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Waterborne Transmission of Enteric Viruses and Their Impact on Public Health

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ABBREVIATIONS

DNA	deoxyribonucleic acid
HAV	hepatitis A virus
HBoV	human bocavirus
HEV	hepatitis E virus
NoV	norovirus
NSP	nonstructural proteins
ORF	open reading frame
PCR	polymerase chain reaction
RDRP	RNA-dependent-RNA-polymerase
RNA	ribonucleic acid
VP	structural proteins

INTRODUCTION

The viruses are infectious agents and mandatory cellular parasites. The viral particle is constituted of a genome [either ribonucleic acid (RNA) or deoxyribonucleic acid (DNA), simple or double stranded], bearer of the genetic information and a protein capsid ensuring its protection in the environment. In some cases the capsid may be surrounded

by a second external layer, the envelope, which is lipido-protein (Koopmans and Duizer, 2004).

The importance of the hydric environment in the transmission of viral infections has been demonstrated in the years 1940–45 with the epidemics of polio (Le Guyader et al., 2000).

Viruses abound in freshwaters and in the marine environments. Among these viruses, those excreted in the feces of infected persons are able to cause infections in humans and therefore have an interest in human health [WHO (World Health Organization), 2013]. These viruses are grouped under the name of enteric viruses [WHO (World Health Organization), 2013]. They are responsible for a considerable mortality in the developing countries, a morbidity equally important in all regions of the world (Parashar et al., 1998). The water contamination by these agents was for domestic wastewater vector, which then can contaminate ground water and surfaces. Human enteric viruses can contaminate humans through the ingestion of contaminated water or other types of contact, such as recreational activities in contaminated marine waters (Abbaszadegan et al., 1999).

Among the foods likely to be contaminated by enteric viruses, there is the shellfish, such as mussels and oysters. These bivalve molluscs feed by filtration of the water. By this mechanism, they accumulate the pathogens contained in the water along with the human enteric viruses. These shells shellfish are mainly consumed raw or undercooked. Due to this, foodborne illness is regularly reported—infections due to viral etiology, following the consumption of shellfish (Lees, 2000).

The control of the sanitary quality of the water and food is currently limited to the surveillance of bacterial indicators of fecal contamination, such as fecal coliforms. Many scientific studies have shown that the so-called indicators were not effective to prove the quality of foodstuffs from the virological point of view. Moreover, the human enteric viruses have been detected in the drinking water free of bacterial indicators of fecal contamination in several industrialized countries. It therefore becomes important to include virological analysis in the routine control of the water and food (Borchardt et al., 2003; Muniain-Mujika et al., 2003).

This work will focus on different enteric virus pathogens of the hydric environment and their characteristics.

PART I: GENERAL OVERVIEW ON ENTERIC VIRUSES

Environmental Virology/Historical Review

The Environmental Virology has taken its real importance since 1965 following the isolation of *poliovirus* in wastewater in epidemics in India (Bosch, 1998). But before this fact, the *poliovirus* was described in 1908.

Thirty years later, it was confirmed that the transmission of *poliovirus* infection was by air where the *poliovirus* would multiply in the olfactory bulb and then borrow the track of the nerve fibers to access directly to the central nervous system (Metcalf et al., 1995). Toward the end of the years 1940 the identification of *Coxsackievirus A* and *B* of the same that the *echovirus* allowed to define a new family of viruses characterized by their human enteric origin, involving their contamination of waters. Then in the year 1950, researchers showed a particular interest for the research on the enteroviruses in the waters. Many of the techniques developed for the purpose of how to concentrate the virus before moving to the cell culture, which is the historical method for the detection of enteroviruses. Research in the field devoted a place of choice to the techniques of concentration (Laveran, 1973; Schwartzbrod, 1984).

The development of molecular biology techniques allowed a considerable expansion of the Environmental Virology from the middle of the year 1980. This expansion could be explained by the fact that the polymerase chain reaction (PCR) becomes a technique of choice because it is faster, less costly, and more specific than the detection method by cell culture (Haramoto et al., 2005). Also, the virus as enteric adenoviruses (40/41), calicivirus, Norwalk-like virus [Norovirus (NoV)], hepatitis A virus (HAV), and other enteric viruses could not be amply sought in the environment. This is due to the fact that the cell lines available did not allow the growth of the so-called pathogens, or at least not enough to give a cytopathic effect. The 1990s will be marked by a real passion for the Environmental Virology, through the technique of PCR for enteric viruses to DNA as adenoviruses and the reverse transcriptase PCR for the RNA viruses (Gilgen et al., 1995; Haramoto et al., 2005).

It is after the involvement of the PCR that research in the food that was previously almost limited to the research of the *enterovirus* developed by research, especially of NoV and virus of hepatitis A. The essential of the scientific production in virology of food is made on the shellfish (bivalve molluscs). During this same period the success of the PCR POSA The problem of its real meaning and the interpretation that it was necessary to make of positive samples by this technique (Haramoto et al., 2005).

Human Enteric Viruses

Human Enteric Viruses and Indicators of Contamination

The development of the Environmental Virology is accompanied by a problem that is to find the indicators of contamination, which would have the same advantage as the bacteriological indicators of fecal contamination (Kittigul et al., 2005). Earlier, the work has indicated clearly

that the bacteriological indicators of fecal contamination could not be used for the monitoring of the virological quality of water and food. The analyses carried out by Jiang and Chu (2004) on the samples of waters of urban rivers showed the absence of enteroviruses and adenoviruses in the samples, the most loaded with fecal Coliforms.

Many scientific works have been undertaken to find an indicator of contamination for these pathogens. The proposals arising from these approaches are varied and not consistent. Many of the authors (Muniain-Mujika et al., 2003; Skraber et al., 2004) have concluded that the fecal coliphages could be satisfactory indicators, in any case better than all the bacteriological indicators. Some authors have concluded the ability of some enteric viruses to play this role of indicator. For this purpose the enteroviruses are the most frequently proposed according. In addition, no particular indicator appears to be unanimous for the moment (Pina et al., 1998).

