Contribution to risk profile on foodborne viruses

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March 3, 2020

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Abstract

Foodborne viruses have been recognized as the highest ranked food safety priority in a recent report by risk assessment experts. Human norovirus (NoV) and hepatitis A virus (HAV), which cause acute gastroenteritis and viral jaundice, respectively, are the predominant pathogenic foodborne viruses with hepatitis E virus (HEV) being a minor contributor to foodborne outbreaks. NoV are responsible for an estimated one third of all global foodborne gastroenteritis cases, making it the lead cause of foodborne illnesses. HAV is endemic in geographical areas with poor hygiene and sanitation infrastructure, and causes 2% of foodborne illnesses worldwide.

The Danish Veterinary and Food Authority is currently developing a risk profile for foodborne viruses and product combinations that have most frequently given rise to disease among consumers. The present report is a contribution to this risk profile and reviews the current knowledge about the biology and occurrence of relevant foodborne viruses, contamination pathways, products at risk and the efficacy of prevention and mitigation methods. The objective of the report is also to identify gaps in our knowledge pointing to research needs for the development of better risk assessments and more targeted control in food production and processing.

Foodborne virus are excreted in high titres in faeces of infected people, and due to their low infectious dose and high environmental persistence, transmission occurs via ingestion of contaminated food and water as well as through direct person-to-person contact. Common contamination routes for food are via infected food handlers and/or exposure to contaminated water and materials during primary production of bivalve shellfish, lettuce, fresh or frozen fruits and vegetables, and products of pork and wild boar meat.

Food safety experts agree that efficient surveillance and virus control measures are required throughout the food production chain from “farm to fork”, i.e., at the sites of primary production, processing, and food preparation in retail or commercial kitchens. However, our understanding of the utility of these controls and how to properly validate their effects is still lacking. For example, we lack insights in the impact of personal hygiene and sanitation practices within food companies, knowledge about the effect of food processing on viral inactivation and accurate methods to distinguish between infective and inactive viruses.

Resumé

Fødevarebårne virus er anerkendt som værende den højest rangerende fødevaresikkerhedsmæssige udfordring i en ny rapport fra eksperter i risikovurdering. Human norovirus (NoV) og hepatitis A virus (HAV), som resulterer i henholdsvis gastroenteritis og viral gulsot, er de mest almindelige patogene fødevarebårne virus, med hepatitis E virus (HEV) som ansvarlig for en mindre andel af fødevarebårne udbrud. NoV er årsagen til cirka en tredjedel af alle globale fødevare-relaterede tilfælde af gastroenteritis, og er dermed den mest almindelige årsag til sygdom forårsaget af fødevarer. HAV findes endemisk i geografiske områder med ringe infrastruktur inden for hygiejne og sanitet og kan på verdensplan tilskrives ca. 2% af fødevarebårne sygdomme.

Fødevarestyrelsen er ved at udarbejde en risikoprofil for de forskellige fødevarebårne virus og produkt kombinationer, som oftest giver anledning til sygdom hos forbrugeren. Denne rapport er et bidrag til denne risikoprofil og gennemgår vores nuværende viden om biologi og forekomst for relevante fødevare-relaterede virus, smitteveje, udsatte produkter og effekten af forebyggende og kontrol metoder. Formålet med denne rapport er også at identificere mangler i vores viden og pege på behov for forskning til at skabe et bedre grundlag for risikovurderinger og målrettede kontrolindsatser i fødevareproduktionen.

Fødevarebårne virus udskilles i et højt antal i fæces fra inficerede individer. Grundet deres lave infektiøse dosis og overlevelse i miljøet foregår smitten ofte ved indtag af forurenet fødevarer og vand så vel som ved direkte overførsel mellem personer. Kendte smitteveje kan relateres til inficerede medarbejdere i fødevarevirksomheder og/eller eksponering til forurenet vand og råvarer i den primære produktion af skaldyr, salat, frisk og frossen frugt og grøntsager, samt svine- og vildtsvinekød.

Eksperter i fødevaresikkerhed er enige om, at effektiv overvågning og metoder til kontrol af virus er nødvendige igennem hele produktionskæden fra ”jord til bord”, inklusiv hos primærproducenterne, i fødevareindustrien, og ved produktion af spiseklare produkter eller måltider i detailledet eller kommercielle køkkener. Vi mangler dog viden om effekten af disse kontroller, og hvordan de kan valideres. For eksempel, så kendes effekten af personlig hygiejne og industrielle rengøringsprotokoller ikke, lige som vores viden om effekten af konserveringsmetoder er mangelfuld. Til slut skal det nævnes, at vi for mange virus (fx NoV) mangler robuste metoder til at skelne mellem aktive (infektiøse) og inaktive virus.

Contents

0. Background and objectives

Illnesses associated with foodborne viruses remain the cause of the majority of foodborne outbreaks. This clearly indicates that we lack proper controls and mitigation strategies. The lack of good detection methods also means that the actual number of virally implicated cases of foodborne illness may be underestimated. Propagation of viruses requires a host, i.e., in this case a human (or mammalian) host. Viruses are inactive outside their hosts and the risk of transmission through contaminated food, water or persons depends on the ability of the viruses to remain infective. The root cause of foodborne outbreaks of viral disease is therefore events where contaminated food and water have become the passive carriers of infectious virus particles from one host to the next.

The Danish Veterinary and Food Authority is currently developing a risk profile for foodborne viruses and product combinations that have most frequently given rise to disease among consumers. The present report is a contribution to this risk profile and reviews the current knowledge about the biology and occurrence of relevant foodborne viruses, contamination pathways, products at risk and the efficacy of prevention and mitigation methods. The objective of the report is also to identify gaps in our knowledge pointing to research needs for the development of better risk assessments and more targeted control in food production and processing.

1. Biology and epidemiology of foodborne viruses

Viruses are obligate intracellular parasites that require susceptible host cells for propagation and host infection. The structure of the extracellular infectious viral particle is simple, as it consists of a nucleic acid molecule comprised of single or double stranded DNA or RNA, covered by a protein coat (a capsid) that for some viruses are further surrounded by an envelope consisting of viral proteins and a lipid bilayer derived from membranes of the host cell. Based on their size and shape, nucleic acid composition and structure of the genome, as well as mode of replication, viruses are distributed into families, a few of which are grouped into orders (Green 2013). In practice, the viruses, which are most commonly implicated in reported viral foodborne illnesses, are human norovirus (NoV) causing gastroenteritis and hepatitis A virus (HAV) causing hepatitis. However, any virus present in the human

gastrointestinal tract is likely to be excreted in high numbers and if it is able to cause disease after ingestion then it could in theory be considered potentially foodborne and/or waterborne (Table 1) (Bosch et al. 2018). Other viral agents, less frequently reported in food and/or waterborne transmission of illnesses are rotaviruses (RV), sapoviruses (SaV), astroviruses (AsV), adenoviruses (AdV) (all causing gastroenteritis), hepatitis E virus (HEV) (causing hepatitis) and tick borne encephalitis virus (TBEV) (causing encephalitis) (Bosch et al. 2018). Extremely high numbers of viruses (10^{13} and 10^{10} virus particles, respectively, per gram of stool) may be shed in stools of patients suffering from gastroenteritis or hepatitis (Costafreda et al. 2006; Ozawa et al. 2007). The symptoms of viral gastroenteritis include nausea, vomiting and abdominal pain and occasionally fever and headache (FAO/WHO 2008a). While bacterial gastroenteritis agents are usually responsible for the most severe cases, viruses such as NoV, are responsible for the largest number of cases (Patel et al. 2009).

Table 1: Viruses documented to be found in the human gastrointestinal tract (Bosch et al. 2018).

Genus	Genome	Popular name	Disease caused
Enterovirus	ssRNA[a]	Poliovirus	Paralysis, meningitis, fever
		Coxsackie A, B virus	Herpangina, meningitis, fever, respiratory disease, hand-foot-and-mouth disease, myocarditis, heart anomalies, rush, pleurodynia, diabetes[b]
		Echovirus	Meningitis, fever, respiratory disease, rash, gastroenteritis
Hepatovirus	ssRNA	Hepatitis A virus	Hepatitis
Kobuvirus	ssRNA	Aichi virus	Gastroenteritis
Parechovirus	ssRNA	Human parechovirus	Respiratory disease, gastroenteritis, central nerve system (CNS) infection
Orthoreovirus	segmented dsRNA	Human reovirus	Unknown
Rotavirus	segmented dsRNA	Human rotavirus	Gastroenteritis
Norovirus	ssRNA	Human norovirus	Gastroenteritis
Sapovirus	ssRNA	Human sapovirus	Gastroenteritis
Hepevirus	ssRNA	Hepatitis E virus	Hepatitis
Mamastrovirus	ssRNA	Human astrovirus	Gastroenteritis, CNS infection
Flavivirus[c]	ssRNA	Tick-borne encephalitis virus	Encephalitis, meningitis
Coronavirus	ssRNA	Human coronavirus	Gastroenteritis, respiratory disease, SARS, MERS
Orthomyxovirus	segmented ssRNA	Avian influenza virus	Influenza, respiratory disease
Henipavirus	ssRNA	Nipah virus, Hendra virus	Encephalitis, respiratory disease
Parvovirus	ssDNA	Human parvovirus	Gastroenteritis
Mastadenovirus	dsDNA	Human adenovirus	Gastroenteritis, respiratory disease, conjunctivitis
Polyomavirus	dsDNA	Polyomavirus	Progressive multifocal leukoencephalopathy, diseases of urinary tract
Alphatorquevirus	ssDNA	TT (Torque Teno) virus	Unknown, hepatitis[b], respiratory disease[b] haematological disorders[b], cancer[b]

[a] The genomes consist of single stranded (ss) or double stranded (ds) DNA or RNA

[b] Uncertain whether the disease is caused by the virus.

[c] Has been found in food (milk) but not in gastrointestinal tract.

1.1. Caliciviruses: Norovirus (NoV) and Sapovirus (SaV)

1.1.1. Virus characteristics

Norovirus (NoV), previously known as 'Norwalk-like virus' or 'small-round-structured-virus', is the major cause of gastroenteritis globally and the most common cause of sporadic infectious gastroenteritis among people of all age groups (Patel et al. 2008, 2009). Moreover NoV is the most frequent cause of foodborne outbreaks of acute gastroenteritis in developed countries (Scallan et al. 2011; Van Duynhoven et al. 2005). Sapovirus (SaV) also causes acute gastroenteritis in humans but is mainly associated with sporadic gastroenteritis in young

children (Hansman, Oka, Katayama, et al. 2007; Johnsen et al. 2009; Khamrin et al. 2007; Monica et al. 2007). Compared to NoV, SaV is in general less commonly reported (Svraka et al. 2010) in foodborne gastroenteritis outbreaks (Hansman, Ishida, Yoshizumi, Miyoshi, et al. 2007; Hansman, Oka, Okamoto, et al. 2007; Hansman, Saito, Shibata, Ishizuka, et al. 2007; Johansson et al. 2005) .

