease and can cause severe epidemic gastrointestinal disease in agriculturally important species such as porcine epidemic diarrhea virus in pigs (Masters and Perlman, 2013).

Transmission, Implicated Foods, Disease Symptoms and Clinical Picture

Transmission: is faecal-oral, respiratory by aerosolised secretions. SARS-CoV was first discovered in 2003, after a pandemic of severe respiratory disease that originated in Guangdong Province, China. It caused disease in 8098 people and of these, 774 died (see "Relevant Websites section"). It is now believed that Chinese Horseshoe bats are the original reservoir host of SARS-like CoVs (Lau *et al.*, 2005; Li *et al.*, 2005). Bats transmit these viruses, probably via faecal contamination of food sources directly to humans or to intermediate hosts, most notably palm civets and raccoon dogs, and these then transmit virus to humans (Guan *et al.*, 2003). These animals are traded in live animal markets as food and it is thought that aerosolisation of faeces and other body fluids caused respiratory infection of humans (Wang *et al.*, 2005). Once SARS-CoV entered humans, it was spread by respiratory droplets or contamination of surfaces by droplets that were then transferred to the mouth, nose or eyes by touching. There was also a cluster of cases in an apartment block in Hong Kong that probably arose from sewage aerosolisation into the ventilation system that proceeded to cause respiratory infection of many of the inhabitants (Tilgner *et al.*, 2003).

The incubation period is 2–7 days but can be up to 10 days. Infection results in symptoms of a high fever, chills, and headache. Some people have mild respiratory symptoms from the beginning that progress to lower respiratory involvement with a non-productive cough, which can lead to hypoxemia and pneumonia. A low proportion of patients (10%–20%) had diarrhea. As stated above, approximately 10% of patients died from the severe respiratory complications, but these were usually older patients or those with other health problems. Up to 20% of patients needed mechanical ventilation to survive. The severe sequela could take many days and weeks to develop. Shedding in faeces occurs for a long time after symptoms are cleared so contact from soiled material from past patients can be a source of infection (Masters and Perlman, 2013).

Risk Reduction, Prevention and Control

There have been no known cases of SARS since 2004 (see "Relevant Websites section"). However, SARS-CoV is not eradicated, as similar viruses are still present in their wild-life hosts. Therefore, continued vigilance must be used to stop the spread of these viruses from their zoonotic hosts to humans. Control of live animal markets and a ban on sales of exotic animals is required (see "Relevant Websites section"), but difficult to introduce due to the cultural background of the communities in which they are found. There is no vaccine or treatment against the virus (Coleman and Frieman, 2014), although several drugs have been developed that could be used in the future (Masters and Perlman, 2013).

Nipah Virus

Classification and Biophysical Properties

Nipah virus is a member of the viral family, *Paramyxoviridae* in the genus *Henipavirus* (ICTV, 2017). It was originally identified in 1999 in Malaysia during an outbreak of encephalitis and respiratory disease in pig farmers and those who had close contact with pigs. Its virions are roughly spherical of about 150 nm diameter but filamentous forms can be seen (Wang *et al.*, 2013). It is a relatively unstable virion (Markey *et al.*, 2013c), but can survive well in pH-neutral fruit bat urine (>4 days at 22°C), on

fruit (up to 2 days) and in artificial date palm sap (de Wit *et al.*, 2014; Fogarty *et al.*, 2008). It is however susceptible to desiccation (Fogarty *et al.*, 2008). It is an enveloped virus that is inactivated by most common disinfectants, lipid solvents, and non-ionic detergents (Markey *et al.*, 2013c).