Resistance of Enteric Viruses

Enteric viruses are generally nonenveloped particles, which gives them a very good stability in the environment. The fact that the virions attach to the suspended material contributes to the protection from the inactivation; these particles can stay in the environment for a long time without being deactivated (Biziagos et al., 1998). These pathogens also have a good resistance to chemical disinfection (Nuanualsuwan and Cliver, 2003). They are much more resistant to chemical treatments such as chlorination and the use of many other disinfectants (Jiang et al., 2001). The limits of the common techniques of disinfection with respect to the elimination of human enteric viruses have led some researchers to focus on physical methods of elimination of viral particles. The membrane ultrafiltration is in this case a way to ensure a good quality of the drinking water (Vaidya et al., 2004). Similarly, the hydrostatic pressure can be used to disable shellfish contaminant virions (Kingsley et al., 2002b; Nuanualsuwan and Cliver, 2003).

Enteric Viruses and Transmission by Food

The viruses are infectious agents and cellular parasites mandatory. Enteric viruses that are transmitted by digestive tract may contaminate food or water (fecal peril). They belong to different families and can be classified according to their genome type by using the classification of Baltimore. Table 40.1 identifies the viruses that can be transmitted by food and waterborne diseases that will be described in a greater detail (Coralie, 2014).

Enteric viruses are transmitted and spread by the fecal–oral route. They come in the gastrointestinal tract, survive the acidity of the stomach, and initiate their infectious cycle.

TABLE 40.1 Transmissible Viruses Via the Food or Water

Classification of Baltimore	Family	Genus	Transmissible virus by food or water	Frequency
I	Adenoviridae	Mastadenovirus	Adenovirus 40 and 41	Regularly
II	Parvoviridae	Erythrovirus	Parvovirus B19	Not well known
		Bocavirus	Bocavirus	Not well known
III	Reoviridae	Rotavirus	Human rotavirus group A	Regularly
	Picobirnaviridae	Picobirnavirus	Picobirnavirus	Not well known
IV	Caliciviridae	Norovirus	Norovirus GG I, II, IV	Very frequent
		Sapovirus	Sapovirus GG I, II, IV, V	Regularly
	Picornaviridae	Hepatovirus	Hepatitis A virus	Regularly
		Kobuvirus	Aichivirus	Regularly
		<i>Enterovirus</i>	<i>Poliovirus, coxsackievirus, echovirus, enterovirus</i>	Regularly
		Parechovirus	Human prechovirus	Not well known
		Casavirus	Cosavirus	Not well known
		Aphthovirus	FMDV	Rare
		Hepeviridae	Hepevirus	Hepatitis E virus
	Astroviridae	Mamastrovirus	Astrovirus	Regularly
	Coronaviridae	Alphacoronavirus	Human coronavirus 229E and NL63	Not well known
			Human coronavirus OC43 and HKU1	Not well known
		Betacoronavirus	SARS coronavirus	Rare
Flaviviridae	Flavivirus	TBEV	Regularly	

(Continued)

TABLE 40.1 (Continued)

Classification of Baltimore	Family	Genus	Transmissible virus by food or water	Frequency
V	Arenaviridae	Arenavirus	Arenavirus	Rare
	Bunyaviridae	Hantavirus	Hantavirus	Rare
	Orthomyxoviridae	Influenza A virus	HSN1	Rare
	Paramyxoviridae	Henipavirus	Nipah virus	Rare

Classification of Baltimore: I = DB DNA; II = Sb DNA; III = DB RNA; IV = Sb RNA; V = Sb RNA., TBEV, *tick-borne encephalitis virus*; FMDV, *foot-and-mouth disease virus*

The viral particles are then excreted at high dose in the stool (10⁷ infectious particles per gram of stool) [FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 2008]. Enteric viruses are characterized by their stability outside of their host, which can generally withstand environmental stresses (with variations according to the virus) such as acid, heat, drought, pressure, disinfectants, and ultraviolet radiation [FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 2008].

Enteric viruses can be transmitted through fecal–oral route directly from person to person or indirectly via the consumption of contaminated food or water (see Fig. 40.1). They can be at the origin of collective foodborne infections.

A foodborne collective infection is defined by the occurrence of “at least two grouped cases, with similar symptomatology, in general digestive, which can bring the case to a same origin of food” (Delmas et al., 2010). The foodborne collective infections are notifiable diseases (DO) (Vaillant et al., 2012).

Transmission by the Water Route

The waterborne transmission of enteric viruses can be at the origin of epidemics in countries where sanitary conditions are weak and a foodborne collective infections in industrialized countries.

The WHO has estimated in 2003 that the impact of the transmission of pathogens by the water route had caused 3.4 million deaths in the world, while the EU considers that 13,548 children under age of 14 years die each year due to these pathogens transmitted by water; however, it is difficult to estimate the real impact of viruses among all pathogens (Gibson, 2014).

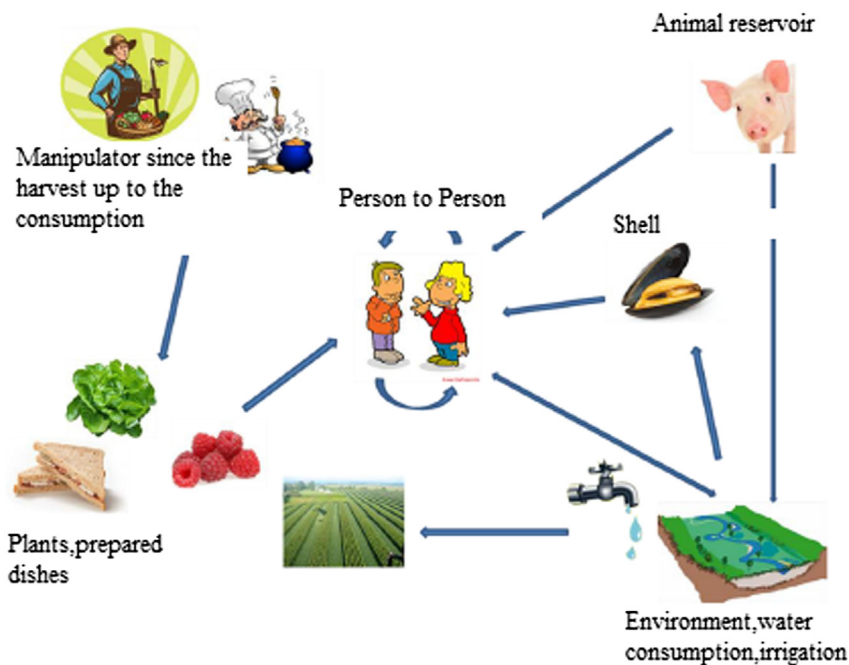


FIGURE 40.1 Routes of transmission of enteric viruses.

