GLOBAL WATER PATHOGEN PROJECT

PART THREE. SPECIFIC EXCRETED PATHOGENS: ENVIRONMENTAL AND EPIDEMIOLOGY ASPECTS

SUMMARY OF EXCRETED AND WATERBORNE VIRUSES

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Summary

There are hundreds of viruses that infect humans and most are released into feces and urine making their way into the environment by excretion or secretion of bodily fluids or skin cells. The viruses infecting the enteric track are known to be excreted in high numbers and many of these viruses are commonly excreted by healthy people often long after symptom resolution.

The most important excreted known pathogens are transmitted by a variety of means including fecal-oral transmission routes and are members of six families, *Picornaviridae*, *Caliciviridae*, *Hepeviridae*, *Reoviridae*, *Astroviridae* (all RNA viruses) and the DNA virus family *Adenoviridae*. Viruses in these families cause asymptomatic infections and also outbreaks or sporadic cases with a wide range of symptoms from mild to severe gastroenteritis to meningitis, respiratory disease, conjunctivitis, miocarditis, paralysis, or hepatitis.

Recent data have shown the presence of new viral pathogens associated with gastroenteritis or other clinical symptoms in a set of novel viral families. In the *Parvoviridae* family, human bocaviruses 1 to 4 (HBoV) and human bufavirus (HBuV) are associated with respiratory and gastrointestinal diseases. Circoviruses are currently known to infect birds and swine, and no human pathogenic circoviruses have been definitively demonstrated yet, nevertheles new phylogenetically diverse Circoviruses have been shown to be present in sewage. A large portion of circular ssDNA viruses similar to the family *Circoviridae* have been revealed primarily through metagenomics in a diverse range of samples. Metagenomics in raw sewage water of United States, Spain and Ethiopia, showed sequences with identities between 20 and 50% to the *Circoviridae* family and in another study sewage from United States showed sequences 35 to 58% identical. The genera *Cyclovirus* have been suggested to cause human enteric infections and, a study identified and characterized the full genome of a novel cyclovirus (tentatively named cyclovirus-Vietnam [CyCV-VN]) in cerebrospinal fluid (CSF) specimens of two Vietnamese patients with CNS infections of unknown etiology.

A wide diversity of viruses is known to be commonly excreted, some are new pathogens recently described and some of them have not been associated yet to human diseases. A study analyzing stool samples from two healthy infant siblings collected at about weekly intervals during their first year of life were analyzed by PCR for 15 different enteric viral genera showed that ninety-two percent (66/72) of the fecal samples tested contained one to five different human viruses. Adenovirus, Aichi virus, Anellovirus, Astrovirus, Bocavirus, Enterovirus, Parechovirus, Picobirnavirus, and Rotavirus were detected. The study also confirmed long-term virus shedding for adenoviruses, anelloviruses, bocaviruses, enteroviruses, parechoviruses, and picobirnaviruses.

Excreted viruses are detected in urban sewage samples and survival is facilitated by organic debris of the clinical matrix in which the virus is shed (feces or vomit) and virus aggregate formation, offering protection in the route to new human hosts. The concentration of viruses observed in urban sewage is high and is related to the epidemiology of each viral infection. Viruses excreted in the population of all geographical areas and without defined seasonability, as it is the case of human adenoviruses, have been detected in wastewater and superficial waters in all geographical areas analyzed with levels of 10^{4-7} GC/100 ml in raw sewage, 10^{3-4} GC/100ml in secondary and tertiary effluent of wastewater treatment plants, 10^{4-7} GC/100 g of biosolids, 10^{1-5} CG/L in river water, and 10^{1-3}CG/L in seawater. Human adenoviruses and human polyomaviruses have been suggested as indicators of human fecal/urine contamination and MST tools in the environment and water based on the affordability of quantification techniques for DNA viruses, and their abundance in all geographical areas and periods of the year. Many classical and emerging viral pathogens have been detected in bathing water, river and seawater and their high stability and low infectious doses support the need for improving control of virus dissemination in water is an important concern requiring improved water treatments and regulations.