NoVs and SaVs constitute two of the five closely related genera within the *Caliciviridae* family (Green 2013; Kroneman et al. 2013). They have a non-enveloped symmetrical icosahedral capsid of 27-40 nm with a single stranded positive sense RNA genome of approximately 7.6 kilobases (Green 2013; Oka et al. 2015). The NoV genome has three open reading frames (ORFs), of which the ORF1 at the 5' end of the genome encodes six non-structural proteins, including the RNA dependant RNA polymerase (RdRp), while ORF2 and ORF3 at the 3' end encode the capsid structural proteins; VP1 and the in between strains highly variable VP2, respectively (Atmar 2010; Green 2013; Seah et al. 1999). The SaV genome is organized into two ORFs, with ORF1 encoding non-structural proteins and the VP1, and ORF2 encoding VP2 (Oka et al. 2015).

Based on variation in the sequence for capsid structural proteins, the NoV genus is divided into seven genogroups (GI-GIIV) of which the GI and GII, as well as GIV although less frequent and more sporadic, are known to infect humans (Atmar 2010; Vinjé 2015). More than 30 human NoV genotypes have been reported, with an intra-genotype nucleotide diversity as high as 15% (Zheng et al. 2006). NoVs from GIII, GV and GVI-GVII infect bovine, murine and canines species, respectively, while besides humans some strains of NoV GII infect porcine species, and some strains of GIV infect feline and canine species. The SaV genus is divided into eight genogroups (GI-GVIII) of which the more than 21 genotypes within GI, GII, GIV and GV have been detected in humans (Oka et al. 2015). SaV has been detected in bats (Tse et al. 2012), dogs (Li et al. 2011), and sea lions (Li et al. 2011). No zoonotic potential has been demonstrated for the NoV and SaV genotypes infecting humans (Atmar 2010; Bank-Wolf et al. 2010; Vinjé 2015).

The diversity of NoV and SaV variants is constantly evolving with the generation of new variants as a result of random mutations in the RNA genome during viral replication, and for NoV the occurrence of inter-genotype recombination events at the junction between the

polymerase and the capsid genes (Farkas et al. 2004; Tsinda et al. 2017; Lindesmith et al. 2011). The different NoV genotypes potentially vary in their ability to cause disease and new variants or recombinants within mainly GII.4 have every 2–3 years through the past two decades been associated with epidemics due to the ability to escape herd immunity (Bull and White 2011; de Graaf et al. 2015; Karst and Baric 2015).

Except for a recently reported replication of NoV in human enteroid cells (Ettayebi et al. 2016), NoV and SaV have not yet been effectively cultivated *in vitro* (Duizer et al. 2004; Oka et al. 2015; Vinjé 2015), which prevents classification of serotypes and detection of viral infectivity or "viability" (Atmar 2010). Due to the lack of cell culture systems, proper risk assessment that requires determination of viability and genotype specification can be a challenge. The detection and determination of the NoV and SaV genotype(s) implicated in outbreaks or detected in contaminated foods have until now relied on the reverse transcription (RT) - PCR amplification, cloning and classical sequencing of selected segments of their genome. The target segments for NoV strain typing are typically located in the polymerase and/or capsid genes to account for possible recombination (Kroneman et al. 2013).

NoV is characterized by long-term stability and persistence in the environment (Glass et al., 2009). NoV appear to survive well on inanimate surfaces. This has frequently been demonstrated in outbreaks occurring in hospitals, residential homes, cruise ships (EFSA 2011; Wu et al. 2005), and in catering and kitchens where contaminated surfaces were detected in food preparation areas (Cheesbrough et al. 2000; Clay et al. 2006; D'Souza et al. 2006; Evans et al. 2002; Kuusi et al. 2002; Lamhoujeb et al. 2008, 2009; Mattison et al. 2007; Taku et al. 2002). NoVs are estimated to exhibit a higher resistance to heat, disinfection and pH changes than most other viruses (EFSA Panel on Biological Hazards (BIOHAZ) 2011) and vegetative bacteria (Duizer et al. 2004; Jimenez and Chiang 2006; Whitehead and McCue 2010) and can survive industrial food preservation methods such as refrigeration, freezing, acidification, reduced water activity and modified atmosphere packaging (Baert et al. 2009). NoV remains infective after heating at 60 °C for 30 min and it is unclear whether NoV can be completely inactivated during pasteurisation (FAO/WHO 2008b). NoV remains infectious for extended periods of time in seawater, especially during the winter months when temperatures are low

(Lees 2000). NoVs are inactivated by 10 mg chlorine/L, a concentration which is commonly used to treat a drinking water supply system after a contamination event, but are considered resistant in to the routinely applied drinking water disinfection dosage of 0.5-1.0 mg/L (Dolin et al. 1972; Keswick et al. 1985).

1.1.2. Outcome of exposure

1.1.2.1. Susceptibility in humans

Particularly young children, elderly, travellers and immunocompromised patients are considered highly susceptible to NoV infection and related complications (Glass et al. 2009). A higher number of outbreaks have, however, been observed in kinder gardens compared with child care and elder care facilities and a greater number of different genotypes have been detected in children (0–14 years old) compared to in older people (>65 years old) (Sakon et al. 2015). Although the excreted median NoV load of any genotype is high, the NoV load decreases with increasing age, especially in young children aged <5 years (Matsushima et al. 2015). It has been speculated that a reason for this could be that infants and children are more susceptible to a greater diversity of NoV genotypes due to a lower acquired immunity compared to the older generation (Kumazaki and Usuku 2016). Thus, it is likely that NoV outbreaks initially spread among young people.

The individual susceptibility to NoV infection relies on the heterogeneous host–virus interactions (Lindesmith et al. 2003), thus some individuals are resistant to infection and disease. The susceptibility to NoV is largely dependent on the specific genotype combined with the presence or absence of specific histo-blood group antigens (HBGA) on the gut epithelial surfaces of the human host (de Graaf et al. 2016). The synthesis of these HBGAs is regulated by the fucosyl- and glycosyltransferases, FUT2 (secretor), FUT3 (Lewis) and ABO(H) genes. Persons having an inactivated FUT2 enzyme, the non-secretors, do not express blood group antigens and are resistant to several NoV genotypes, including the predominant GII.4. Significant genotypic and phenotypic diversity in HBGA expression exist between different human populations, with non-secretor individuals occurring in approximately 5–50% of different populations worldwide (Bucardo et al. 2009; Castanys-Muñoz et al. 2013; Le Pendu et al. 2006). Bacteria that express HBGA and induce fucosylation in the gut may also be

intermediary factors that govern NoV susceptibility (Jones et al. 2014; Meng et al. 2007; Miura et al. 2013; Wacklin et al. 2014).

1.1.2.2. Disease

The pathogenesis of NoV illness is not well understood (de Graaf et al. 2016). Infection by NoV and SaV, and the resulting symptoms of acute gastroenteritis can occur among people of all age groups including neonates (Menon et al. 2010; Patel et al. 2008, 2009). The incubation times for NoV and SaV are usually 12–48 hours; with a median 1.1 and 1.2 days for NoV GI and GII, respectively, and 1.7 days for SaV (Lee et al. 2013). NoV and SaV cause similar symptoms, which typically are self-limited vomiting, (explosive) non-bloody diarrhoea and abdominal gurgling and pain, but also nausea, fever, and headache, (de Graaf et al. 2016; Robilotti et al. 2015; Yamashita et al. 2010). The severity of symptoms of NoV and SaV illnesses vary among people receiving the same titre of inoculum (Dolin et al. 1971; Oka et al. 2015). Vomiting has been reported to occur more frequently among children than diarrhoea (Green 2013). In one study, 74% of patients experienced onset of vomiting on the first day of NoV infection, while this was less common in young children below 1 year (59%) (Rockx et al. 2002). The symptoms last on average 12-60 hours (Green 2013; Kaplan et al. 1982; Rockx et al. 2002) .

While NoV illness is typically self-limiting, it may be life threatening for children, elderly people, and for immunocompromised patients (Green 2013). Thus, the majority of morbidity and mortality occurs among children, older adults and immunocompromised individuals (Koo et al. 2010). NoV infection in neonates have been associated with necrotizing enterocolitis (Turcios-Ruiz et al. 2008), diarrhoea associated benign infantile seizures (Chen et al. 2009) and inflammatory bowel disease (Khan et al. 2009). Among children (<5 years old), NoV causes 12% of all severe (hospitalized) gastroenteritis cases and an estimated 200,000 fatalities in developing countries, which is second highest for this age group after Rotaviruses (Green 2013; Patel et al. 2008). NoV infection may cause acute diarrhoea, serious illness, increased hospitalization and death in elderly (>64 years) (Mattner et al. 2006) (Ruzante et al. 2011; van Asten et al. 2011). An estimated 80 fatalities per year in UK (Harris et al. 2008) make infections life threatening in institutional settings or nursing homes (Estes et al. 2006; Green et al. 2002). Underlying conditions like cardiovascular disease, renal transplant and

immunosuppressive therapy have been suggested to be co-factors in cases with severe complications associated with NoV illness (Mattner et al. 2006).

NoV infections were shown to lead to symptoms lasting more than two weeks in 20% of cases in a community-based cohort study in the Netherlands (Rockx et al. 2002). Older patients (79-94 years) experienced persisting non-specific symptoms like headache, thirst or vertigo for 19 days past the initial diagnosis (Goller et al. 2004). This concurs with NoV infections in patients having underlying secondary illnesses, like immunodeficiency, being reported to cause prolonged and recurring illness and shedding (up to 182 days) (Siebenga et al. 2008), and a higher risk for nosocomial diseases (Lemes et al. 2014).

Asymptomatic infections, where people are shedding virus without showing any clinical symptoms, have been described for both SaV and NoV in all age groups (Phillips et al. 2010; Yamashita et al. 2010). Asymptomatic NoV infections have been reported in 7% of infants in developed countries (Ahmed et al. 2014), 7-30% of the population in some African countries (Huynen et al. 2013) and for more than 5% of adults in England (Phillips et al. 2010).

Among community cases of gastroenteritis, 4.7% had mixed infections, primarily involving adenovirus, NoV, and SaV (Tam et al. 2012).

1.1.2.3. Incidence rate in humans

NoV causes the largest number of foodborne disease illnesses and overall burden in the world (Ahmed et al. 2014; Bitler et al. 2013; Fankhauser et al. 2002; Green 2013; Karst et al. 2014; Vinjé 2015; WHO 2015a). The exact number of illnesses and fatalities are difficult to determine with a high level of accuracy due the disease being self-limited and often not reported to the medical system. Various researchers have however, come up with a range of estimates, which are described in the following section. NoV is estimated to being associated with nearly 50% of all-cause acute gastroenteritis outbreaks (Patel et al. 2009) and the leading cause (12% estimated) of mild to moderate acute diarrheal illness globally in all age groups (Patel et al. 2008). The World Health Organization (WHO) has estimated NoV to be responsible for approximately one third of an 1.8 billion diarrheal diseases caused by nine etiological agents commonly transmitted by food (Pires et al. 2015). Of an estimated 677

million cases of diarrheal disease caused by NoV, an estimated 213,515 cases result in fatalities every year (Pires et al. 2015). In the USA between 1996-2007, the annual mean number of hospitalizations due to illnesses associated with NoV infections was estimated to be 71,000 (swelling up to 110,000 cases in epidemic seasons) at an annual cost of 493 million USD to the healthcare system (Lopman et al. 2011). Another estimate is for NoV to be responsible for more than 124 million foodborne illnesses (one fifth of the estimated >600 million cases of foodborne illnesses) and 34,929 fatalities every year (WHO 2015a).

1.1.3. Treatment and vaccination

NoV infection is self-limiting in general and does not typically require medical intervention for remedy, but in rare severe cases of dehydration interventions including oral electrolyte replacement therapy may be necessary (Green 2013).