The viruses transmitted by the water route are frequently involved in gastrointestinal diseases outbreaks and acute hepatitis. The epidemics are associated with the recreational water, drinking water, and the aquifers water. Depending on the type of water, these epidemics are mainly due to the introduction of fecal material in the water or to an inadequate or interrupted treatment of drinking water (Gibson, 2014). In addition, the treatment of wastewater does not inactivate 20%–80% of the enteric viruses, which allows a significant viral load in the environment, including the river water, sea water, and groundwater (La Rosa et al., 2012). The most frequently transmitted viruses by water route are NoVs, HAV and hepatitis E virus, adenovirus, astrovirus, enteroviruses, and rotavirus (Gibson, 2014).

Transmission by Food Route

Food can be contaminated by the surrounding water, irrigation water, or at different stages of life (cultivation, harvesting, storage, transportation, sales, food preparation, etc.) via a hand-borne contamination [Koopmans and Duizer, 2004; FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization), 2008]. Plants and fruits can be contaminated via the water irrigation source

TABLE 40.2 Pathologies Induced by the Major Enteric Viruses

	Gastroenteritis	Hepatitis aigues	Other pathologies
The major viruses	Norovirus, rotavirus, sapovirus, aichivirus, <i>enterovirus</i> , astrovirus, adenovirus	Hepatitis A virus, hepatitis E virus,	<i>Enterovirus</i> , coronavirus, TBEV, parvovirus, cosavirus
Suspected virus	Bocavirus, parvovirus, picobirnavirus, cosavirus, coronavirus	/	/

(groundwater or contaminated wells, water contaminated network, etc.) as well as via organic fertilizers (manure and sludge that has not been heat treated) which can be used in traditional culture (Morin and Picoche, 2008). The sea water may be contaminated by a leak of sewers, or by poorly treated sewage. Shellfish (filter feeders) can then be contaminated by sea water that they filter inducing the concentration of virus within their digestive tissues (Morin and Picoche, 2008).

In the case of a zoonotic transmission the contamination is carried out either by direct contact with the infected animal or by the consumption of foods from infected animals (consumption of meat or meat products from these animals). The zoonotic power of some viruses has been demonstrated [as for the hepatitis E virus (HEV) transmitted by pork in particular], and it has been suspected for a few other viruses such as rotavirus and NoV (Martella et al., 2010; Midgley et al., 2014; Bank-Wolf et al., 2010) (Table 40.2).

Human diseases associated with enteric viruses vary as well as the severity of the associated symptoms. The most common pathology associated with enteric viruses infections is the gastroenteritis (with vomiting and/or diarrhea). However, some of these viruses can also be responsible for various pathologies, such as hepatitis, respiratory diseases, conjunctivitis, infection of the central nervous system (meningitis, encephalitis, poliomyelitis), muscular syndromes (fibromyalgia, myocarditis), and be involved in chronic diseases such as diabetes and chronic fatigue syndrome (La Rosa et al., 2012).

Acute Gastroenteritis Viruses Aigues

Today it is admitted that the most common acute viral gastroenteritis are due to rotavirus in young children and the NoV in adults. The viruses responsible for gastroenteritis are a significant cause of mortality and morbidity in the world, but their importance is often underestimated. The distribution of cases between five enteric viruses in function

of the age of the patients is represented in Fig. 40.2 for the first study and in Fig. 40.3 for the second.

In the first study (FSA, 2000) the sapoviruses (SAVs) are detected under the appellation calcivirus. We note that very little of calciviruses are then detected in adults in comparison to the second study (FSA, 2012). This can be explained by the progress in terms of sensitivity of

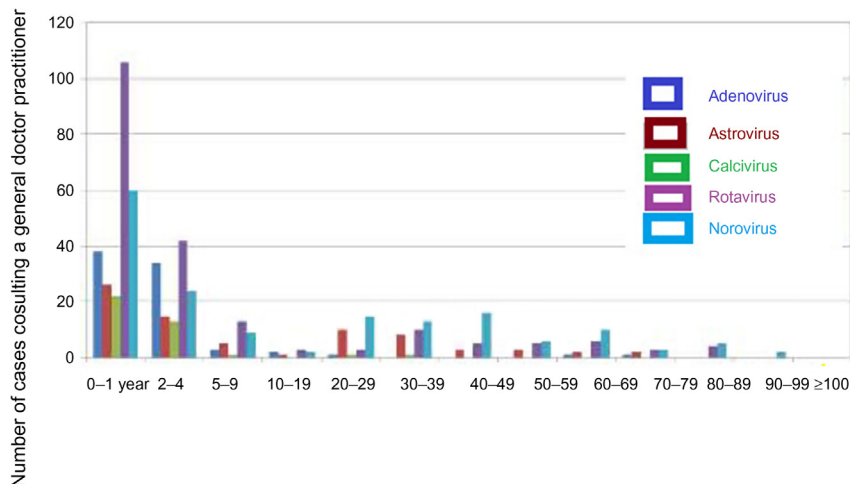


FIGURE 40.2 Virus detected in patients consulting their general practitioner for gastrointestinal infection, according to the age, for the period 1993–96 (FSA, 2000).

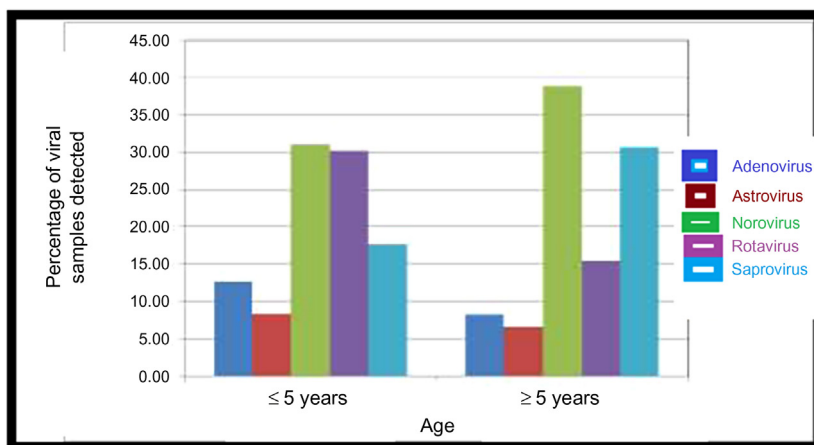


FIGURE 40.3 Viruses detected in patients consulting their general practitioner for gastrointestinal infection, according to the age, for the period 2008–09 (FSA, 2012).

detection methods between these two studies. In the first study, 26.5% of consultations among general practitioners for intestinal viral infection involved children less than 5 years of age with a rotavirus infection. This figure rises to approximately 12% during the second study. This difference can be explained by the fact of the improvement of techniques for the detection of the whole of the enteric viruses between the two studies (FSA, 2012).