There are hundreds of viruses that infect humans and are released into the environment by excretion or secretion of bodily fluids or skin. The viruses infecting the gastrointestinal tract also known as enteric viruses, are excreted in high numbers (10^7 10^9 g-1 of feces) by infected individuals with or without disease, and in some cases long after the resolution of disease. These viruses can be transmitted by contaminated water via the fecal-oral route.

1.0 TAXONOMIC CLASSIFICATION OF THE VIRAL AGENTS

The most important waterborne viruses are members of six families, including RNA virus families such as *Picornaviridae*, *Caliciviridae*, *Hepeviridae*, *Reoviridae*, *Astroviridae* and the *Adenoviridae* within the family of DNA viruses. Viruses in these families cause asymptomatic infections and also outbreaks or sporadic cases with a wide range of symptoms from mild to severe gastroenteritis to meningitis, respiratory disease, conjunctivitis, myocarditis, paralysis, or hepatitis (http://ictvonline.org).

Table 1. Main viral waterborne pathogens

Family (genome, size)	Genus	Most important human pathogens	Related diseases
Adenoviridae (dsDNA, 70-90nm)	Mastadenovirus	Human adenovirus A-G (HAdV)	Gastroenteritis, respiratory disease, conjunctivitis, cystitis
Astroviridae (ssRNA, 28-41nm)	Mamastrovirus	Astrovirus 1-9 (HAstV)	Gastroenteritis, related to respiratory infections
Caliciviridae (ssRNA, 27-38nm)	Norovirus	Norovirus GI, GII (NoV)	Gastroenteritis
	Sapovirus	Sapovirus GI, GII, GIV, GV (SaV)	Gastroenteritis
Hepeviridae (ssRNA, 25-30nm)	Orthohepevirus	Hepatitis E virus G1,2,3,4,7 (HEV)	Acute hepatitis
Picornaviridae (ssRNA, 24-30nm)	Enterovirus	Enterovirus A-D (EV-68 and EV-71), Rhinovirus A-C, Poliovirus 1-3, Coxsakievirus A-B	Paralysis, meningitis, hand-foot-and-mouth disease, heart anomalies, skin rush
	Hepatovirus	Hepatitis A virus GI-III (HAV)	Acute hepatitis
	Kobuvirus	Aichivirus A to C (AiV)	Gastroenteritis
	Parechovirus	Parechovirus 1 to 16 (PeV)	Gastroenteritis, respiratory infections, encephalitis, meningitis, hepatitis
Reoviridae (dsRNA, 70-75nm)	Rotavirus	Rotavirus A to G (RoV)	Gastroenteritis

1.1 Viral pathogens of primary concern for waterborne diseases

1.1.2 Other groups containing new water-borne emerging viruses

Recent data has shown evidence of new viral pathogens in the *Parvoviridae* family associated with gastroenteritis in humans. The clinical manifestations of parvovirus 4 (PARV4) remain unknown whereas human bocaviruses 1 to 4 (HBoV) and human bufavirus (HBuV) are associated with respiratory and gastrointestinal diseases (Väisänen et al., 2014)

New viruses with DNA in circular form that are phylogenetically diverse have been detected in sewage. These viruses have been included within the family *Circoviridae* which comprises virus species that infect birds and swine (Blinkova et al., 2009). A large portion of circular ssDNA viruses, similar to the family *Circoviridae,* was elucidated by metagenomics of a diverse range of samples. Metagenomics of urban sewage in the United States, Spain and Ethiopia, showed virome contigs with 20 to 50% similarities to viruses with circular genomes characteristic of the *Circoviridae* family (Cantalupo et al., 2011). In addition, PCR screening of viral nucleic acid recovered from sewage in the United States revealed genetic variants of DNA circoviruses (Blinkova et al., 2009). The genus *Cyclovirus* has been suggested to cause human enteric infections, and a study identified and characterized the full genome of a novel cyclovirus (tentatively named cyclovirus-Vietnam [CyCV-VN]) in cerebrospinal fluid (CSF) specimens of two Vietnamese patients with CNS infections of unknown etiology (Li et al., 2010; Phan et al., 2015). The authors suggested the potential for fecal-oral as well as foodborne transmission while high detection rates in feces from pigs and poultry (average, 58%) suggested the existence of animal reservoirs for such transmission routes (Tan et al., 2013).