NoV does not naturally induce long term immunity after infection (Esposito et al. 2014) and despite the severity of infections and outbreaks, and attempts to develop vaccines, no commercially available safe and clinically efficient prophylactics are yet available (Arias et al. 2013; Atmar et al. 2011; Debbink et al. 2014; Green 2013). Successful development of NoV vaccines and other therapeutics have been limited due to the poor understanding of human immunity against NoV (Arias et al. 2013), the lack in NoV tissue culture systems, high diversity of strains and frequent antigenic shifts and genomic drift (Kaufman et al. 2014). Passive immunization using antibodies that block binding of NoV to human histo-blood groups may provide protection against the virus (Richardson et al. 2013), as reported in a study using antibodies from egg yolks from anti-NoV antibodies immunized chickens (Dai et al. 2012).

Diagnosis of SaV and NoV infections is based on molecular analysis of faecal samples from patients (Oka et al. 2015). The same method can be used to detect - and distinguish between - the presence of SaV or NoV in food samples.

1.1.4. Epidemiology

NoVs and SaVs are primarily transmitted via the faecal–oral route including direct person-to-person transmission or indirectly through aerosols from projectile vomiting contaminating food, water, or environmental surfaces (Franck et al. 2015b; Glass et al. 2009; Hall et al. 2013;

Lian et al. 2019). NoV is highly contagious with an infectious dose of 18–2800 viral particles. Infected persons including asymptomatic carriers, exhibit a prolonged period (4 weeks on average; range of 13–56 days) of viral shedding in faeces and vomitus as determined in human feeding trials (Ao et al. 2018; Teunis et al. 2008). In outbreaks, the average attack rate is high - typically 45% or more (Vinjé et al. 1997) and limited long-term immunity increases the risk of secondary spread through person-to-person transmission (Teunis et al. 2008). NoV is therefore easily transmitted and spread via the environment, food and water, factors which sometimes result in large outbreaks (Atmar et al. 2008, 2014; Hall et al. 2013; Patel et al. 2009).

Factors that contribute to NoV transmission are high population density, crowding, high contact rates and social mixing in closed populations (Rohayem 2009). Other factors are consumption of food prepared by infected food handlers and consumption of contaminated foods and water produced in insanitary conditions (Franck et al. 2015). For these reasons, NoV has repeatedly been implicated in disease outbreaks in institutional settings such as hospitals, nursing homes for elderly, schools and day-care centres, military-camps, cruise ships, restaurants and events with catered meals (Fankhauser et al. 2002; Green 2013; Green et al. 2002). The most common setting for NoV outbreaks in the United States and Europe are the acute and long-term healthcare facilities (e.g., nursing homes) (Division of Viral Diseases, National Center for Immunization and Respiratory Diseases 2011; Franck et al. 2015; Fretz et al. 2005; Hall et al. 2012; Vega et al. 2014; Wikswo et al. 2012). In Asian countries (Japan, Taiwan, Hong Kong and China), schools and childcare facilities account for >90% of all NoV outbreaks (Kumazaki and Usuku 2016; Lau et al. 2004; Lian et al. 2019; Wu et al. 2015).

Consumption of ready-to-eat food contaminated by infected and asymptomatic food handlers are the most common cause of foodborne NoV outbreaks (Daniels et al. 2000; Franck et al. 2015; Safaa Lamhoujeb et al. 2008). Bivalve shellfish grown and harvested in wastewater polluted areas can concentrate NoV, which are inadequately eliminated by standard depuration procedures (Muniain-Mujika et al. 2002); leading to outbreaks of gastroenteritis after consumption of shellfish (Le Guyader et al. 2006, 2008; Webby et al. 2007).

NoV outbreaks generally peak in winter and early spring (between October and March) (Greer et al. 2009; Lian et al. 2019). This is in particular the case for GII.4 strains, while non-GII.4

strains appears to exhibit a weaker seasonal pattern (Kroneman et al. 2008), and non-GII.4 outbreaks caused by person-to-person transmission occur significantly less in the fall and winter seasons than in the spring-summer season (Vega et al. 2014).

The increase of gastrointestinal diseases by e.g. NoV during winter has been associated with lower temperatures and greater rainfall (Rohayem 2009). However, a further explanation might be that NoV accumulates more efficiently in oyster tissue during fall and winter, which could significant increase the exposure of NoV amongst consumers of oysters during that period, and thus contribute to efficient re-circulation of the virus back to the human population (Maalouf et al. 2010).

GI strains are detected less frequently in clinical samples than GII strains although GI strains are clearly present in the environment (Boxman et al. 2006; Hasing et al. 2013; Lopman et al. 2004; Vega et al. 2014; Williams and Zorn 1997). GI strains have been reported to be found relatively more often in school children than in infants (Kroneman et al. 2008), which could be due to school children coming into contact with more various genotypes including GI strains than infants, because school children have a wider sphere of activity than infants.

In addition to the food association, numerous outbreaks of NoV have originated from sewage-polluted drinking water (Hewitt et al. 2007; ter Waarbeek et al. 2010; van Alphen et al. 2014) and recreational water bodies (Hoebe et al. 2004; Sartorius et al. 2007). This may be due to the resistance of NoV towards wastewater treatment and its ability to remain infectious in the aquatic environment (Bae and Schwab 2008; La Rosa et al. 2009; Nordgren et al. 2009; Skraber et al. 2009).

1.2. Hepatitis A virus (HAV)

Hepatitis A virus (HAV) causes viral jaundice and is an important water- and foodborne pathogen (Collier et al. 2014; WHO 2016).

1.2.1. Virus characteristics

The 30 nm diameter icosahedral non-enveloped HAV with a single stranded positive sense RNA genome of approximately 7.5 kb is the only member of the *Hepatovirus* genus in the family of *Picornaviridae* (Hollinger and Martin 2013). The genome consist of an untranslated region (UTR) at the 5' end and a single ORF encoding a protein, which is cleaved and processed into the non-structural and structural proteins, VP1, VP2, VP3 and VP4 (Hollinger and Martin 2013; Stuart et al. 2018; Weitz et al. 1986). Host susceptibility to the HAV is reported to be exclusive to humans and several monkey species (Hollinger and Martin 2013).

HAV is highly persistent and can survive for long periods in the environment notably in water, food and soil (Rzezutka et al. 2004). Water is considered to be the most important source of transmission, as the virus can remain infectious after up to 60 days and 30 weeks in tap- or sea water, respectively (Crance et al. 1998; Enriquez 1995), and for more than six and eight weeks in river- or ground-water, respectively (Sobsey et al. 1989; Springthorpe et al. 1993). HAV is also able to survive in various types of soil, where it can remain infectious for 12 weeks (Sobsey et al. 1989). Due to the ability to resist drying, freezing, food preservatives and acidification, HAV is persistent in the environment and has frequently caused food-borne outbreaks among susceptible populations worldwide (Baert et al. 2009; Collier et al. 2014; Linder and Malani 2017; Mollers et al. 2018; Rossati et al. 2017; Severi et al. 2015; Werber et al. 2017). HAV is therefore considered a major food hazard (FAO/WHO 2008b).

1.2.2. Outcome of exposure

1.2.2.1. Susceptibility

Age dependent immunity and susceptibility against HAV infection has been reported, while sex does not play a role in susceptibility to HAV (Jacobsen 2010).

HAV transmission, infection and illnesses are highly associated with regions of poor sanitation and hygiene practices (Hollinger and Martin 2013). In low income regions, such as Asia and sub-Saharan Africa, where the level of endemicity is high, almost all people contract immunity to HAV infection and illness (Jacobsen and Wiersma 2010). In contrary, in high income regions with better sanitation, e.g., Australia, Canada, Japan, New Zealand, Republic of Korea,

Singapore and Western Europe, a very low level of HAV infections are reported with a consequently high proportion of susceptible adults (Jacobsen and Wiersma 2010). In the Western and South-western regions of United States, consistent higher incidence rates have been observed compared to other parts of the country (Fiore 2004). WHO reported that in high income countries in the Asian Pacific region, nearly 100% of the children between the age of 1-10 are at risk of HAV infection (Jacobsen 2010).

In recent years, the geographic distribution of HAV infections has been changing due to improved sanitation and personal hygiene in endemic countries (Hollinger and Martin 2013). Between 1975-1990, approximately 95% of the population of EU/EEA countries were living in high endemic areas, whereas the number was reduced to 20% in 2014 (ECDC 2016). In 2016 ECDC classified 28 EU/EEA countries' 'susceptibility-in-adults profile' of HAV infection for which seroprevalence data were available. Three countries were graded 'Low' (>20 cases per 100,000 populations) (Romania, Bulgaria, Portugal), ten countries 'Moderate' (Spain, Malta, Lithuania, France, Italy, Poland, Cyprus, Slovakia, Greece, Slovenia), ten countries 'High' (Croatia, the Netherlands, Ireland, Czech Republic, UK, Germany, Luxembourg, Belgium, Austria and Estonia) and five countries 'Very high' (Norway, Sweden, Iceland, Finland and Denmark) (ECDC 2016).

1.2.2.2. Disease

The general incubation period of HAV infection is 15-50 days before onset of symptoms. Acute HAV illness may include symptoms such as fever, malaise, anorexia, nausea, abdominal discomfort, dark urine and jaundice (Fiore 2004; Pintó et al. 2010). Recovery can be expected within two months (Fiore 2004; Pintó et al. 2010), although a small number (6-10%) of cases may experience prolonged relapsing symptoms of HAV illness over a period of up to 40 weeks (Glikson et al. 1992; Schiff 1992; Sjogren et al. 1987). Symptoms of HAV infection are age dependent, where children below the age of 5-6 experience asymptomatic to subclinical infections and less than 10% cases of jaundice, compared to the usually symptomatic infection and often evident hepatitis in 80% of adults (Jeong and Lee 2010; Lednar et al. 1985). Between 21-53% of HAV infected patients needs hospitalization, where the rates are lowest for children and highest for persons over 60 years. Once hospitalized, the mortality rate

among HAV infected patients is 0.23% below the age of 30 and 1.8-2.21% above the age of 49 (Hollinger and Martin 2013).

In HAV infected individuals, the virus is excreted in the bile and shed in the stool. The shedding peaks two weeks prior to onset of jaundice, a fact which may increase the risk of large outbreaks. Although a chronic carrier state does not exist in children, they may excrete the virus for longer than adults. The stool concentration of virus drops after the appearance of jaundice (Koopmans and Duizer 2004; Tassopoulos et al. 1986).

1.2.2.3. Incidence rate in human

Worldwide HAV infections are estimated to cause 14 million cases of illness yearly and approximately 28,000 deaths in 2010 (Havelaar et al. 2015; WHO 2015a).

1.2.3. Epidemiology of HAV

HAV transmits primarily via the faecal-oral route through person-to-person contact or through contaminated food and water (Bitler et al. 2013; Hollinger and Martin 2013; Iorio and John 2018; Linder and Malani 2017; Martínez et al. 2015; Severi et al. 2015; Werber et al. 2017).

HAV is frequently implicated with recurring epidemics and is the most common cause of foodborne viral jaundice (Hollinger and Martin 2013).