The NoV represents the most important cause of epidemics of non-bacterial gastroenteritis in the world (housing, 2005). These viruses infect adults as well as children, as shown in Figs. 40.2 and 40.3. They represent 40%–50% of gastroenteritis related to food in the United States (Dolin, 2007). The main viruses infecting the adults in the United Kingdom in 2008–09 are the NoV and SAV (FSA, 2012).

The rotavirus infections represent the major cause of diarrhea among children 6–24 months (Schaechter et al., 1999). Almost all of the children have at least had a rotavirus infection of Group B before the age of 5 years (Schaechter et al., 1999).

Rotavirus is responsible for about 2 million of hospitalizations and cause 352,000–592,000 deaths among children under 5 years of age each year in the world (Parashar et al., 2003). The children of the poorest countries account for 82% of the dead by rotavirus (Parashar et al., 2003).

The astrovirus is a significant cause of gastroenteritis in young children (Dennehy et al., 2001; Herrmann et al., 1991). In 1978 Kurtz and Lee have conducted a study for anti-astrovirus antibodies in an English hospital; they have found that 75% of children 5–10 years had antibodies against this virus. The astrovirus is also an important cause of gastroenteritis in the elderly in association with other viruses, such as rotavirus or calicivirus (Lewis et al., 1989; Gray et al., 1987).

For the adenovirus, it is essentially serotypes 40 and 41 that are responsible of gastroenteritis. The infection is most often asymptomatic in healthy adults (Coralie, 2014).

PART II: ENTERIC VIRUSES

Human Enteric Viruses

Common Characteristics

Human enteric viruses are those that colonize the gastrointestinal tract. These organisms are excreted in large amounts in the stool of infected persons. These viruses have a high serotypic variability. Indeed, more than 140 different serotypes of human enteric viruses have been detected in the domestic releases. These viruses can infect both surface and groundwater. In the environment, these organisms do not multiply,

because their multiplication requires adapted host cells such as the intestinal epithelial cells. The effectiveness of water treatment methods remains limited with respect to these microorganisms. This is the case for all oral–fecal transmission viruses via drinking waters and contaminated foods, but also other vectors of fecal–oral transmission. These viruses are responsible for various pathologies (Haramoto et al., 2005).

Enteroviruses

Descriptions of the Enteroviruses

The enteroviruses are the viruses of the Picornaviridae family. They are characterized by a single-stranded RNA genome, of 2.5×10^6 Da that ends by a poly-A chain at the 3' end. The other 5' end is blocked by a protein called V of approximately 2.4 kDa. The capsid of the Picornaviridae consists of 60 under protein units. Each of these subunits is formed of four polypeptides. The enteroviruses are nonenveloped viruses; their capsid has a diameter of 27 N m (Ehlers et al., 2005).

The human enteroviruses are divided in five species (Table 40.1): human *poliovirus* with three serotypes; *Coxsackievirus A* including the serotypes 1–22, and also 24 are infectious to humans; the *Coxsackievirus B* of serotypes 1–6; echoviruses of serotypes 1–7, 9, 11–27, 29–33 and enteroviruses 68–71 (Ehlers et al., 2005).

Poliovirus Species

Polio is this acute infectious disease that may have the effect destroying the neuron, motor of the spinal cord. The result is the flaccid paralysis that characterizes this viral disease. The disease had a high incidence in the world until the development of reliable attenuated strains that led to an oral vaccine designed by Sabin. This vaccine is trivalent and also gives a good humoral immunity. This vaccine, still in use, had raised so much hope that WHO has set for objective of the eradication of poliomyelitis before 2000. It is clear that this objective has not been achieved. However, in the countries where polio has been eradicated, the injectable vaccine is the only one used because the maintenance of the use of oral vaccine could cause reversion to virulent strains in the environment (Khalfan et al., 2001; Herremans et al., 2002; Horie et al., 2002a,b).

The Coxsackievirus A and B

The Coxsackievirus was classified in two species: the *Coxsackievirus A* with 23 serotypes and the *Coxsackievirus B* with 6 serotypes based on histopathological studies (Lum et al., 2002).

TABLE 40.3 The Species of the Genus *Enterovirus* and Pathologies Associated

Species	Serotypes	Pathologies associated
<i>Poliovirus</i>	1–3	Meningitis, encephalitis, poliomyelitis
<i>Coxsackievirus A</i>	1–22, 24	Meningitis, encephalitis, paralysis, fever
<i>Coxsackievirus B</i>	1–6	Meningitis, encephalitis, paralysis, myalgia, pericarditis, myocarditis, gastroenteritis
<i>Echovirus</i>	1–9, 11–21, 24–27, 29–34	Meningitis, encephalitis, paralysis, gastroenteritis, conjunctivitis
<i>Enterovirus</i>	68–71	Meningitis, encephalitis, paralysis, conjunctivitis

Echoviruses

This species has been identified for the first time in 1955 (enteric cytopathogenic human orphan virus). They cause encephalitis (Lum et al., 2002) (Table 40.3). The site of initial replication of *echovirus* is the intestinal tract. From there the virus can invade other organs (Lum et al., 2002).

The infections with *echovirus* are usually asymptomatic. However, these viruses remain capable of causing serious and very varied pathologies. These disorders can be transmitted according to an epidemic mode similar to the polio cases. Some echoviruses are attacking the central nervous system causing aseptic meningitis. Echoviruses are also responsible for myocarditis and hemorrhagic conjunctivitis and even some chronic diseases such as diabetes (2006). It should be noted that notwithstanding their replication in the intestinal tract, it is observed that echoviruses do not cause gastroenteritis (Lum et al., 2002).

Caliciviruses: Norovirus and Sapovirus

Caliciviruses are single-stranded RNA viruses of positive polarity. They have an icosahedral capsid of approximately 30 nm in diameter. These viruses are found in a large number of hosts, such as humans, primates, cats, pork, and chicken. The Caliciviridae family includes two kinds that can infect humans: NoV and SAV (Adler and Zickl, 1969).