Table 2. Emerging viruses with potential for water-borne transmission

Family (genome, size)	Genus	Human pathogens	Related diseases
Anelloviridae (ssDNA, 30-32nm)	Alphatorquevirus	Torquetenovirus (TTV)	Asymptomatic. May be associated with various diseases: hepatitis, pulmonary diseases, hematologic disorders, myopathy and lupus.
Circoviridae (ssDNA, 15-20nm)	Cyclovirus	Human Associated Cyclovirus 1-11 (HuACyV)	Systemic infections, may play a role in development of paraplegia
Parvoviridae (ssDNA, 18-26nm)	Erythroparvovirus	Parvovirus B19 (PaV)	Fifth disease in children, arthropathy, hepatitis
	Bocaparvovirus	Human bocavirus 1-4 (HBoV)	Gastroenteritis, related to respiratory infections
	Protoparvovirus	Bufavirus (HBuV)	Gastroenteritis
Papillomaviridae (dsDNA, 50-60nm)	Alpha-papillomavirus	Human Papillomavirus 16, 18 (HPV)	Cervix, penis, anus and vulva cancers
	Beta-papillomavirus	HPV 66	Related to genital warts
Picobirnaviridae (ssRNA, 33-41nm)	Picobirnavirus	Human picobirnavirus (HPBV)	May be implicated in gastroenteritis in humans
Polyomaviridae (dsDNA, 50-60nm)	Betapolyomavirus	Polyomavirus JC (PyV)	Progressive multifocal encephalopathy (PML)
		BKPyV	Mild respiratory infection, polyomavirus-associated nephropathy polyomavirus-associated haemorrhagic cystitis
	Alphapolyomavirus	Merkel cell PyV (MCPyV)	Associated to merkel cell carcinoma

1.2 EXCRETION OF VIRUSES

The excretion of viruses in feces is high and viruses are commonly excreted by healthy people even after resolution of symptoms. Stool samples from healthy infants showed that ninety-two percent (66/72) of the tested fecal samples contained one to five different human viruses (Kapusinszky et al., 2012). Adenoviruses, aichi viruses, anelloviruses, astroviruses, bocaviruses, enteroviruses, parechoviruses, picobirnaviruses and rotaviruses were the viruses most frequently detected. Vaccination schedules have an effect on the excretion of viruses (Laassri et al., 2005). The summary of the level of excretion of the most important waterborne viruses is shown in Table 3.

Table 3. Summary of the excretion characteristics of main water-borne viral pathogens

Viral Pathogen	Excretion concentrations	Clinical characteristics	Prevalence in feces/urine	Reference
Adenovirus	E+07 to E+11 GC/g of stool	IP: 3 to 10 days ID: 1 to 4 days DE: 11 days (1 to 192)	2.6% to 16% in fecal gastroenteritis samples	Bozkurt et al., 2015; Lion et al., 2010; Rimoldi et al., 2011
Aichivirus	E+06 to E+12 GC/g of stool	IP: 12 to 54h ID: 2 to 3 days DE: Undetermined	0.8% in fecal gastroenteritis samples	Bozkurt et al., 2015; Drexler et al., 2011; Le Guyader et al., 2008