Contaminated fruit imported from endemic areas has in recent years been identified as the source of several large, and often multistate, outbreaks of HAV in Europe (EFSA 2014). Consumption of frozen raspberries and/or blueberries were the suspected sources of HAV outbreaks in the Netherlands in 2017, in four Nordic countries including Denmark in 2012-2013 and in Italy, Germany, Ireland and Norway 2013-2014 (Lassen et al. 2013; Mollers et al. 2018; Severi et al. 2015). The last mentioned outbreak resulted in 1,589 hepatitis A cases, including two deaths. In 2018, dates were for the first time linked to a transnational HAV outbreak in Denmark and Norway (Migley et al., *in prep*; Rajiuddin et al., *in review*; Rajiuddin 2019).

Besides, consumption of contaminated green onions (Dentinger et al. 2001; Wheeler et al. 2005), semidried tomatoes (Donnan et al. 2012; Gallot et al. 2011; Petrignani et al. 2010), pomegranates (Collier et al. 2014) and bivalve shellfish have been associated with foodborne HAV outbreaks (Boxman et al. 2016; Guillois-Bécel et al. 2009; Manso and Romalde 2013).

1.3. Hepatitis E virus (HEV)

Hepatitis E virus (HEV) causes liver infection and continuously poses a serious threat especially in developing countries with many large hepatitis outbreaks and approximately 20 million cases occurring every year (Hakim et al. 2017; Rein et al. 2012).

1.3.1. Virus characteristics

HEV is a 30-34 nm diameter spherical non-enveloped, 7.2 kb positive sense single-stranded RNA virus with a morphology that is similar to *Calicivirus* (Cook and van der Poel 2015), although they belong to the *Hepeviridae* family, Hepevirus genus (Balayan et al. 1983; Emerson and Purcell 2013). Although there seems to be only one serotype, HEV has based on the genomic sequence been divided into four genotypes Gt1-4 (Lu et al. 2006). HEV Gt1 and Gt2 are relatively conserved and reported to primarily infect humans, while Gt3 and Gt4 are infectious to a whole range of mammalian animals including swine, wild boar and domestic pigs which occasionally may cross-transmit to humans (EFSA 2017; Meng 2010; WHO 2015). Of all animal species, domestic pigs are most abundantly examined worldwide, and found to be massively infected with HEV belong to mainly Gt3 and Gt4, which also has been detected in wild boars (EFSA 2017).

The Gt1 and Gt2 cause the majority of human HEV infections and epidemics in Asia, Africa and Mexico, while only sporadic cases of human Gt3 and Gt4 infections are observed in more industrialized countries, including the USA, Japan, China and Europe (Herremans et al. 2007; Mushahwar 2008; Zhou et al. 2004).

HEV has at least two distinct epidemiological profiles: (1) large outbreaks and epidemics in developing countries, usually caused by HEV Gt1, resulting in high morbidity and mortality among pregnant women and young children, and (2) very few symptomatic cases of HEV Gt3,

most cases without symptoms or clear source(s) of infection, but frequent seroreactivity in 5%-21% of asymptomatic persons in developed countries. Though the first is largely considered to be the result of a water-borne infection, the latter is suspected to result from frequent contact with pigs or consumption of meat and meat products from pig or wild boar.

HEV can be detected using serological assays. However, RT-PCR is increasingly used for detection (Garson et al. 2012; Jothikumar et al. 2006). Although an internationally validated standard (Althof et al. 2019) including standard material (WHO 2019) is available for HEV RNA detection in meat and meat products, no formal international standard exists for the detection of HEV in food products. HEV has been detected in various foods such as pork products (Di Bartolo et al. 2012), shellfish (Diez-Valcarce et al. 2012) and leafy vegetables (Kokkinos et al. 2012). There has also been progress in development of a cell-culture assay for HEV (Okamoto 2013) although it seems to be selective for a limited number of HEV strains (Johne et al. 2016).

1.3.2. Outcome of exposure

1.3.2.1. Susceptible populations

Sporadic HEV infections have been identified in at least 63 countries, half of which are large epidemics (WHO 2010, 2015b). HEV is prevalent all over the world, although epidemics and outbreaks are mainly reported in developing countries where the more virulent HEV strains, Gt1 and Gt2, are transmitted through water (Emerson and Purcell 2013; Meng 2010).

In the developing HEV endemic countries, sporadic hepatitis is believed to predominantly be caused by HEV with the young adults in highest risk of severe illness and death among in particular pregnant women (Emerson and Purcell 2013; Meng 2010; Rein et al. 2012). Pregnant women, immunosuppressed or pre-existing liver diseased persons, as well as refugees, travellers and displaced persons suffer the highest attack rates of HEV Gt1 and Gt2 due to their weakness or nature of living conditions that include poor hygiene and overcrowding (WHO 2015b).

HEV is endemic in swine all over the world (Meng 2003). In industrialized countries with better sanitation and food safety, the less virulent HEV strains, Gt3 and Gt4, are clinically

predominant and mainly observed in individuals, who are in contact with swine and swine products, such as pig-farmers, handlers and veterinarians (Emerson and Purcell 2013; Meng 2010; Pavio et al. 2010). The incidence of HEV infection has however, increased in industrialized countries (EFSA, 2017); with locally acquired infections in men over 60 years of age in UK believed to be associated with the consumption of processed pork products.

1.3.2.2. Disease

HEV infection in humans can be asymptomatic, as many individuals in industrialized countries are seropositive for antibodies against HEV without a history of prior illnesses (Drobeniuc et al. 2001; Meng et al. 2002). The incubation period of HEV infection before disease onset may be 2-8 weeks (Aggarwal and Naik 2009; Emerson and Purcell 2013). HEV infected patients may have jaundice, anorexia and hepatomegaly in general, while abdominal pain, tenderness, nausea and vomiting has been reported in approximately half of the cases (Emerson and Purcell 2013). Viremia in patients have been reported from 1 week prior to onset of clinical symptoms of the disease and 3 weeks post exposure of HEV, which is also concurrent with faecal shedding that may continue for weeks (Emerson and Purcell 2013). Despite that the clinical symptoms of HEV infection varies among infected species, the histopathological lesions have been reported to be similar in infected humans, pigs and chickens (Meng 2010).

While HEV Gt3 initially was thought to only cause acute infection where most patients remain asymptomatic (Hoofnagle et al. 2012), chronic infection rapidly leading to cirrhosis and liver failure has been demonstrated mainly in immunocompromised organ transplant recipients (Zhou et al. 2013).

In general, the mortality due to HEV illness is 0.1-4%, while in pregnant women in their third trimester the fatality rate is between 10-50% (WHO 2015b). HEV infection in patients with chronic liver disease may cause fatalities in up to 30% cases (Emerson and Purcell 2013).

After 7-8 weeks post HEV infection, viremia may reduce, while liver enzyme values are at their highest. Khuroo et al. (1993) reported that anti-HEV antibodies in patients might persist for years after exposure.

Compared to a 0.2% fatalities among HAV infected patients, the in general infrequent HEV infections with mild onset of symptoms in immune competent patients may be more severe, as they may cause up to 1% fatality (Emerson and Purcell 2013; WHO 2015b).

1.3.2.3. Annual incidence rate in humans

In developing countries the prevalence of HEV can be very high. For example in Egypt, the general population shows a more than 70% prevalence of HEV antibodies (Stoszek et al. 2006).

In Asia and Africa, an estimated 20.1 million HEV infections may occur annually, which may result in 3.4 million symptomatic cases, 70,000 deaths and 3000 stillbirths. Among all age groups, the highest increase in prevalence of HEV was observed among children and young adults between 5-20 years of age, while the highest numbers of symptomatic cases and fatalities were observed in East and South Asia compared to the accounted nine Global Burden of Disease (GBD) areas (Rein et al. 2012). In Asian and African regions, the rate of HEV incidents is highest (1.0-1.4%) for ages 15-20, and decreases for ages 0-15 (0.5-1.0%) and further for ages older than 30 years (≤0.2%) (Rein et al. 2012).

1.3.3. Treatment and vaccination

HEV infection and illness is normally self-limiting and immune competent persons recover without complications (Emerson and Purcell 2013). No anti-HEV treatment or guideline from WHO exists and treatment for acute HEV is generally supportive (WHO 2015b).

Clinical trials have demonstrated that anti-HEV antibodies can be induced by vaccination. A subunit vaccine (Hecolin®) approved by the China Food and Drug Administration (Bin Park 2012), containing recombinant truncated capsid proteins of HEV Gt1 have been demonstrated to be highly effective in providing nearly lifelong prevention of the disease of HEV Gt1 - with possible cross reactivity to Gt4 – infections (Chen et al. 2015; Zhang et al. 2015; Zhu et al. 2010). It remains unknown whether Hecolin® could confer protection against HEV Gt2 or Gt3 and thus provide protection against the foodborne zoonotic Gt3 infections mainly acquired in Europe. The safety and efficacy of the HEV vaccines in pregnant women, among which a high case fatality rate has been observed, remains to be studied (Wu et al. 2012).

Such trials with Hecolin® are currently being conducted in a rural area in Bangladesh (NCT02759991). An additional HEV Gt1 vaccine candidate has shown efficient protection against HEV in a phase II clinical trial conducted in Nepal (Shrestha et al. 2007) and more HEV vaccines are now in different stages of development (Cao et al. 2017; Kulkarni et al. 2016; Wen et al. 2016; Xia et al. 2016)

1.3.4. Epidemiology

HEV is relatively stable and excreted in the environment through faeces of infected persons and animals, thus primary transmission of HEV is faecal-oral through water and food, particularly when faecal contaminated by e.g. manure (Krog et al. 2017; Van der Poel et al. 2018). However, since many cases are not obviously associated with travel to HEV endemic areas, or can be directly linked to live pigs or pork products, the route of transmission is not fully elucidated (EFSA 2017).

Five main routes of HEV transmission has been described (WHO 2010): i) faecal-oral transmission through contaminated water, ii) foodborne transmission through ingestion of food derived from infected animals, iii) zoonotic transmission through exposure to infected animals and their bodily fluids, iv) transmission through infected body fluids, and v) vertical transmission from mother to fetus.

Faecal contamination of drinking water has been reported to be the major route of HEV transmission in endemic regions (Rein et al. 2012). Waterborne transmission of HEV Gt1 or Gt2 have been reported in at least 30 countries in Asia, Africa and North America, (WHO 2015b).

In developed countries, where drinking water is safer, HEV transmission is largely zoonotic, through uncooked or undercooked pork products and wild boar meat (Li et al. 2005; Masuda et al. 2005; Kamar et al. 2012). In Japan, where 2% of pig livers sold to consumers are contaminated with HEV, sporadic cases of HEV infection have been associated by ingestion of raw or uncooked pig liver (Yazaki et al. 2003; Meng 2010). In USA, 11% of pig livers sold to consumers are contaminated of HEV (Feagins et al. 2007). In Denmark, infection of HEV was suggested to be through zoonotic transmission, which in one study was reported to involve largely asymptomatic cases (Christensen et al. 2008).

In both developed and developing countries contaminated shellfish, meats and direct contact with infected animals have been implicated in HEV diseases (Emerson and Purcell 2013; Meng 2010; Pavio et al. 2010)

1.4. Tick-borne encephalitis virus (TBE)

Tick-borne encephalitis virus (TBEV) is a zoonotic virus transmitted via tics to rodents, goats, sheep and cows with potential further transmission to human consumers of unpasteurized dairy products from endemic areas (Kríz et al. 2009).