Norovirus

The name NoV refers to the city of Norwalk in Ohio in the United States, where an outbreak of gastroenteritis involving children and adults occurred in 1968 (Adler and Zickl, 1969). The viral particles only have been clearly identified in the samples of this epidemic in 1972. An

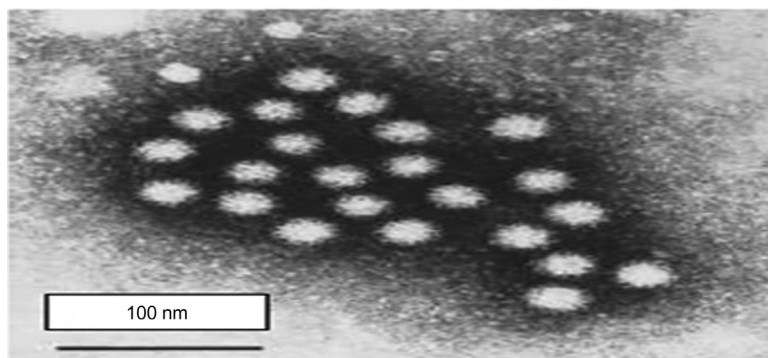


FIGURE 40.4 Aggregates of Norwalk virus observed in electron microscope (Kapikian, 2000) (Curry, 2003).

observation with the electron microscope was possible after the agglutination of particles by antibodies from the serum of a convalescent patient (Kapikian et al., 1972). Fig. 40.4 represents the aggregates of NoV observed in electron microscope (Kapikian, 2000). Thanks to the analysis of the genome, which is a single-stranded RNA of 7–8 kb, the Norwalk virus was then classified in the *Caliciviridae* family and in the gender NoV. This genus includes five genogroups whose genogroups I, II, and IV are pathogenic for humans (Kapikian, 2000).

The diversity of the gene sequence of the capsid has allowed the definition of genotypes that are, respectively, 8, 17, and 1 for the genogroups I, II, and IV (Zheng et al., 2006).

The NoV is responsible for acute gastroenteritis with diarrhea and sudden onset vomiting.

The incubation period for the genogroups I and II has a median value of 1.2 days, and 95% of symptomatic cases are observed before 2.6 days (Lee et al., 2013).

Vomiting is very common in children over 1 year old, while diarrhea dominates the clinical picture in children under 1 year of age. Fever is observed in 37%–45% of patients, the latter being often solved spontaneously in 24 hours. Healing is also spontaneous after 2 or 3 days; however, more severe clinical forms can be observed in immunocompromised individuals (Lee et al., 2013).

Sapovirus

The SAVs have been identified for the first time during an outbreak of gastroenteritis in an orphanage in the city of Sapporo, Japan (Chiba et al., 1979). Fig. 40.5 represents the SAV observed in electron microscopy. The genome of these viruses is a single-stranded RNA of positive

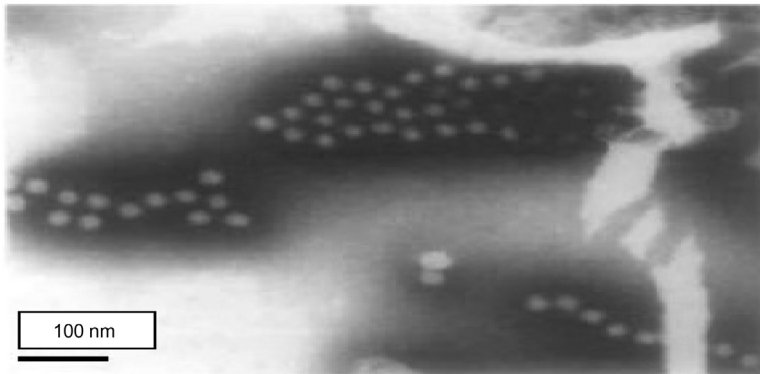


FIGURE 40.5 Sapovirus in the stool of a child with gastroenteritis, electron microscopy (Curry, 2003).

polarity of size between 7 and 8 kb. The SAVs are divided into five genogroups, themselves divided into genotypes (Hansman et al., 2007).

The SAVs are also responsible for gastroenteritis. The incubation period is 24–48 hours with symptoms often less marked than the NoV (Cubitt, 1989). The healing is spontaneous in less than 3 days (Cubitt, 1989).

Rotavirus

Rotavirus belongs to the Reoviridae family. Their icosahedral capsid measures between 70 and 100 nm in diameter (Weisberg, 2007). These viruses are classified into eight groups, A–H (Desselberger, 2014), but only the Groups A, B, and C infect humans, and the Group B is mainly found in China (housing, 2005).

Its genome is composed of 11 segments of double-stranded RNA of total size between 19 and 32 kb pairs some of which encode for structural proteins (VP1–4, VP6, VP7) and the other for nonstructural proteins (NSP) (NSP 1–5) (Fig. 40.6) (Parashar et al., 1998).

The transmission is done primarily from person to person. A transmission by aerosols is possible. Rotavirus can survive for several hours on the hands, up to 9 days in aerosols and several tens of days in water at 20°C [AFSSA (French Food Safety Agency), 2007]. Despite this resistance in water, any epidemic related to water has been reported to date for rotavirus (Singer et al., 2010).

Epidemiological Review of Pathologies Caused by Rotavirus

Nearly 95% of children in the world are infected by the rotavirus before the age of 5 years (Parashar et al., 1998). The Rotavirus Group A

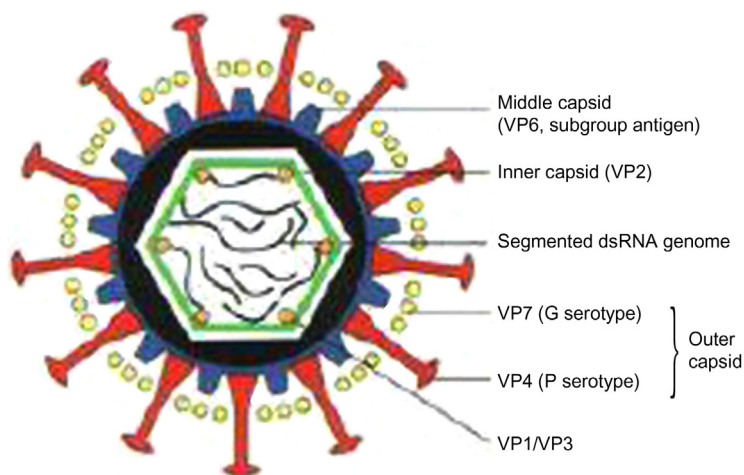


FIGURE 40.6 Schematic representation of a rotavirus virion (Singer et al., 2010).