Viral Pathogen	Excretion concentrations	Clinical characteristics	Prevalence in feces/urine	Reference
Astrovirus	E+08 to E+13 GC/g of stool	IP: 3,9 to 5,2 days ID: 1 to 4 days DE: 2 to 30 days	11% mean incidence of gastroenteritis worldwide, with 7% and 23% incidences in urban and rural areas	Bosch et al.,2013; Caballero et al., 2003; Desselberger and Gray, 1995; Lee et al., 2013
Bocavirus	E+04 GC/ml of fecal supernatant	IP: Undetermined ID: 1 to 4 days DE: weeks	1.3% in fecal gastroenteritis samples	Lau et al., 2007; Proenca-Modena et al., 2013; Rimoldi et al., 2011
Enterovirus	Coxsackievirus: E+03 to E+06 TCID50/g of stool	IP: 2 days ID: 2 to 3 days DE: 50 days (44 to 142)	22.1% coxsackievirus in fecal gastroenteritis samples	Bozkurt et al., 2015; Melnick and Rennick, 1980; Khetsuriani et al., 2009
Hepatitis A	E+07 GC/ml of fecal supernatant	IP: 7 to 50 days ID: 3 to 6 months DE: 8 days (4 to 42)	20% of clinical hepatitis	Arankalle et al., 2006; Lee, 2000
Hepatitis E	E+03 to E+07 GC/ml of fecal supernatant	IP: 2 to 10 weeks ID: 2 to 6 weeks DE: 22 days (14 to 33)	70% of fecal samples from hepatitis patients	Chandra et al., 2010.; Kim et al., 2014; Takahashi et al., 2007
Norovirus	E+07 to E+09 GC/gr of stool	IP: 1,1 to 1,2 days ID: 12 to 60h DE: 28 days (13 to 56)	16.2 to 42.8% in fecal gastroenteritis samples	Atmar et al., 2008; Bozkurt et al., 2015; Kaplan et al., 1982; Lee et al., 2013; Rimoldi et al., 2011
Polyomavirus	E+05 GC/ml urine	Reactivation in patients with immunosuppressive conditions DE: Several months or years	62.7% of helthy adults and 13.2% of children excrete polyomaviruses in theurine, mostly JC virus (41.2%)	Bofill-Mas and Girones, 2001; Kling et al., 2012; Polo et al., 2004
Rotavirus	E+10 to E+12 GC/gr of stool	IP: 2 days ID: 3 to 8 days DE: 10 days (4 to 57)	33 to 38.2% in fecal gastroenteritis samples	Bozkurt et al., 2015; Desselberger and Gray, 1995; Ramani et al., 2014; Richardson et al., 1998; Rimoldi et al., 2011
Sapovirus	E+07 to E+08 GC/g of stool	IP: 1,7 days ID: 1 to 4 days DE: 4 days (4 to 21)	3.8% in fecal gastroenteritis samples	Bozkurt et al., 2015; Lee et al., 2013; Rimoldi et al., 2011; Rockx et al., 2002; Torner et al., 2016

IP: Incubation Period, ID: Illness duration, DE: days excretion

1.3 TRANSMISSION

1.3.1 Global routes of transmission for viral infections

Water and food are the main vehicles for transmission of viruses that replicate in the gastrointestinal tract causing the wide spectrum of diseases described in Table 2. Contaminated drinking water is an important cause of gastrointestinal disease (Altzibar et al., 2015; Braeye et al., 2015; Craun et al., 2010; Kauppinen et al., 2017). The burden of water-borne diseases directly related to viruses, was estimated at 136 outbreaks in Europe during 2000 and 2007 (39% of all diarrhea cases due to unsafe water) and at 64 outbreaks in the U.S. during 1971 and 2006 (Craun et al., 2010; ENHIS, 2009). The risk of emerging waterborne diseases increases where standards of water, sanitation and personal hygiene are low. More than half of the waterborne disease outbreaks linked to drinking water have been associated with untreated or inadequately treated ground water, indicating that contamination of ground water remains a public health problem (Yoder et al., 2011).

The global public health impact is higher when considering the food-borne transmission route. The American and European surveillance reports on the food-borne outbreaks estimate that between 45 and 51% of the total food-borne outbreaks are caused by water-borne viruses (Gould et al., 2013; Price-Hayward and Hartnell, 2016). The route from food production to consumption is very complex, with many points where pathogens can enter and reach the consumers (e.g. at the farm, during slaughter, during processing, in the kitchen). Of the viral pathogens that can contaminate food, HAV, HEV and NoV in bivalve shellfish, fresh produce, and prepared foods have been identified as the highest risk pathogens (EFSA, 2012). Foodborne cases of hepatitis E in humans are increasingly common and likely underestimated in the medical community (Meng, 2013). Sporadic and cluster cases of hepatitis E occur after consumption of undercooked or raw animal meats.