1.4.1. Virus characteristics

TBEV is an enveloped, single stranded RNA virus, which belongs to the genus *Flavivirus* and is maintained in forests, which is the habitat for the tick vectors and their main hosts, rodents. A significant increase in reported cases (including foodborne) in the last 30 years due to ecology and climate changes, has led to an increased focus on this virus.

Three major subtypes of TBEV exist: the European or Western (TBEV-Eu), the Siberian (TBEV-Sib), and the Far Eastern or spring-and-summer-encephalitis (TBEV-Fe). The vectors of TBEV act as long term reservoirs of the viruses (Hubálek and Rudolf 2012). The vector of TBEV-Eu is *Ixodes ricinus* which is predominantly distributed in the mid to western regions of the European Union (EU) including Denmark (Lindquist and Vapalahti 2008; Demina et al. 2010; Lindquist 2014; Michelitsch et al. 2019). In the Netherlands in 2016, an endemic TBEV was reported, through the detection of a TBEV strain that was genetically different from the common TBEV (Weststrate et al. 2017).

The virus genome itself can be infectious and has in the appropriate host been shown to be capable of producing progeny viruses with same virulent characteristics as of a wild type TBEV (Mandl et al. 1997).

Simulation of a typical thermal regime utilized for cheese production could not completely reduce the infectivity of a tick-borne *Flavivirus* (Langat virus (TP21 strain)) inoculated in milk. Infectious TP21 was shown to be maintained for days in goat milk kept at refrigeration

conditions, and be stable for at least 24 hours in acidified dairy products and 24-48 hours in sour milk (Gresíková-kohútová 1959). However, the infectivity of TP21 in milk was reduced markedly at room temperature (22°C) after 24 hours and completely after 48 hours (Offerdahl et al. 2016). Further, infectious TP21 in goat milk could be completely inactivated after 20 min at 65˚C, as well as by HTST pasteurisation (72˚C, 15 sec following by cooling to refrigeration temperature) (International Dairy Foods Association 2016; Offerdahl et al. 2016). Similary, infectious TBEV in goat milk was shown to be reduced by up to 6.7 log after heating the milk at 72°C for 10 sec (Gresíková et al. 1961).

Another study using a Western TBEV strain Hypr suspended in milk, showed a slightly different reduction pattern in which the virus remained stable during storage at 8°C for five days, and could be reduced 4-4.5 log by heat treatments in the range of 60 to 80 °C (Saier et al. 2015).

Thus, TBEV infectivity in goat milk may persist for days at refrigerated temperatures, but is not likely to survive pasteurization. The kinetics may vary according to the virus tested and the study. However, it is clear, that proper milk handling and pasteurization processing in areas endemic for TBEV are important.

1.4.2. Outcome of exposure

The incubation period of tick-bite acquired TBEV infections can be 2-28 days (Bogovic and Strle 2015; Taba et al. 2017), while individuals affected by foodborne TBEV may show clinical symptoms already after 2-4 days (Dumpis et al. 1999; Taba et al. 2017). TBEV infection is normally asymptomatic but may be acute neuroinvasive (Taba et al. 2017). The clinical onset of TBEV is biphasic. In 2/3 of infected patients, a first phase may be induced showing influenza-like illness with fever, headache, muscle pain and fatigue that last 2-7 days. In 30% of cases, a second phase is induced that lasts up to 10 days with reappearing high fever and symptoms of inflammation of the central nervous system. Encephalitis developing during this second phase may result in paralysis, permanent sequelae or death (Taba et al. 2017). The clinical severity varies by subtype with a lower fatality rate of European TBEV (approximately 1%), than the other two subtypes of TBEV (Taba et al. 2017). Patients do not shed TBEV in faeces (Veje et al. 2018) .

On average, up to 3% ticks can be carriers of TBEV in endemic areas and approximately 0.3% of tick bites lead to disease manifestation (Kaiser 2016). Approximately half of TBEV infections develops into meningitis, 40% cases develop meningoencephalitis and the remaining 10% of cases develop encephalomyelitis (Kaiser 2016). TBE can be mistaken for nonspecific inflammatory disease due to the unspecific clinical presentation as shown for infected Swedish children (Hansson et al. 2011).

1.4.2.1. Susceptibility

In endemic areas, every case of meningitis, encephalitis or myelitis has the potential to be TBE (Taba et al. 2017). Non-vaccinated tourists in endemic regions is at risk of contracting TBE with an estimated 1 in 10,000 persons/month (similar to the risk of typhoid fever or malaria among tourists in India). With increased tourism, particularly in warm months to endemic areas, the risk of TBEV infection may increase (Bogovic and Strle 2015).

Among German patients in 2001-2018, increased severity of TBEV infections was shown to correlate with age, as well as fatalities increased from average 0.4% in all age groups to 2.1% among patients aged 70 years or older (Hellenbrand et al. 2019). This study further showed a highest mean incidence rate of TBE among 40-69 year olds, and confirmed that male patients in all age groups had more severe manifestations of the disease compared to females (Bogovic and Strle 2015).

1.4.2.2. Annual incidence rate in humans

According to European Academy of Neurology (EAN) consensus, an estimated 13,000 cases of TBE can occur in Eurasian northern hemisphere (Taba et al. 2017). In EU and Asia, 10,000 to 15,000 TBE cases are reported per year, with more than 10,000 complications that needs hospitalization (Kaiser 2016; Dobler 2010). This number is likely underestimated, as many countries do not have concrete case definitions and mandatory system of reporting TBE cases (Bogovic and Strle 2015). Considering the frequency of fatalities per year, TBEV illness are second highest among neurotropic *Flaviviruses* after Japanese encephalitis (Lindquist and Vapalahti 2008).

In EU, TBE disease has been notifiable since 2012 and a case definition has been proposed by ECDC only recently (Taba et al. 2017). In the European countries during the period of 2005-2009, pronounced yearly variations of registered TBE cases occurred with the following highest incidences per 100,000 inhabitants: 14.1 cases for Slovenia, 11.1 cases for Estonia, 10.6 cases for Lithuania and 8.8 cases for Latvia (Süss 2011). According to the latest available epidemiological data for Slovenia the incidence of the disease in 2013 was 15.0 cases per 100,000 inhabitants (Institute of Public Health of the Republic of Slovenia 2014). Between 2012-2016 in EU, 12,500 cases of TBE were reported, among which Czech Republic and Lithuania together accounted for 38.6% of cases (Beauté et al. 2018). In Denmark, 37 cases of TBE was reported during the period 1998 – 2009, which was lowest among the European countries, Belarus and Russia (Lindquist 2014). No data on TBE illnesses was reported from Denmark between 2012-2016 (Beauté et al. 2018).

In Czech Republic, 1997-2008, 7,288 TBE cases were reported, of which approximately 1% were foodborne (Kríz et al. 2009).

1.4.3. Treatment and vaccination

Patients infected with TBEV may require symptomatic treatment and in severe cases emergency management and intensive care (Taba et al. 2017). European TBEV is vaccine-preventable by two effective vaccines based on the European TBEV subtype (Šmit and Postma 2015; WHO 2011). However, effective treatment is not available for all TBEV (Kaiser 2016; Taba et al. 2017). The first developed veterinary vaccine for TBEV was reported recently, and showing promise in laboratory experiments (Salát et al. 2018).

1.4.4. Epidemiology

The predominant route of TBEV transmission is horizontal through bite of infected ticks, however foodborne transmission of TBEV by ingestion of raw milk or milk products from endemic areas have also been reported (Kríz et al. 2009; Taba et al. 2017). Person-to-person spread, except rarely through blood transfusion and breastfeeding, has not been reported (Mansfield et al. 2009). In central EU, the TBE mostly occur during the warm months coinciding with the highest tick activity period between April and November (Lindquist 2014; Lindquist and Vapalahti 2008).

TBEV RNA has been detected in samples of raw milk of goats (21%), sheeps (22%), and cows (11%) from Poland (Cisak et al. 2010) and in 5.4 of % of milk samples from cows in three municipalities in Norway (Paulsen et al. 2019).

Alimentary transmission of TBEV has been reported by consumption of unpasteurized goat milk in Austria, Estonia, Slovenia (Hudopisk et al. 2013; Kerbo et al. 2005; Markovinović et al. 2016), cow milk in Hungary (Caini et al. 2012), and goat and sheep cheese in e.g. Croatia (Dorko et al. 2018; Holzmann et al. 2009; Markovinović et al. 2016).

Pasteurization of milk products and vaccination of veterinary animals may prevent alimentary TBEV infection and transmission to humans (Salát et al. 2018).

1.5. Rotavirus (RV)

Human rotaviruses (RV) cause severe diarrheal disease in children all over the world (Estes and Greenberg 2013). RV is a 100 nm diameter icosahedral, non-enveloped and triple capsid structured virus with 18.5 kb segmented double stranded RNA genome (Rodríguez-Lázaro et al. 2012). Belonging to the genus *Rotavirus* in the *Reoviridae* family of viruses (Estes and Greenberg 2013), RV consist of 10 different species (A-J) based on genome sequence and antigenic variances (Crawford et al. 2017). Most human infections are caused by group A RV, although infections and outbreaks also occur to a lesser extent due to group B RV and C RV. Diverse genotypes of RVs are found in the intestinal tracts of many young mammals which can act as reservoir for human infections (Estes and Greenberg 2013).

Most children are infected by RV by the age 5, regardless of the socio-economic status of the region (Crawford et al. 2017), although most fatalities occur in the developing countries due to poor sanitation (Tate et al. 2016). Childhood infection may lower the risk of subsequent infection and disease onset (Velázquez et al. 1996). In spite of adults frequently becoming infected by RV, they seldom manifest clinical symptoms (Estes and Greenberg 2013). However, an estimated annually 24,000 hospitalizations still occur due to RV infection in individuals above 5 year (Lopman et al. 2011).

Rotavirus causes gastroenteritis with vomiting, diarrhoea, malaise and fever (Crawford et al. 2017).

Oral treatments, like rehydration therapy using oral saline and other liquid supplements may be challenged by the typical symptomatic vomiting (Hagbom et al. 2011; Leung and Robson 2007). In 2006, live attenuated vaccines against RV were licenced and are now used globally in more than 100 countries (Crawford et al. 2017). The introduction of vaccines may lead to the emergence of novel RV genotypes or the re-emergence of old strains, particularly from animal reservoirs (Iturriza-Gómara et al. 2004; Kang et al. 2005; Rzezutka et al. 2004; Steyer et al. 2008).

Being responsible for approximately 450,000 fatalities in children below 5 years of age, RV is the major cause of severe gastroenteritis in children globally (Tate et al. 2012). Even after the introduction of a global universal vaccination program, RV still causes considerable mortalities particularly in developing countries. Of an estimated 215,000 deaths in 2013 globally, 49% occurred in India, Nigeria, Pakistan and the Democratic Republic of Congo alone (Tate et al. 2016).

RV persist similarly to NoV, HAV and HEV in fresh water (Hurst and Gerba 1980) even when subjected to light exposure, which can seriously affect the stability and viability of other enteric RNA viruses, e.g., astrovirus (Fujioka and Yoneyama 2002; Lytle and Sagripanti 2005). Inactivation of virus infectivity in different types of water has been consistently found to correlate with higher temperatures (John and Rose 2005).