is recognized as the most common enteric pathogens identified in children hospitalized for diarrhea. The infection is universal and quasi-independent of socioeconomic status. This results in huge mortality in the developing countries, with more than 800,000 annual deaths among children in the 1990s. In the industrialized countries, diarrhea related to the enteric infections involves only a limited mortality. This is explained by a better symptomatic treatment of the so-called affection. Indeed, the infant mortality due to diarrhea to do enteric usually occurs only in the event of default of this enteric situation which can be of times aggravated by the states of current malnutrition in some poor countries (Fig. 40.7). It is for this reason that the mortality in question is concentrated in the developing countries (Schwartzbrod, 1984).

Enteric Adenovirus

Description

Adenoviruses belong to the Mastadenovirus genus within the family Adenoviridae. Their genome consists of linear double-stranded DNA. Adenoviruses are the particles with 60–90 nm diameter, without envelope, including the capsid. It is formed of 252 capsomeres (240 hexons and 12 pentons). The genome is double-stranded DNA of 26–45 kb approximately, coding for 40 proteins, including the proteins of the capsid, the proteins of cores, and the proteins that are essential for the infectious viral cycle (Fig. 40.8).

The human adenoviruses are responsible for respiratory, ophthalmic, and enteric diseases. The human adenoviruses are subdivided into six

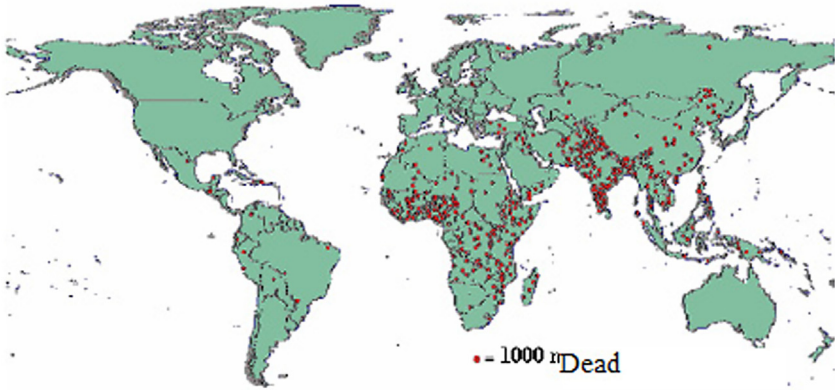


FIGURE 40.7 Estimate of the overall distribution of the annual mortality caused by the rotavirus (Parashar et al., 2003).

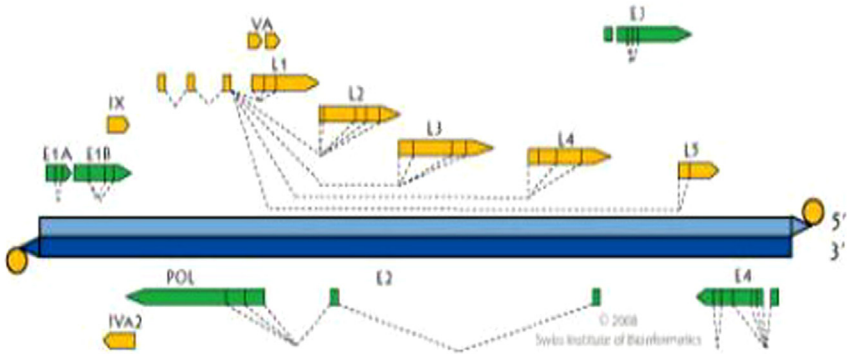


FIGURE 40.8 Genomic organization of adenovirus (Coralie, 2014).

subgroups (A–F) comprising 51 serotypes. Subgroup F includes both serotypes 40 and 41, which are genetically very close and are involved in enteric pathologies.

The serotypes 40 and 41 adenovirus, called enteric adenoviruses, are responsible of acute gastroenteritis, especially among children. Considered an emerging pathogen, it has been added to the list of “Contaminant Candidate List (CCL3 and 4)” of the “US Environmental Protection Agency” in 2004.

The incubation period is 3–10 days, and the symptoms are fever, diarrhea, vomiting, abdominal pain, and possibly the respiratory symptoms. The infection lasts for approximately 10 days (Rovida et al., 2013).

In a hospital study, Rovida et al. (2013) demonstrated that enteric adenoviruses were the primary agents responsible for gastroenteritis with 17.5% of the cases for which they were assigned. They are detected

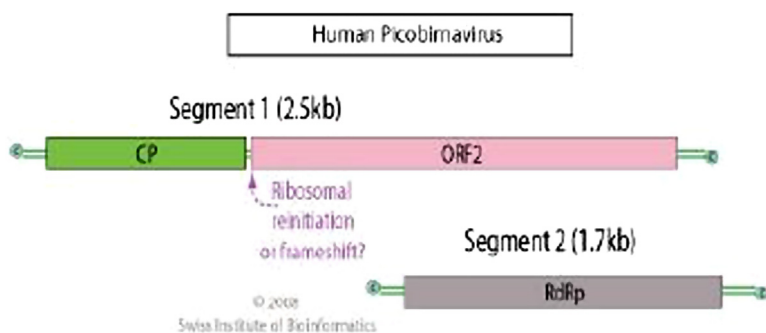


FIGURE 40.9 Genomic organization of Picobirnavirus (Fregolente and Gatti, 2009).

throughout the year but more frequently on the periods of October–November and January–February (Rovida et al., 2013).

Picobirnavirus

Description

Discovered in rats in 1988, this virus has been called Picobirnavirus, “pico” because it is small in size (virion 35 nm) and “birna” because its genome is a double-stranded RNA (Pereira et al., 1988). It belongs to the Picobirnaviridae family, composed of a single kind Picobirnavirus, with two species: Human picobirnavirus and Rabbit picobirnavirus (Fregolente and Gatti, 2009). It is a nonenveloped virus.