Table 4. Transmission routes of the principal waterborne viruses

Viral Pathogen	Transmission routes	Seasonality	Reference
Adenovirus	Fecal-oral: contaminated food, person-to-person, drinking water Airborne: respiratory secretions Bathing water	Without clear seasonality	Mena and Gerba, 2009; Vetter et al., 2015
Aichivirus	Fecal-oral: contaminated food, person-to-person, drinking water	Without clear seasonality	Kitajima and Gerba, 2015
Astrovirus	Fecal-oral: contaminated food, person-to-person, drinking water	Higher incidence in the cold-weather period	Bosch et al., 2014
Bocavirus	Fecal-oral: drinking water Airborne: aerosol, respiratory secretions Vertical transmission?	Higher prevalences in cold months	Hamza et al., 2009; Schildgen et al., 2008
Enterovirus	Fecal-oral: drinking water Respiratory secretions	Higher prevalences in warm/wet seasons	Sedmak et al., 2005
Hepatitis A	Fecal-oral: contaminated food, person-to-person	No clear seasonality	Fares, 2015; Ouardani et al., 2016
Hepatitis E	Fecal-oral: contaminated food, drinking water Foodborne: raw meat	Occurs more frequently in winter	Inoue et al., 2009; Kotwal and Cannon, 2014
Norovirus	Fecal-oral: contaminated food, person-to-person, drinking water	Higher prevalences in cold months	de Graaf et al., 2016
Polyomavirus	The route of intra-human transmission is still unknown	Without seasonal distribution	Fratini et al., 2014
Rotavirus	Fecal-oral: contaminated food, person-to-person, drinking water	Year-round infection in countries within 10 degrees of the equator, Winter peaks in all other regions of the world	Estes et al., 1983
Sapovirus	Fecal-oral: drinking water	Peak observed mainly in the cold season	Dey et al., 2012

1.3.2 Animal Reservoirs of viral infections in humans

Humans are the main reservoirs of enteric viruses. With exception of rotavirus and hepatitis E virus, zoonotic transmission of water-borne viruses is rare. It is a well-known fact that animal RoV-A infect humans. Nowadays, there is convincing genetic evidence that interspecies transmission of RoV occurs. Animal RoV can infect humans via direct interspecies transmission events or reassortment between a human and animal rotavirus. Recent reviews on porcine, bovine and equine rotaviruses indicate that there are some globally important genotype specificities of RoVs in each of these host species. (Papp et al., 2013a; Papp et al., 2013b). Nevertheless, zoonotic viruses can emerge from animal reservoirs and affect humans only incidentally.

Hepatitis E virus is an emerging zoonotic water- and foodborne pathogen (Ricci et al., 2017; Uddin Khan et al., 2013). HEV-1 and HEV-2 are restricted to humans whereas HEV-3 and HEV-4 are naturally present in several animal species and can cross the species barrier. The zoonotic transmission of HEV-3 and HEV-4 from swine, wild boar and deer to human via the consumption of raw meat has been proven (Bouquet et al., 2012, 2011; Cook et al., 2017). In 2016, a small outbreak in China was related to HEV-4 found in food from the company's cafeteria (Zhang et al., 2016). There is also an increasing evidence for zoonotic transmission of hepatitis E from camels (Sridhar et al., 2017).

2.0 DATA ON OCCURRENCE OF VIRUSES IN WASTE WATER

Waterborne viral diseases are of major concern in both developing and developed countries and wastewater treatment plays a crucial role in mitigating viral pollution of aquatic environments. A summary of representative available data on the occurrence of viral pathogens in raw sewage, secondary and tertiary effluents of wastewater treatment plants is shown in Tables 5, 6 and 7.

Table 5. Viral concentrations in wastewater effluents worldwide

Area	Viral Pathogen	Percent Positive (# of samples)	Mean concentration (GC/L)	Max concentration (GC/L)	Reference
Asia	Norovirus GGII	36	2.51 E+06	NR[a]	Eftim et al., 2017
Bolivia	Rotavirus	NR	3.1 E+07	NR	Symonds et al., 2014
Brazil	Hepatitis A	25% (6/22)	5.1 E+02	NR	Villar et al., 2007
Brazil	Polyomavirus	96% (23/24)	4.6 E+05	3.2 E+05	Fumian et al., 2010
Brazil	Rotavirus	70.6% (17/24)	NR	2.9 E+08	Prado et al., 2011
Canada	Adenovirus	100% (16/16)	9.16 E+06	NR	Qiu et al., 2015
	Enterovirus	100% (16/16)	4.08 E+04	NR	
	Norovirus GGII	100% (16/16)	1.2 E+06	NR	
	Sapovirus	12.5% (2/16)	E+07	NR	
Europe	Norovirus GGII	305	E+05	NR	Eftim et al., 2017
France	Astrovirus	82% (14/17)	4.1 E+06	3.1 E+07	Le Cann et al., 2004
Germany	Adenovirus	100% (13/13)	1.24 E+06	NR	Leifels et al., 2016
	Enterovirus	92% (12/13)	2.27 E+05	NR	
Italy	Bocavirus	76% (102/134)	4.7 E+04	E+05	Iaconelli et al., 2016
Japan	Adenovirus	100% (72/72)	5.5 E+06	NR	Katayama et al., 2008