1.6. Aichi virus (AiV)

Aichi virus (AiV) belongs to the genus *Kobuvirus* in the *Picornaviridae* family and is responsible for human gastroenteritis (Racaniello 2013). The non-enveloped ~30 nm diameter icosahedral virus particles contain a single stranded positive sense RNA genome of approximately 8.25 kbs (D'Souza 2015; Yamashita et al. 1998). AiV has been detected in human faecal samples from all over the world (Kitajima and Gerba 2015). Studies suggest high (80-99%) and

widespread seroprevalence of AiV-1 antibodies in adults in countries such as Japan, Germany, France, Spain and Tunisia (Kitajima and Gerba 2015).

AiV has been detected in raw or treated sewage and surface water (Di Martino et al. 2013; Haramoto and Kitajima 2017; Kitajima and Gerba 2015; Lodder et al. 2013) and shellfish (Hansman et al. 2008; Terio et al. 2018). Kitajima and Gerba (2015) suggested that AiV may cause no or subclinical symptoms while circulating, or may be involved in mixed viral infections causing gastroenteritis.

The clinical symptoms of AiV infection may include diarrhoea, abdominal pain, nausea, vomiting, and fever (Yamashita et al. 2001). The onset of symptoms, however, may depend on patient condition (Yamashita et al. 2001). Another study suggested no association between AiV and gastroenteritis in children in China, proposing that the virus may replicate in humans without causing disease (Li et al. 2017).

In Thailand, 2.6% of paediatric gastroenteritis patients were found to be infected by AiV in one study of 923 cases (Chuchaona et al. 2017).

1.7. Astrovirus (ASV)

Astrovirus (AsV) is a member of the family *Astroviridae* with icosahedral non-enveloped capsid of 28-35 nm diameter and a 6.4-7.7 kbs positive sense single stranded RNA genome (Arias and DuBois 2017; Bosch et al. 2014; D'Souza 2015). The virus is prevalent in stool samples of symptomatic or asymptomatic individuals from around the world (Storch 2013). AsV is a major cause of acute gastroenteritis in children, elderly and immunologically compromised patients (Bosch et al. 2014; Johnson et al. 2017). The majority of the children have been reported to carry antibodies against AsV type-1 which makes adults less susceptible to infection (Bosch et al. 2014; Johnson et al. 2017). Bats and pigs carry the largest diversity of AsV strains and are suggested to be potential reservoirs (Vu et al. 2017). Common genetic features have been found among chicken, turkey and duck AsVs, which may suggest frequent cross-species transmission (Bosch et al. 2014; Johnson et al. 2017). The high genetic

variability of AsV and recombination due to simultaneous infection with multiple strains suggest AsV as major candidates of emerging zoonotic infections (Vu et al. 2017).

AsV infection has an estimated incubation period of 3-6 days (Lee et al. 2013) until the onset of symptoms such as watery diarrhoea, abdominal pain, fever, headache and anorexia (Johnson et al. 2017). Though AsV are in general self-limiting and asymptomatic in adults and adult children, AsV may cause fatal encephalitis and meningitis in immunocompromised patients (Pérot et al. 2017).

In Australia, an average of estimated 17,500 foodborne gastroenteritis illnesses occurred a year (in circa 2000) due to AsV and adenovirus (AdV) infections (Hall 2005).

Detection of AsV in fresh fruit and vegetables is not common (Shin et al. 2019). However, the virus has been detected in mussels in a 2014-2015 surveillance study in Italy (Fusco et al. 2017) and in patient stool samples obtained in connection with a foodborne disease outbreak in Japan (Mori et al. 2017).

1.8. Adenovirus (AdV)

Adenovirus (AdV) belong to the genus *Mastadenovirus* and are divided into subgroups (A-G) (Harrach et al. 2012). They have an icosahedral, 70-90 nm in diameter non-enveloped capsid and a single double stranded DNA genome of 26-49 kbp (Harrach et al. 2012). All AdV serotypes of these subgroups can cause gastrointestinal infections except for subgroup E (Wold and Ison 2013). Human AdV commonly cause infection in the gastrointestinal and respiratory tracts, as well as in the eyes, and occasionally the urinary tract, liver and pancreas (Wold and Ison 2013). AdV subgroup F and G consisting of serotypes 40, 41 and 52, exclusively cause gastrointestinal infections in humans (Wold and Ison 2013).

The incubation period for AdV is 8-10 days, before onset of the primary symptoms, watery diarrhoea and vomiting, which last for 7-8 days (Wood 1988; Uhnoo et al. 1990).

Worldwide an estimated 8% of clinically relevant viral disease are caused by AdV (Wold and Ison 2013), whereas in industrialized countries, 4-17% of acute diarrhoea among infants may

be due to AdV infection (Uhnoo et al. 1990). One study conducted in Thailand between 2011-2017 showed that children aged between 1-2 years had the highest rate of AdV illnesses among other age groups (Kumthip et al. 2019). In Australia, an average of estimated 1650 foodborne gastroenteritis illnesses occurred every year in 2010's due to AdV infections (Kirk 2014).

AdV are an important cause of nosocomial infection and gastroenteritis (Krajden et al. 1990; Rodriguez-Baez et al. 2002), in which non-enteric AdV may play an important role (Kumthip et al. 2019). The majority of human AdV infections are subclinical (Harrach et al. 2012), which in children has been suggested to produce lifelong immunity (Wold and Ison 2013).

2. Detection methods for viruses in foods

Methods for cell culture detection and titration of infective NoV and HAV in complex matrices such as foods have not yet been established. However, unreliable and time-consuming cell culture assays to test for NoV or HAV in clinical samples do exist (Ettayebi et al. 2016; Yeh et al. 2008). Therefore, detection of NoV and HAV in foods relies on the detection of viral genomes extracted from the food matrix (de Roda Husman et al. 2009). In general, these methods consist of two parts, i) elusion, concentration and extraction of viruses from the matrix followed by purification of the viral genome, and ii) molecular detection of specific sequences of the viral genome in question typically by the highly sensitive and specific reverse transcription-quantitative Taqman real-time PCR (RT-qPCR) (Vinjé 2015).

The first validated standard method for extraction and detection of viral RNA from foods was published in 2017 (ISO 2017).

For fresh produce, the method includes viral elution from the food matrices using a protein rich alkaline buffer requiring concurrent pH adjustments, followed by viral particle concentration, extraction and capsid lysis to release viral genomes. The viral genomes are then absorbed to magnetic silica particles forming a complex which are purified by several washing steps, before the genome is finally eluted from the particles prior to being analysed for the presence of genomic sequences of the virus in question using RT-qPCR (ISO 2017).

The number of steps in the ISO standard makes it laborious and time consuming and prone to loss of viral genomes. Thus, the method often fails to achieve the desired efficiency in viral genome recovery from the tested samples. In addition, food matrices such as fruits and vegetables contain organic or inorganic substances, which if remaining in the purified nucleic acid extracts may act as PCR inhibitors that hamper RT-qPCR amplification of target viral sequences (Bartsch et al. 2016; Perrin et al. 2015; Schrader et al. 2012).

To improve viral RNA recovery in extracts from soft fruits processed by ISO 15216 (ISO 2017), Bartsch et al. (2016) included a purification step using the commercially available MobiSpin-400 column (MoBiTec, Göttingen, Germany). This improved the detection frequency of target viruses, although it failed to comply with the extraction efficiency criteria described in the ISO standard method (15216). Therefore, the ISO standard method, although being a complex procedure, still faces major challenges with low viral RNA recoveries and inhibited RT-qPCR detection of target viral sequences, in extracts processed from diverse categories of foods.

Relevant and sensitive qPCR methods exist for all the viruses described in this document. However, the challenge of how to best isolate viral genomes from different food matrices remains the same for detection of all foodborne viruses and is an area of active research. Having reliable detection methods is naturally of great consequence both for the surveying food and health authorities and for the food industry.

3. Transmission routes of foodborne viruses

3.1. Transmission via food handler

The origin of most foodborne virus outbreaks can be pin-pointed to events in kitchens, where the food is prepared by symptomatic or asymptomatic food handlers, who are infected or have infected relatives, and served to the consumer without prior heat treatment (EFSA Panel on Biological Hazards (BIOHAZ) 2011; Kuo et al. 2009;Todd et al. 2007a). Buffet meals may also be contaminated by guests with subsequent transmission to other buffet guests (Franck et al. 2015). Food handler transmission of foodborne viruses have most often been reported

for NoV and HAV and to a lesser extent for SaV and RV, see Table 2 (EFSA Panel on Biological Hazards (BIOHAZ) 2011; Fiore 2004; Franck et al. 2015).

A study of foodborne disease outbreaks caused by infected food handlers, identified three main causes of NoV and HAV contamination: i) handling of food by infected person or carrier, ii) bare hand contact, and iii) lack of proper hand hygiene (Todd et al. 2007b). Among foodborne NoV outbreaks, infected food handlers could be identified as the origin of NoV transmission in 34% of 191 reported outbreaks in Denmark during 2005-2011 (Franck et al. 2015), and in 61% of 74 selected published outbreaks during 2003-2017 (Hardstaff et al. 2018). In both these studies, the transmitted NoV by food handlers involved a diverse range of foodstuffs in a wide variety of settings. In the Danish study, the implicated food handlers were reported as asymptomatic during food handling in the majority of outbreaks (64% out of 41). Before handling the food, some food handlers had been in contact with ill relatives and remained asymptomatic, while others developed symptoms shortly after or were post-symptomatic (Franck et al. 2015). That asymptomatic food handlers are more often reported to cause NoV disease outbreaks than symptomatic food handlers is not an uncommon observation (Boxman et al. 2007).

Practically all types of foods served after personal handling without prior heat treatment (i.e., ready-to-eat foods), may pose a risk of transmitting viruses to consumers, and a great number of such events have been described for both NoV and HAV (Chironna et al. 2004; Fiore 2004). For NoV, infected food handlers could be identified as the vectors in outbreaks due to e.g., contaminated sliced ham affecting 125 cases (Texas, 1998) (Daniels et al. 2000), side salads involving 333 persons (13 states, USA, 2001) (Anderson et al. 2001), sandwiches causing 59 cases (Spain) (Godoy et al. 2005), and bakery product affecting 231 cases (The Netherlands, 2001) (de Wit et al. 2007).

Similarly for HAV, transmission through infected food handlers affected 91 consumers of uncooked food served at a catered event in Kentucky in 1994 (Massoudi et al. 1999) and 269 people consuming raw beef in Belgium (Robesyn et al. 2009). Glasses, which became contaminated by pub staff, led to infection of eight drink-consumers (England, 2002) (Sundkvist et al. 2000). An interesting study, which reviewed all reports of salsa or guacamole

associated (SGA) disease outbreaks during 1984-2008, concluded that 32 outbreaks (987 illnesses) were caused by NoV, of which nearly all (30) were caused by foods prepared in restaurants or delis (Kendall et al. 2013). Fresh salsa and guacamole require careful preparation and storage and this study pointed to the importance of focussing on prevention strategies, which involve food handlers, in order to reduce virus transmission and the risk of illness among consumers.