Transmission, Implicated Foods, Disease Symptoms and Clinical Picture

Transmission is respiratory and oral. The wild-life reservoir host of Nipah virus are *Pteropus* fruit bats (Chua *et al.*, 2002; Yadav *et al.*, 2012) and transmission may be by direct infection of humans, after the virus has passed through an intermediate host e.g., pigs, or from fomites. It is thought that bat saliva or urine is the major source of virus and so food such as partially eaten fruit contaminated with saliva or contamination by faeces and urine may be the source of infection for other hosts. In the Malaysian outbreak of 1998–99, it is thought that contaminated fruit from trees adjacent to pig farms encroaching into forest were dropped into enclosures where they were eaten by the pigs or that there was direct contamination of enclosures with urine. The pigs amplified the virus (they also showed clinical respiratory and neurological disease), so that farmers and workers in direct/close contact were infected and were the population where the majority of cases was seen (Parashar *et al.*, 2000). However, in the Indian sub-continent, especially Bangladesh, where Nipah virus infection was first recognized in 2001, the major risk factor for contracting Nipah virus is drinking raw palm sap (Luby *et al.*, 2006). There is photographic evidence of fruit bats licking sap from the cuts in the trees from which the sap is collected, and contamination by faeces is seen in or on the pots (Khan *et al.*, 2010; Rahman *et al.*, 2012).

Human infection may be asymptomatic, but there can be acute respiratory disease with fatal encephalitis, leading to mortality rates of 40%–75%. The incubation period is believed to be 4–14 days or longer (see "Relevant Websites section"). The Malaysian outbreak saw more cases of encephalitis than respiratory disease and there was little evidence for human to human transmission. In the Indian sub-continent, especially Bangladesh, the symptoms of infection manifested more with respiratory disease with fewer cases of encephalitis (Luby *et al.*, 2009). The aerosolisation of respiratory secretions (droplets) and close contact with the sufferer allows respiratory transmission to lead to human to human transmission chains (Gurley *et al.*, 2007; Yadav *et al.*, 2012).

Risk Reduction, Prevention and Control

Nipah virus will be maintained in its bat reservoir and so it is unlikely to be eradicated. Slaughter and burial of pigs in the affected regions controlled the Malaysian and Singapore outbreak. Routine cleaning and disinfection on pig pens with detergents may reduce exposure of pigs but if an outbreak is suspected, quarantine and culling can reduce the spread of disease (Wang *et al.*, 2013). In Bangladesh, the use of bamboo skirts to restrict access of bats to the sites on trees where sap is collected reduces the risk of contamination (Khan *et al.*, 2010). Heat treatment of sap also inactivates the virus and this, along with stopping the feeding of raw palm sap to humans and domestic animals reduces the risk of infection and transmission (Luby *et al.*, 2009). Continual surveillance for re-occurrences must be in place to monitor possible incursions into humans. There is no vaccine and no specific treatment at present (see "Relevant Websites section").

H5N1 Influenza a Virus

Classification and Biophysical Properties

Influenza viruses are members of the *Orthomyxoviridae* family, and the H5N1 genotype is in the *Alphainfluenzavirus* genus and is of the *influenza A* species (ICTV, 2017). Influenza viruses are negative stranded RNA viruses that have a segmented genome (Shaw and Palese, 2013). Influenza A nomenclature uses the 2 genomic segments that encode the envelope glycoproteins, haemagglutinin (H) and neuraminidase (N) because these proteins are major contributors to the pathogenicity of the viruses. The wildlife reservoir for these viruses is wild birds, especially waterfowl, in which a subclinical gastroenteric infection is usually seen. Thus, these viruses are often called avian influenza. There are several high pathogenicity avian influenza A (HPAI) virus genotypes but one of the most pathogenic for humans and other animals are those in the H5N1 genotype (Wright *et al.*, 2013). With widespread sequencing, the ability to group viruses as 'clades', i.e., those viruses that are derived from a common ancestor, has now allowed a numerical naming system to be instituted. The Eurasian-African H5N1 viruses that are circulating and causing human and animal disease can be split into several (≥20) clades (see "Relevant Websites section"). Within all the different clades, the original H5 genotype has remained, despite re-assortment of the other gene segments.