Its genome (Fig. 40.9) consists of two segments, a large segment (2.2–2.7 kb) coding for two open reading frames (ORFs), the first coding for a precursor of the capsid and the second is not yet characterized, and a small segment (1.2–1.9 kb) with a single ORF coding for the RNA-dependent-RNA-polymerase (RDRP) (Rosen et al., 2000; Wakuda et al., 2005).

Two genogroups (GI and GII) are described on the basis of the sequence of the RDRP (Fregolente and Gatti, 2009).

The picobirnavirus has been detected in the feces of animals or humans, introducing or not a diarrhea, sometimes in the presence of other enteric pathogens, and is as well qualified as opportunistic virus (Gallimore et al., 1995; Rosen et al., 2000; Bányai et al., 2003; Fregolente et al., 2009). The picobirnaviruses are excreted in the feces during a long period (45 days to 7 months) (Kapusinszky et al., 2012).

It has been identified in samples from two outbreaks of gastroenteritis in retirement homes in Florida (Rosen et al., 2000), as a single pathogen in patients with gastroenteritis (Cascio et al., 1996), as well as in 20% of patients Dutch with gastroenteritis (Picobirnavirus IM)

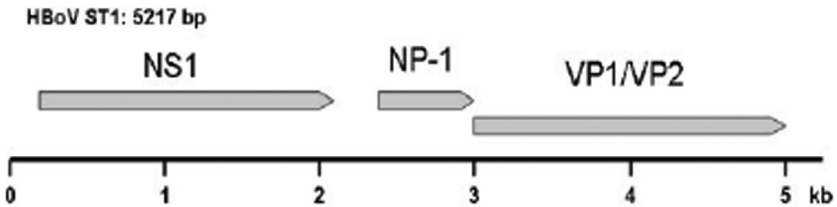


FIGURE 40.10 Genomic organization of Bocavirus (Allander et al., 2005).

(van Leeuwen et al., 2010). Its prevalence in the United Kingdom is estimated to be between 9% and 13% (Gallimore et al., 1995).

Bocavirus

Description

The Parvoviridae family is subdivided into two subfamilies, the Densovirinae infecting arthropods and Parvovirinae infecting birds and mammals. Within the Parvoviridae subfamily, five genera are described, including the Bocavirus. The human Bocavirus (HBoV) has recently been found in respiratory samples (nasopharyngeal) of young Swedes. The HBoV is the second viral species of the Parvovirinae subfamily known to be pathogenic to humans after Parvovirus B19 (Allander et al., 2005).

The HBoVs are simple DNA strand viruses, not wrapped. The size of its genome is approximately 5.3 kb and includes three ORFs (Fig. 40.10), two coding for two NSP (NS1 and NP1) and an ORF coding for two structural proteins (VP1 and VP2) (Allander et al., 2005).

The transmission is fecal–oral and air. The HBoV is found in respiratory specimens of patients hospitalized for respiratory disorders (Allander et al., 2005). The first study describing the presence of HBoV in the stools of children with gastroenteritis has identified this virus as the only pathogen and therefore the only responsible for the pathology (Vicente et al., 2007). Since then, three other species of HBoV have been described: HBoV2 (Kapoor et al., 2009; Arthur et al., 2009), HBoV3 (Arthur et al., 2009), and HBoV4. The genomic sequence of HBoV2 varies by 23% compared to that of HBoV, while that of HBoV3 varies from 18% compared to those of HBoV and HBoV2 (Arthur et al., 2009).

HBoV is associated most often with the symptoms of gastroenteritis that is the HBoV2 (Arthur et al., 2009) and is more rarely detected in the breath samples. A study on patients with gastroenteritis has demonstrated that HBoV was involved as a pathogen in 2% of the cases of gastroenteritis in the hospital (Rovida et al., 2013). HBoV is frequently detected in the feces of sick or healthy children and adults, which suggests the idea that the period of shedding of virus is long and that there is

frequent infections, often in coinfections. Epidemiological data indicate an early infection by the virus, with a seroprevalence of 90% at the age of 5 years (Endo et al., 2007). HBoV was detected in clinical and/or environmental samples in all regions of the globe: Europe (Allander et al., 2005; Kapoor et al., 2009; Hamza et al., 2009; Vicente et al., 2007), Asia (Kapoor et al., 2009), Africa, Australia (Arthur et al., 2009), and America. The different species of HBoV seem to have a worldwide distribution.

Viruses Responsible of Hepatitis

Hepatitis A Virus

Description

The HAV belongs to the family of the Picornaviridae and is classified in the genus Hepatovirus. It is a nonenveloped virus consisting of an icosahedral capsid. Its genome of about 7500 nt is composed of a single-stranded RNA of positive polarity. It is composed of two noncoding regions located in the 5' and 3' ends of NTR, as well as of a single ORF comprising the region P1, coding for the structural proteins VP1, VP2, and VP3 (VP4 putative), which constitute the capsid and regions P2 and P3, encoding for NSP involved in the replication of the virus (Fig. 40.11), including the protein 3b, also called VPg, which binds to the 5' NTR and probably plays a role as a primer for the synthesis of RNA; the protein 3c is a protease; the protein 3D is an RDRP (Cristina and Costa-Mattioli, 2007).

Only one serotype of HAV has been identified but several genotypes are described. The genotyping based on the sequence of the junction VP1–2 revealed 7 genotypes (Robertson et al., 1992), the genotypes I, II, III, and VII infecting humans, and genotypes IV, V, and VI infecting monkeys. More recently, Costa-Mattioli et al. (2002) and Read (2004) have proposed a new classification based on the complete analysis of the 900 nt of the sequence of the protein VP1: genotypes I and III are divided into two subgenotypes A and B, whereas the former genotypes II and VII are grouped into subgenotypes IIA and IIB, respectively.

The different genotypes of HAV have different geographic distributions (Nainan et al., 2006), and the subgenotype IA is the most prevalent in the world (Fig. 40.12).