Indeed, the most frequent cause of foodborne outbreaks due to NoV and HAV have been documented to originate from catering, canteens or restaurants where the surfaces of the kitchen environment and foods have been contaminated by infectious food handlers (Fankhauser et al. 2002; Franck et al. 2015). Surfaces of community buildings like hospitals, day care centres, offices, apartment houses, nursing homes, hotels, day care centres, schools, animal care facilities, bars, coffee shops and paediatric wards have been reported to be contaminated by foodborne viruses (Boone and Gerba 2007). Transmission of viruses between hands, melamine surfaces, door handles, telephone receivers or cleaning cloth has been reported in households (Barker et al. 2004). Transmission of foodborne viruses between hands and contaminated fomites have been demonstrated in several studies as reviewed by Barker et al. (2001). Two experimental transmission studies using hands inoculated with infectious virus showed transfers of 46, 18 or 13% of NoV surrogates (feline calicivirus) to ham, lettuce or steel disks, respectively (Bidawid et al. 2004), and 9.2% of HAV to lettuce (Bidawid et al. 2000).

Table 2: Some reported outbreaks of foodborne viruses due ill food handlers, 2009-2018

Cause of transmission	Virus	Year	Country of OB	Settings	No. OB	No. cases	Detection (Epi/stool/swab)	Reference
Kitchen stuff	NoV	2009	Austria	Healthcare facility	1	204	Epi	(Schmid et al. 2011)
Catered lunch	SaV	2010	Japan			3827	Epi/stool	(Oka et al. 2017)
Food served by ill cook and water	NoV	2011	France	Military canteen	1	147	Epi/stool(chef)/food	(Mayet et al. 2011)
Grain salad and beetroot dip (indicated food handler contaminated)	NoV	2014	Australia	Restaurant	1	46	Epi/stool	(Coutts et al. 2017)
Pork liver and lamb chops (indicated food handler contaminated)	NoV	2015	Taiwan	distillery	1	169	Epistool/food/swab	(M.-Y. Chen et al. 2016)
Schools & colleges (71.9%), kindergartens (23.4%), and factories (4.7%)	NoV	2016-2017	China		64	2953	Stool	(Fu et al. 2017)
Person to person	NoV	2017	China	Primary school		19	Stool	(J. Li et al. 2018)
Environmental surfaces and infected food handlers	NoV	2017	USA	Wedding event		159	Epi/stool	(Free et al. 2019)
Food handler	NoV	2017	Italy	cafeteria	2	45	Epi/stool/swab/	(Monini et al. 2019)
Food supplying chain	NoV	2017	Portugal	Army base	3	31	Stool	(Lopes-João et al. 2019)
Turkey dinner (indicated)	NoV	2018	Spain	Nursing home		137	Epi/stool	(Parrón et al. 2019)

3.2. Transmission during primary production

Fresh produce

Virus contamination of food during primary production can be due to inefficient sanitation of water and equipment or improper practice of personal hygiene among symptomatic or asymptomatic food handlers (pickers and packers), who shed virus particles (EFSA Panel on Biological Hazards (BIOHAZ) 2011; Kuo et al. 2009; EFSA Panel on Biological Hazards (BIOHAZ) 2014b). Examples of fruits, vegetables and lettuce, which became contaminated during primary production and later resulted in viral disease outbreaks among consumers, are listed in Table 3.

Fresh food, such as soft-fruits, are sold as ready-to-eat food in the market place, and come directly from production establishments, therefore risk evaluation of food contamination at primary production level is a key factor in foodborne disease control (Macori et al. 2018). Fresh produce may be subjected to both pre- and post-harvest contamination (Beuchat 1996).

Before harvest, fruits and vegetables may be contaminated by faeces, soil, water used for irrigation or to apply insecticides or fungicides, green or inadequately composed manure, air (dust), wild or domestic animals, insects and human handling (Beuchat and Ryu 1997). After harvest, fruit and vegetables may be contaminated by faeces, improper human handling by workers or consumers, harvesting equipment, transport containers, wild or domestic animals, insects, air (dust), wash or rinse water, processing equipment, ice, transport vehicles, storage condition, packaging condition, cross-contamination, and improper handing after purchase (Beuchat and Ryu 1997).

Often fresh produces such as berries are picked by hand, which may facilitate contamination and entry of human pathogenic viruses in the food chain (Alegbeleye et al. 2018; Anderson-Coughlin and Kniel 2019; Beuchat and Ryu 1997). The type of cultural or irrigation techniques may also play a role in contamination of fresh produces (Macori et al. 2018). At the production level, irrigation with contaminated water has been reported to have contaminated fresh lettuce (Barker et al. 2013; Werneck et al. 2017), and leafy greens and berry fruits (Bouwknegt et al. 2015). Domesticated animals have also been reported to be the source of contamination at the farm level (Salaheen et al. 2015).

Foodborne viruses, which are known to be transmitted via primary production of fresh produce, are primarily NoV and HAV but also HEV and RV. Contaminated water is the most common cause of NoV, HAV and HEV transmission (Jacobsen 2010). Waterborne transmission of HEV (genotype 1 or 2) have been reported in at least 30 countries in Asia, Africa and North America (WHO 2015b).

In a study in Mexico, NoV was found on 31% of workers' hands during the harvest of green bell peppers, while 45 or 30% of field or packed green bell peppers were found contaminated with NoV (León-Félix et al. 2010).

Seaweed has just recently been reported associated with NoV illness (Kwan et al. 2017), see Table 3. The first reported outbreak of NoV gastroenteritis was in South Korea in 2012, where both the seaweed implicated in disease outbreak and seawater used to wash seaweeds were found contaminated by NoV (Park et al. 2015). Investigations suggested that the seaweed

were likely contaminated by either seawater before harvest, due to NoV contaminated wastewater disposal near seaweed farm, or during washing of seaweed after harvest using contaminated seawater (Park et al. 2015). In Japan, seven large outbreak of NoV gastroenteritis was reported due to dried seaweed possibly being contaminated by an infected food handler during packaging. This led to illness in 2094 persons (Sakon et al. 2018). More recently, in 2019, imported contaminated seaweed has been reported to have caused a NoV disease outbreak in Norway (RASFF 2019:3003). Seaweed may be processed in geographical areas, where NoV contaminated seawater may be used for washing (Park et al. 2015), or seaweed may be processed and packed by infected food handlers (Kusumi et al. 2017). These products, despite containing preservatives or being processed by desiccation, may still harbour high titres (360-2900 genome copies/g) of NoV, which could remain infectious even after a long preservation period (Kusumi et al. 2017; Park et al. 2015; Sakon et al. 2018).

Table 3: Some reported outbreaks of foodborne viruses due to produce, 2009-2018

Food Vehicle	Virus	Year	Country of OB	Settings	No. OB	No. cases	Detection (stool/epi?)	Source region	Reference
Semidried tomatoes	HAV	2009	Australia			562	case-control studies + serum + food		(Donnan et al. 2012)
raspberries	NoV	2009	Finland	Restaurant +day care + cafeteria	3	~200	Specimen + food	Poland	(Maunula et al. 2009)
Raspberries (indicated)	NoV	2009	Finland	School	15	525	Epi + stool	Poland	(Sarvikivi et al. 2012)
Salad (indicated)		2009	Germany	Military base	1	101	Epi + stool + environmental swab		(Wadl et al. 2010)
Raspberries	**NoV**	2009	Denmark		**1**	**6**	Epi + Stool + Food	**Serbia**	(Franck et al. 2015)
Semidried tomatoes	HAV	2009-2010	The Netherlands			66	Case-control study +		(Petrignani et al. 2010)
Semidried tomatoes	HAV	2010	France	Domestic	1	59	Serum+epi	Turkey	(Gallot et al. 2011)
Lettuce (Lollo Bionda)	NoV	2010	Denmark				France		(Ethelberg et al. 2010)
Romaine	NoV	2010	Denmark		1	40	Epi + Stool + Food	**Germany**	(Franck et al. 2015)
Lolo bionda	NoV	2010	Denmark		11	260	Epi + Stool + Food	**France**	(Ethelberg et al. 2010)
Raspberries	NoV	2010	Denmark		1	10	Epi + Stool + Food	**China**	(Franck et al. 2015)
Raspberries	NoV	1010-11	Denmark		7	224	Epi + Stool + Food	**Serbia**	(Franck et al. 2015)
Raspberries,	NoV	2010-2011	Denmark	Hospital canteen+	6	27	Epi + Stool + Food	Serbia	(Müller et al. 2015)
Raspberries	NoV	2011	Denmark		1	8	Epi + Stool + Food	**China**	(Franck et al. 2015)
Strawberries	NoV	2012	Germany		1	11000	Epi + Stool + Food	China	(Bernard et al. 2014)
Green seaweed	NoV	2012	South Korea	School	2	91	cohort study + stool + food	South Korea	(Park et al. 2015)
Strawberries	NoV	2012	Germany			10950	Epi + specimen + food	China	(Mäde et al. 2013)
Strawberries	HAV	2012-13	Denmark /Scandinavia		1	103	Epi + Stool + Food	**N Africa**	(Nordic outbreak investigation team 2013)
strawberries	HAV	2012-13	Denmark, Finland, Norway and Sweden			103	Epi + patients' specimen (	Egypt, Morocco and Turkey	(Lassen et al. 2013; Nordic outbreak investigation team 2013)
Pomegranate arils	HAV	2013	USA			165	Patients' specimen + food	Turkey	(Collier et al. 2014)
mixed frozen berries	HAV	2013-2014	13 EU/EEA countries (90% in Italy)			1589	Epi + microbiological	Possibly: Bulgaria (blackberries) and Poland (red currants)	(Severi et al. 2015)
Environment + mixed salad	NoV	2014	Germany	Restaurant	1	3	Stool + food + environmental swab		(Mäde et al. 2016)
green coral (Lollo Bionda) lettuce)	NoV	2016	Denmark		23	412	Cohort Study + Stool + food	France	(Müller et al. 2016)
strawberries	HAV	2018	Sweden			20	patients specimen + food	Poland	(Enkirch et al. 2018)
strawberries	HAV	2018	Austria			14		Poland	Enkirch et al., 2018)
Seaweed (Laver)	NoV	2017	Japan	School	4	1193	Specimen + food		(Somura et al. 2017)
Seaweed (dried shredded)	NoV	2017	Japan	School + office	7	2094	Epi + stool + food		(Sakon et al. 2018)

3.3. Bivalve shellfish

Bivalve shellfish are at constant risk of being exposed to pathogens from their surrounding water as a consequence of human or animal discharge originating from wastewater treatment plants and run offs from manured land (EFSA Panel on Biological Hazards (BIOHAZ) 2012; Krog

et al. 2014). Pathogens are taken up through the bivalve shellfish indiscriminate filter-feeding behaviour and will bioaccumulate to varying degrees in the digestive tissue (DT) of the different species (Carver and Mallet 1990; Winter 1973). If present in the growing water, NoV, HAV and HEV will be accumulated due to specific binding affinities to the tissue in the digestive gland, gills and mantle, with an efficiency depending of the species of shellfish, virus family and strain type, and seasonality (water temperature) (Burkhardt et al. 1992; Burkhardt and Calci 2000; Le Guyader et al. 2012; Maalouf et al. 2010, 2011; Muniain-Mujika et al. 2003).

The hygienic control of faecal contamination in shellfish beds is based on sanitary surveys (EU 2017) and the levels of the indicator bacteria, *Escherichia coli*, in shellfish meat (European Communities 2005). However, despite compliance with legislative requirements (European Communities 2004), NoV, HAV and HEV among other foodborne viruses are frequently detected in oysters and mussels during winter in European areas (EFSA Panel on Biological Hazards (BIOHAZ) 2011, 2012; Mesquita et al. 2016; Pol-Hofstad et al. 2014). Reasons for this are partly that bacteria are eliminated from shellfish more quickly than are viruses (Holm et al. 2015; Schwab et al. 1998). Also, the main foodborne viruses are more resistant to seawater conditions than most vegetative bacteria (Griffin et al. 2003; Mattioli et al. 2017). Besides, lying dormant in the sediment, viruses can be resuspended upon disturbance of the seabed and thus be absorbed by the shellfish long after first entering the sea (Meschke and Boyle 2007). For these reasons, viral and bacterial loads in shellfish correlate poorly.