The virions are spherical (80–120 nm diameter) or filamentous (up to 20μm long) (Noda, 2011). The virus is present in the faeces of wild waterfowl, water contaminated by their faeces, domestic poultry secretions (respiratory and faeces) and aerosolised respiratory secretions from infected animals. The virion is usually very labile (Markey *et al.*, 2013b) but it has been shown that avian influenza virus is infectious for months in low temperature water and for over a week in water at 22°C (Hinshaw *et al.*, 1979; Markwell and Shortridge, 1982) with increased survival when water has neutral to basic pH (7.0–8.5) and low ammonia concentrations (Keeler *et al.*, 2014). It is also stable in frozen lakes (Shoham *et al.*, 2012), allowing maintenance in the environment and infection of waterfowl from year to year. The seasonality of epidemics in humans is affected by temperature and humidity with the virus surviving better at 20°C in low humidity conditions but at 30°C requiring higher humidity. Thus, the cool,

dry conditions of winter favour transmission in temperate zones and humid, rainy conditions favour transmission in tropical and sub-tropical zones. The presence of salts and proteins in respiratory droplets allows virus survival in aerosolised droplets for up to 1–24 hr (Sooryanarain and Elankumaran, 2015). Contamination of fomites may also occur allowing transfer by hands.

Transmission, Implicated Foods, Disease Symptoms and Clinical Picture

Transmission is via inhalation of small aerosol droplets, faecal contamination from poultry and water borne infection. In Asia, contamination of the environment by the faeces of waterfowl leads to infection of domestic poultry including chickens, ducks and geese which are often kept in the same environment. This usually causes severe disease and high titres of virus to be secreted from the domestic birds promoting infection of those working with or in contact with them, or in the food chain. Farming of poultry and pigs together increases the risk of transmission to pigs and they can amplify and increase the risk of human infection. Influenza virus A causes seasonal outbreaks with occasional severe epidemics/pandemics in humans and animals. The Asian-African H5N1 lineage is thought to have originated from commercial geese in the Guangdong province of China in 1996. This has since been spread across the globe by wild birds and infected people. There is evidence that H5N1 has infected humans directly by drinking duck blood or eating duck meat, however, aerosolisation and inhalation is the more common route (Shao *et al.*, 2011; Tumpey *et al.*, 2002). This virus has evidence of direct bird to human transmission without the need for adaptation through a secondary species such as pigs (Wright *et al.*, 2013).

In humans, the symptoms it causes are an acute respiratory tract infection with fever and sore throat, cough and malaise. If the virus becomes systemic there may also be vomiting and abdominal pain. H5N1 viruses are highly pathogenic and there is a high case mortality rate with these infections (Wright *et al.*, 2013).

Risk Reduction, Prevention and Control

Reducing the exposure of domestic poultry to wild waterfowl i.e., increased biosecurity reduces the risk of infection of these poultry and so exposure of workers to the virus. Quarantine and culling of premises as well as closing live bird markets also reduces the risk of spreading the infection (see "Relevant Websites section"). In humans, there is a killed vaccine against annual strains of influenza A and B, and a live attenuated influenza A and B nasal spray vaccine. However, none is specifically against the H5N1 strains. There are several antiviral drugs (amantadine, rimantadine, zanamivir, oseltamivir) available to treat those infected with influenza A, but there is the risk of resistance occurring, with some of the circulating H5N1 strains showing resistance to amantadine and rimantadine and oseltamivir resistant strains have been isolated from patients treated with the drug (Wright *et al.*, 2013).

Methods of Detection

Infections by Severe Acute Respiratory Syndrome (SARS) virus, Nipah virus (NiV), H5N1 virus, Hepatitis A virus (HAV), Hepatitis E virus (HEV), Adenovirus, Astrovirus, Norovirus (NoV) and Rotavirus (RVA) in humans and animals are detected by nucleic acid amplification tests and serologic tests. For example, a standardised method based on quantitative real-time PCR (RT-qPCR) for the detection of NoV and Hep A in food has been developed by the European Committee for Standardisation (CEN) working group (TC 275/WG6/TAG 4 – Detection of viruses in food) (Lees and CEN WG6 TAG4, 2010) and provides a tool to quantify NoV concentration in shellfish. It has been used to demonstrate that the risk of gastrointestinal illness associated with consumption of oysters increases with increasing concentrations of NoV genome copies present (Lowther *et al.*, 2012). Costantini *et al.* (2010) demonstrated that a commercially available NoV enzyme immunoassay showed excellent specificity but low sensitivity both for outbreaks as well as for samples from sporadic cases. The assay detected 18 of the 21 genotypes evaluated and that at least 10^7 virus particles g^{-1} of faecal sample were required for a positive signal. This assay may be useful for rapid screening of faecal samples collected during an outbreak of acute gastroenteritis.