Hepatitis E Virus

Description

The HEV was discovered in the 1980s as the agent of viral hepatitis non-A and non-B was transmitted by fecal–oral route (Wong et al., 1980; Khuroo et al., 1980). It has been classified in 2004 as the only member of the genus Hepevirus in the Hepeviridae family. HEV is a nonenveloped

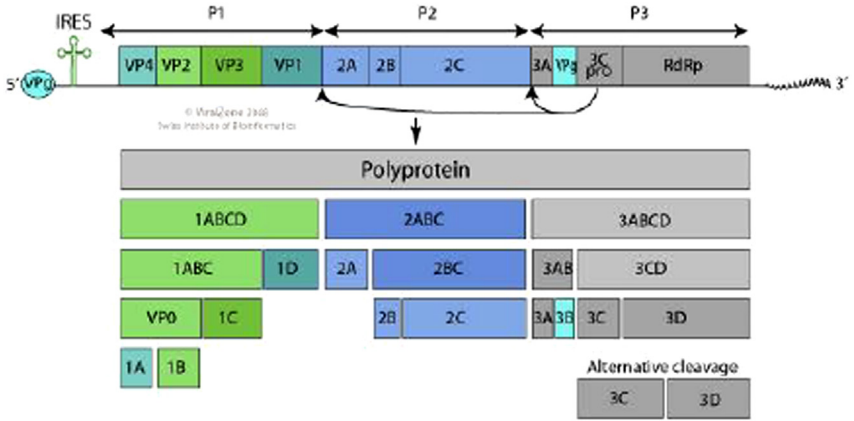


FIGURE 40.11 Genomic organization of HAV. HAV, Hepatitis A virus.

virus, icosahedral capsid, and 27–30 nm in diameter. Its genome consists of a positive polarity single strand RNA, approximately, 7300 nt (Tam et al., 1991; Aye et al., 1992; Reyes et al., 1993). Three ORFs are described (Fig. 40.13), overlapping partially, surrounded by a share of a 5' not encoding and a cover necessary for its viability and, on the other hand, of a 3' noncoding, followed by a poly-A tail (Pelosi and Clarke, 2008; Smith et al., 2013). The coding sequences cover 95% of the genome of HEV (Smith et al., 2013).

The ORF 1, long of approximately 5 kb, codes for a nonstructural polyprotein, involved in the replication of the viral genome and the manufacture of viral proteins (methyltransferase, helicase, RDRP, and protease) (Pelosi and Clarke, 2008). The ORF 2, long of approximately 2 kb, codes for the capsid protein (which interacts in particular with the 3' of the viral RNA for its encapsidation and contains a signal peptide of endoplasmic reticulum as well as glycosylation sites) (Pelosi and Clarke, 2008; Yugo and Meng, 2013). The ORF 3, more small, overlaps in part the 5' end of the ORF2 and codes for a phosphoprotein whose function is still poorly known, but who could be involved in the modulation of cell signaling in associating with the capsid protein and the cytoskeleton (Pelosi and Clarke, 2008; Smith et al., 2013).

The HEV has a worldwide distribution. It is endemic in the regions where sanitary conditions are low, responsible for large-scale outbreaks of viral hepatitis (Pelosi and Clarke, 2008). It is also found in the developed countries but is at the origin of sporadic cases. The genotypes of HEV have different geographic distributions. Genotype 1 is endemic in Asia and is also found in Africa. Genotype 2 was originally identified with a strain responsible for an epidemic in Mexico City and has since been found mainly in Africa. The Genotype 3 is associated with sporadic

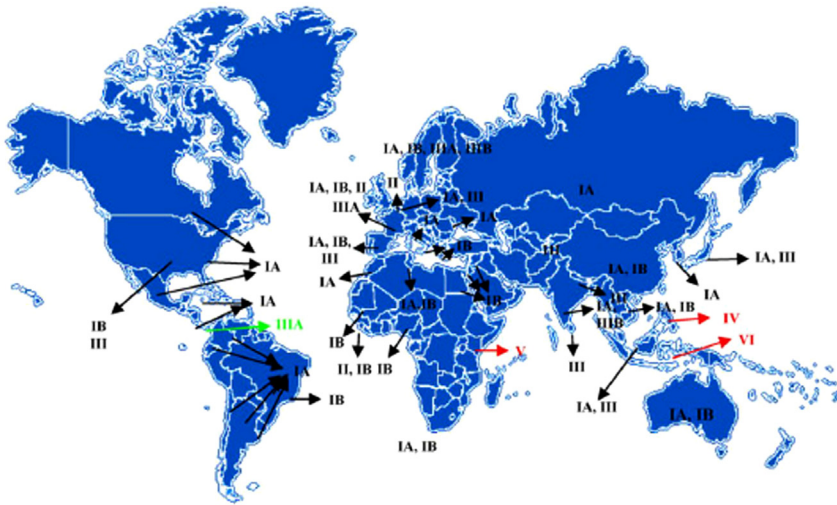


FIGURE 40.12 Geographic distribution of HAV genotypes (black, the genotypes isolated from humans, in red those isolated in monkeys, green strain PA21, first identified in the monkey but being a human strain) (Cristina and Costa-Mattioli, 2007). For interpretation of the references to color in this figure legend, the reader can refer web version of this chapter.

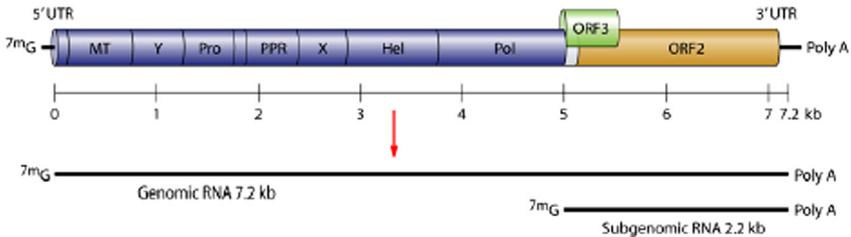


FIGURE 40.13 Structure of the HEV genome (Kamar et al., 2014). *HEV*, Hepatitis E virus.

cases, mainly in the industrialized countries despite its world distribution, and the genotype 4 is associated with sporadic cases and circulates mainly in Asia (Pelosi and Clarke, 2008; Yugo and Meng, 2013). Approximately 150 cases of viral hepatitis due to HEV are reported each year in France, 50–100 in Germany, and 30 in Italy, the seroprevalence is 6% in the Netherlands, 7.3% for adults in Spain, and 15%–30% in the United States.

CONCLUSION

The viruses associated to a waterborne transmission are enteric viruses, it means that they infect the cells of the intestinal tract and are excreted in the feces of infected persons. These viruses pose significant

problems in terms of public health; they are responsible for gastroenteritis, hepatitis, paralysis, meningitis, or respiratory diseases. These viruses are excreted in large quantities through fecal and will contaminate the environment; they can be transmitted by water route or during the consumption of contaminated food.

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