Area	Viral Pathogen	Percent Positive (# of samples)	Mean concentration (GC/L)	Max concentration (GC/L)	Reference
Japan	Astrovirus	36% (10/28)	1.7 E+06	NR	Kobayashi et al., 2017
	Hepatitis A	7% (2/28)	9.7 E+02	1.8 E+03	
	Hepatitis E	11% (3/28)	1.7 E+02	6.4 E+03	
Japan	Enterovirus	65% (47/72)	2.95 E+05	NR	Katayama et al., 2008
	Norovirus GGI	94% (68/72)	3.6 E+07 winter 2.39 E+04 summer	NR	
	Norovirus GGII	92% (66/72)	3.9 E+07 winter 8.3 E+04 summer	NR	
Japan	Sapovirus	100% (12/12)	1.8 E+04	1.3 E+05	Haramoto et al., 2008
Japan	Polyomavirus	7% (2/28)	2.7 E+02	7.2 E+02	Kobayashi et al., 2017
Nepal	Aichivirus	100% (1/1)	NR	4.0 E+09	Haramoto and Kitajima, 2017
New Zealand	Enterovirus	100 (30)	NR	4.7 E+06	Hewitt et al., 2011
New Zealand	Norovirus GGII	13	6.31 E+03	NR	Eftim et al., 2017
North America	Norovirus GGII	107	5.01 E+04	NR	Eftim et al., 2017
Spain	Adenovirus	89% (33/37)	8.38 E+05	2.9 E+07	Rusiñol et al., 2015
	Polyomavirus	100% (37/37)	7.47 E+05	1.7 E+07	
Spain	Norovirus GGI	91% (49/54)	NR	5.9 E+08	Pérez-Sautu et al., 2012
	Norovirus GGII	98% (53/54)	NR	3.4 E+09	
Sweden	Adenovirus	100% (7/7)	4.42 E+06	9.3 E+06	Hellmér et al., 2014
Switzerland	Hepatitis E	31% (5/31)	7.81 E+04	NR	Masclaux et al., 2013
Uruguay	Astrovirus	45 (19/45)	NR	4.3 E+07	Victoria et al., 2014
USA	Adenovirus	100% (48/48)	1.55 E+07	NR	Schmitz et al., 2016
USA	Aichivirus	100% (11/11)	1.18 E+04	NR	Rachmadi et al., 2016