To detect and quantify HEV virus present in environmental and food samples, a RT-qPCR method was developed by Jothikumar *et al.* (2006). This TaqMan assay was designed to target a conserved region in ORF3, allowing the detection of four different genotypes of HEV. A number of commercially ELISA (enzyme-linked Immunosorbent assay) kits for the HEV detection of IgM and IgG antibodies which can be used early diagnosis of patients suspected for infection with HEV, for the screening of blood units and the follow-up of HEV-infected patients are also available.

A Taqman assay for the detection of Multiple Rotavirus Genotypes was designed, targeting the rotaviral VP2 gene (Gutiérrez-Aguirre *et al.*, 2008). This method was able to detect the presence of 17 different G-P types which were divided into 7 of human origin (G1P[8], G2P[4], G3P[8], G4P[8], G8P[8], G9P[8], and G12P[8]), 3 of bovine origin (G6P[1], G6P[1] G6P[5], and G6P [11]), and 7 of porcine origin (G2P[13], G3P[6], G4P[22], G5P[7], G5P[13], G9P[13], and G11P[13]). This method, when applied to environmental samples, was able to detect rotavirus at a level 2.6×10^4 and 2.6×10^5 particles/ml in tap water and environmental water, respectively. A competitive RT-PCR SYBR green assay was designed based on conserved regions of the VP6 gene of group A rotaviruses, producing a 433 base pair fragment (Schwarz *et al.*, 2002). An in vitro synthesised RNA with a 43-base deletion with respect to the wild-type sequence of this fragment was used as an internal control. Using these transcripts as templates, 10 RNA molecules were amplified and reproducibly detected. Using this protocol, the assay could be used to investigate the presence of rotavirus in environmental, food and water samples. Immunochromatography tests are also available for detecting

rotaviruses in stool samples. A study undertaken by de Grazia *et al.* (2017) compared the performance of two commercially available one-step chromatographic immunoassays that detect both rotavirus and adenovirus. Both tests were able to detect the wide range of RVA genotypes circulating over the study period (including G1P[8], G2P[4], G3, G4, G9 and G12P[8]). The results of the present study showed a satisfactory efficacy of the two diagnostic tests analyzed using real-time PCR as a reference test.

The case fatality rate for NiV is estimated to be 40%–75%. In addition, there is no treatment or vaccine available for either people or animals. The main tests used are real time RT-PCR from bodily fluids and antibody detection via enzyme-linked immunosorbent assay ELISA (see "Relevant Websites section"). For example, a TaqMan assay as described by Guillaume *et al.* (2004) for NiV detected a wide range of virus concentrations from $1.2 \times l0^5$ pfu to 1.2 pfu per reaction, corresponding to a threshold of 200 pfu/ml for rapid, accurate and quantitative diagnosis. The specificity of the NiV Taqman assay was determined by the absence of amplification using measles and Hendra Paramyxovirus RNA. An antigen capture ELISA was developed by Chiang *et al.* (2010) for the viral detection of *Henipavirus* and for the differentiation between NiV and Hendra virus. This assay allows for the rapid detection and differentiation between the *Henipaviruses* and could be used in any future outbreaks of *Henipaviruses.*

Astroviruses are classified into two genera: mammalian viruses (Mamastroviruses, MAstVs) and avian viruses (Avastroviruses, AAstVs). Human astroviruses are found in four MAstV species (MAstV 1, 6, 8, 9) (Pérot *et al.*, 2017). An RT-PCR assay was designed by Finkbeiner *et al.* (2009), based on the astrovirus RNA polymerase (ORF 1 b) that allows for the detection of the eight human astroviruses serotypes found in MAstV 1, a common cause of viral gastroenteritis in children. This primer set also detects viruses in MAstV 6. These two groups also contain astroviruses from cats, pigs, dogs and rabbits (Pérot *et al.*, 2017). To date, there is no universal pan-astrovirus RT-PCR assay. Immunochromatography (IC) tests are also available for detecting astroviruses. An IC test for the detection of astrovirus was evaluated in 44 stool samples of pediatric patients with acute gastroenteritis in Japan, during January to March 2007, and it is a rapid method for the detection of astroviruses and may be useful for screening astroviruses during outbreaks of food-borne and person-to-person transmission (Khamrin *et al.*, 2010).

A broad-spectrum PCR assay was developed by Sibley *et al.* (2011) for the detection of Mastadenovirus (MaAdV) and Atadenovirus (AtAdV), based on the adenovirus hexon gene. MaAdV, which comprises human and bovine adenoviruses and a large variety of mammalian adenoviruses. AtAdV includes bovine adenovirus (BadV) as well as adenovirus infecting ducks, goats, sheep, deer, and reptiles (Sibley *et al.*, 2011). This assay has been shown to demonstrate natural BAdV excretion in urine, BAdV detection in groundwater, and recombination in AdV of livestock origin (Sibley *et al.*, 2011) and has the potential to be used in screening samples during outbreaks of food-borne disease.

For the detection of H5N1 Influenza viruses, the World Health Organisation (WHO) (see "Relevant Websites section") provides updated information on the molecular detection/diagnostic protocols for the surveillance of influenza viruses in humans. For example, the WHO provides primers and probes sequences for real-time RT-PCR procedures for the detection of:

(1) Influenza type A viruses (Matrix gene).
(2) A(H1N1)pdm09 viruses (Haemagglutinin (HA) gene).
(3) Former seasonal influenza A(H1N1) (HA gene).
(4) A(H3N2) viruses (HA gene).
(5) A(H5N1) viruses (Clade 1, 2, 3) (HA gene).
(6) Influenza type B viruses (Non Structural gene).
(7) A(H7N9) viruses (HA gene).
(8) A(H9N2) viruses (HA gene)
(9) Influenza type B Victoria lineage viruses (HA gene).
(10) Influenza type B Yamagata lineage viruses (HA gene).

A Taqman based assay was designed for the detection of SARS and Middle East respiratory syndrome (MERS) coronaviruses (CoVs) by Noh *et al.* (2017), based on the conserved spike S2 region of human SARS-CoV, MERS-CoV, and their related bat CoVs. This assay can detect SARS-CoV and MERS-CoV in humans but also several bat CoVs that are closely related to these viruses in bats. A monoclonal antibody-based capture enzyme immunoassay for the detection of nucleocapsid antigen in sera from patients with SARS was developed by Che *et al.* (2004). This assay used a mixture of three monoclonal antibodies for capture and rabbit polyclonal antibodies for detection of serum antigen. The sensitivity of the assay was 84.6% in 13 serologically confirmed SARS patients with blood taken during the first 10 days after the onset of symptoms (11 of 13). The specificity of the assay was 98.5% in 1272 healthy individuals (1253 of 1272). There was no cross-reaction with other human and animal coronaviruses in this assay.

Conclusions

- Food can become contaminated by viruses at source and through contaminated food handlers and environments.
- Good food hygiene and personal hygiene, especially hand washing, are essential to help minimise the spread of these viruses within the food chain.
- Since foodborne viruses tend to be more resistant to physical and chemical treatments than bacteria, their control represents a challenge for the food industry.
- Ongoing research is required, for example, current laboratory detection methods can be modified to allow differentiation between e.g., infectious and non-infectious viruses.

- There are a number of knowledge gaps in terms of how, for example, NoV, HAV and HEV are transmitted through the food chain, the contribution they make to overall foodborne illness and their survival and elimination from food.
- Emerging trends indicate that viruses play an important role in foodborne illness. This has implications for the whole of the food chain.

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