[a] NR: Not reported

Table 6. Viral concentrations in secondary effluents worldwide

Area	Viral Pathogen	Percent Positive (# of samples)	Mean concentration (GC/L)	Treatment	Reference
Brazil	Adenovirus	70% (5/7)	3.78 E+03	CAS	Prado et al., 2011
	Norovirus GGII	28.5% (4/14)	2.4 E+06	CAS	
	Rotavirus	71% (3/5)	1.9 E+04	CAS	
Brazil	Polyomavirus	39% (9/23)	4.3 E+04	CAS	Fumian et al., 2010
Canada	Adenovirus	100% (16/16)	9.08 E+04	CAS	Qiu et al., 2015
France	Aichi virus	84% (231/275)	1.55 E+03	CAS	Prevost et al., 2015
	Astrovirus	84% (231/275)	1.08 E+05	CAS	
	Enterovirus	64% (175/275)	1.0 E+02	CAS	
	Norovirus GGI	98% (270/275)	5.0 E+03	CAS	
	Rotavirus	84% (231/275)	2.11 E+05	CAS	
Germany	Enterovirus	46% (6/13)	8.63 E+03	CAS	Leifels et al., 2016
	Rotavirus	77% (10/13)	1.3 E+04	CAS	
Italy	Hepatitis A	14% (3/21)	Undetermined	CAS	Iaconelli et al., 2015
Japan	Aichi virus	71% (20/28)	5.5 E+02	DHS	Kobayashi et al., 2017
	Astrovirus	32% (9/28)	6.3 E+03	DHS	
	Enterovirus	21% (6/28)	8.0 E+02	DHS	
	Hepatitis A	4% (1/28)	1.5 E+03	DHS	
	Hepatitis E	0% (0/28)	Non detected	DHS	
	Norovirus GGI	14% (4/28)	6.5 E+01	DHS	
	Norovirus GGII	57% (16/28)	7.2 E+01	DHS	
	Rotavirus	11% (3/28)	4.3 E+02	DHS	
Japan	Sapovirus	58% (7/12)	1.5 E+02	CAS	Haramoto et al., 2008
Norway	Bocavirus	54% (14/26)	2.72 E+04	CAS	Myrmel et al., 2015
	Hepatitis E	8% (2/26)	Undetermined	CAS	
	Norovirus GGI	100% (26/26)	3.8 E+06	CAS	
Singapore	Astrovirus	100% (18/18)	3.9 E+04	CAS	Aw and Gin, 2010
	Hepatitis A	28% (5/18)	Undetermined	CAS	

Area	Viral Pathogen	Percent Positive (# of samples)	Mean concentration (GC/L)	Treatment	Reference
Spain	Adenovirus	78% (25/32)	1.2 E+05	CAS	Rusiñol et al., 2015
	Norovirus GGII	65% (21/32)	5.05 E+05	CAS	
	Polyomavirus	59% (19/32)	1.6 E+05	CAS	
Sweden	Norovirus GGII	100% (12/12)	1.0 E+05	CAS	Nordgren et al., 2009
United Kingdom	Adenovirus	10% (5/48)	1.1 E+01	MBR	Purnell et al., 2016
	Norovirus GGI	3% (1/48)	1.1 E+01	MBR	
	Norovirus GGII	6% (2/48)	1.1 E+01	MBR	

CAS: conventional activated sludge; MBR: membrane bioreactor; DHS reactor: down-flow hanging sponge (DHS) reactor

Table 7. Viral concentrations in tertiary effluents worldwide

Area	Viral Pathogen	Percent Positive (# of samples)	Mean concentration (GC/L)	Treatment type	Reference
Brasil	Adenovirus	50% (3/6)	2.88 E+03	Cl2	Prado et al., 2011
	Hepatitis A	100% (4/4)	2.8 E+04	Cl2	
	Rotavirus	66% (3/4)	1.20 E+05	Cl2	
Canada	Adenovirus	100% (16/16)	8.71 E+04	UV	Qiu et al., 2015
	Adenovirus	6% (1/16)	1.86 E+04	UF and Cl2	
	Astrovirus	6% (1/16)	3.54 E+03	UF and Cl2	
	Rotavirus	38% (6/16)	7.94 E+02	UF and Cl2	
	Enterovirus	6% (1/16)	7.41 E+02	UF and Cl2	
Germany	Enterovirus	8% (1/13)	6.0 E+03	UV	Leifels et al., 2016
	Rotavirus	0% (0/13)	Non detected	UV	
Spain	Adenovirus	72% (16/22)	1.9 E+03	Actiflo® and UV	Rusiñol et al., 2015
	Hepatitis E	0% (0/22)	Non detected	Actiflo® and UV	
	Norovirus GGII	54% (12/22)	3.09 E+05	Actiflo® and UV	
	Polyomavirus	21% (5/22)	4.67 E+02	Actiflo® and UV	

Area	Viral Pathogen	Percent Positive (# of samples)	Mean concentration (GC/L)	Treatment type	Reference
USA	Adenovirus	13% (3/23)	1.0 E+01	UV and Cl2	Francy et al., 2012
	Enterovirus	0% (0/23)	Non detected	UV and Cl2	
	Norovirus GGI	8% (2/23)	1.0 E+01	UV and Cl2	

UV: Ultraviolet, UF: Ultrafiltration, Cl_2: Chlorination

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