As a consequence, consumption of raw or undercooked oysters, mussels and clams are regularly associated with disease of NoV, but also HAV and less commonly HEV (EFSA Panel on Biological Hazards (BIOHAZ) 2012), see Table 4. The first association with shellfish-borne viral gastroenteritis was already made in the UK in 1976/1977, when cooked cockles were epidemiologically linked to 33 clusters of nearly 800 people (Appleton et al. 1981; Appleton and Pereira 1977). Since then enteric viruses causing gastroenteritis have been epidemiologically linked to outbreaks of shellfish-vectored illness on numerous occasions in several countries (Bellou et al. 2013). In a study reviewing the 368 published shellfish borne viral outbreaks occurring between 1980 and 2012, NoV accounted for the majority (83.7%, n=300) of outbreaks followed by HAV (12.8%, n=46), AsV (0.5%, n=2), HEV, SaV, RV, AiV, EV (each virus 0.3%, n=1). Oysters were the most commonly involved type of shellfish (58.4%,

n=215) followed by clams (22.6%, n=83), cockles (1.1%, n=3) and mussels (0.5%, n=2). The reported outbreaks occurred in 17 different countries, with East Asia accounting for most of the NoV outbreaks (72.7%) while Europe accounted for most of the HAV outbreaks (83%). The one HEV outbreak was due to mussels from UK.

Human SaV has been detected in an 18-months surveillance study of Spanish mussels (Varela et al. 2016) and in catered lunch suspected to be the cause of disease outbreaks in Japan in 2010 (Oka et al. 2017).

Table 4: Some reported outbreaks of foodborne viruses due to bivalve shellfish, 2009-2018

Cause of transmission	Virus	Year	Country of OB	Settings	No. OB	No. cases	Detection (Epi/stool/food)	Source region	Reference
oysters (steamed) (indicated) + 2nd transmission	NoV	2009	USA	Restaurant	1	177	Epi/ study/stool	USA	(Alfano-Sobsey et al., 2012)
Shellfish	NoV	2009	UK	Restaurant	1	240	Epi/stool/food/ swab		(Smith et al., 2012)
Oysters	NoV	2010	Ireland			>70	Eoi/Stool/food		Marine Institute Ireland* (see Efsa 2011/2012 (EFSA Panel on Biological Hazards (BIOHAZ) 2011)
Oysters	NoV	2007-10	UK		6	287	Epi/Stool/Food	UK	(Lowther et al. 2012)
Oysters	NoV	2010	DK, UK, SE, Fr, NO				Epi/Stool/Food		(Westrell et al. 2010)
Oysters	NoV	2010	UK	Restaurant	1	11	Stool/ swab/food		(Baker et al. 2011)
Mussels	HAV	2012	The Netherlands	Domestic	2	89	Epi/serum	The Netherlands/UK	(Boxman et al. 2016)
Clams (carpet shell) (Tapes rhomboides)	NoV	2013	Norway	company Christmas celebration		43	Epi/food		(Lunestad et al. 2016)
Oysters	NoV	2013	Australia			306	Epi/stool/food		(Lodo et al. 2014)
Oysters (fermented)	NoV	2013	South Korea	School		8	Epi/ stool/food/swab		(Cho et al., 2016)
Raw oysters, Clams	NoV	2016	Denmark				Epi/Stool/Food	France	(Rasmussen et al. 2016)
Scallops	HAV	2016	Hawaii			292		Philippines	(CDC 2016; Disease Outbreak Control Division 2017)
Oysters (*G. gigas*) (raw)	NoV	2017	Denmark			10	Eoi/Stool/food	Denmark	Unpublished

3.4. Meat products

Foodborne transmission of HEV by meat and meat products may be attributed to for example consumption of raw liver from infected pigs or wild boar, or contamination of food products during preparation (BIOHAZ 2017). The exact stage, where meat become contaminated from infected animals, is not known. However, since the virus is shed in animal faeces and urine, poor evisceration practices have been assumed to be the main source of meat contamination by HEV (Velebit et al. 2015).

The European population are sporadically infected with HEV, due to the pig, wild boar and deer reservoirs of the virus, which can reach the food chain (Clemente-Casares et al. 2016). The seroprevalence of HEV in the populations of 11 EU countries have been estimated to be between 2.2 to 52.2% (Clemente-Casares et al. 2016), while in Denmark it is 19.8% among blood donors (Holm et al. 2015). In Denmark, infection of HEV was suggested to be through zoonotic transmission, which in one study was reported to be largely asymptomatic (Christensen et al. 2008). Apart from pigs, ferret, and rat reservoirs in Denmark, farmed minks were reported to carry distinct variants of HEV (Krog et al. 2013). In the USA, consumption of undercooked meat was reported to be the highest risk factor for HEV infection (Cossaboom et al. 2016). Consumption of wild boar meat have been reported to be connected with HEV infection in Japan in at least 2 studies (Li et al. 2005; Masuda et al. 2005). In UK, in 2009-2010, HEV was detected in slaughterhouses, processing plants and point of sale in pork food chain, suggesting pork meat to be a possible risk factor for foodborne transmission of HEV (Berto et al. 2012). HEV RNA has been detected in samples of pig liver (1-21%), meat (0-6%) and sausage (0-47%), in samples of wild boar liver (2-38%), meat (0-12%) and sausage (10%), and in samples of deer liver (0-22%) and meat (0-5%) collected in predominantly developed countries (Pavio et al. 2017). In a screening study in 2016 in Switzerland, approximately 11, 19 or 6% of meat products, liver sausages or raw meat sausages, respectively, were found to contain HEV RNA (Moor et al. 2018). Even exposure to pigs or pig-environment may increase risk of HEV transmission. In Netherlands, 11% of swine veterinarians were seroprevalent for HEV, while seroprevalence was 6% among non-swine veterinarians and only 2% in general population (Bouwknegt et al. 2008).

Table 5: Selected reported outbreaks of foodborne hepatitis E viruses due meat products, 2009-2018, (Extract of ECDC member state survey; ECDC, 2017)

Cause of transmission	Virus	Year	Country of OB	No. OB	No. cases	Reference
Unknown, assumed pork and pork products at pig-slaughtering feasts	HEV	2009–2011	Czech Republic	2	13, 8	(Trmal et al. 2012)
Raw figatelli	HEV	2010	France		2	(Renou et al. 2011)
Probably raw figatelli	HEV	2011	France		1	(Anty et al. 2012)
Tripe sausages made in farm and selling in butcher shop	HEV	2011	Czech Republic		36	(EFSA Panel on Biological Hazards (BIOHAZ) et al. 2017)
Raw pig liver sausage (figatelli)	HEV-3	2011	France		1	(Moal et al. 2012)
Possible factors: pork meat (3), butcher, home pig slaughter (3), excessive pork intake, minced meat/ liver sausage, brawn, liver sausage (3), raw pork meat, grilled pork meat, contact with HEV (2), greaves, minced meat, precooked sausage, home-made sausage, wild boar goulash, sausage	HEV	2009–2012	Czech Republic		27	(Chalupa et al. 2014)
Raw pork liver sausage, not thoroughly cooked pig meat	HEV-4	2011–2012	France		4	(Colson et al. 2012; Tessé et al. 2012)
Undercooked pig liver-based stuffing in spit-roasted piglet	HEV-3	2013	France		17	(EFSA Panel on Biological Hazards (BIOHAZ) et al. 2017; Guillois et al. 2016)
Raw pig liver sausage (figatelli)	HEV-3	2013	France		2	(Renou et al. 2014)
Likely raw pig liver sausage (figatelli)	HEV-3	2014	France		1	(Doudier et al. 2015)

3.4. Dairy products

Transmission through dairy products is relevant for TBEV, which can be acquired by milk producing domesticated animals being bitten by ticks carrying the virus. It should be noted as explained in section 1.4. that proper pasteurization will inactivate the virus.

Table 6: Some reported outbreaks of foodborne viruses due dairy products, 2009-2018

Cause of transmission	Virus	Year	Country of OB	No. OB	No. cases	Detection (stool/epi?)	Source region	Reference
Unpasteurised cow milk	TBE	2011	Hungary	1	7	Epi + blood (not in food)	Hungary	(Caini et al. 2012)
Unpasteurised goat milk (råw)	TBE	2012	Slovenia		3	Epi + blood + food	Slovenia	(Hudopisk et al. 2013)
Raw goat milk + cheese	TBE	2015	Croatia		7	Specimen (cerebral fluid) + serum + epi	Croatia	(Markovinović et al. 2016)
Unpasteurised goat milk, cheese	TBE	2016	Germany	1	32	Goats, Tick, cheese	Germany	(Brockmann et al. 2018)

3.5. Drinking water.

Although not the primary focus of this review, contaminated drinking water can also be the cause of virus outbreaks. This is highly relevant for the food industry, as the regulations require that drinking water is used in the handling and processing of foods.

Table 7: Some reported outbreaks of foodborne viruses due to contaminated drinking water, 2009-2018

Cause of transmission	Virus	Year	Country of OB	Settings	No. OB	No. cases	Detection (Epi/stool/water)	Source region	Reference
Water	NoV GI	2011	Sweden			173	Epi + stool + water		(Riera-Montes et al., 2011)
Tap water	NoV	2012	Denmark	Community	1	15	Epi + stool + water	Denmark	(van Alphen et al. 2014)
Tap water	NoV GI	2015	Greece			230	Stool + water		(Tryfinopoulou et al. 2019)
Private well connected to public water supply	HEV	2015	France			7			(EFSA Panel on Biological Hazards (BIOHAZ) et al. 2017)
Tap water	NoV	2016	Denmark	Community	1		Epi + Stool + water	Denmark	(Hellmér 2018)

4. Mitigation

Strategies to mitigate foodborne viruses can be divided into prevention of the occurrence in the raw material, and mitigation of the viruses in the food processing environment. The latter can be achieved through attention to the hygiene in processing facilities and where possible through food processing to inactivate the virus particles without compromising the quality of the food product.

In terms of decontaminating surfaces or foods, limited efficiency in disinfection of NoVs has been reported when using common disinfectants such as quaternary ammonium compound (QAC) or ethoxylated alcohols (Girard et al. 2010) and for HAV using commercial QAC (Jean et al. 2003). Sodium hypochlorite (50 ppm) or peracetic acid (85 ppm) have been demonstrated to reduce NoV surrogate murine norovirus (MNV) on surfaces of blueberries, strawberries and lettuce by up to 4 logs after 1 min of treatment (Girard et al. 2016). Free chlorine inactivation of HAV and bacteriophage MS2 on strawberries, cherry tomatoes and lettuce has been demonstrated to be effective, however, highly dependent on contact time (2-10 min) and type of food matrix (Casteel et al. 2008; Fraisse et al. 2011). Solomon et al. (2009) showed

that QAC at a concentration of 10 times (8480 ppm) the recommended level (848 ppm) reduced HAV by only 0.4 log, while oxidative disinfectant Virkon required an 1% concentration to achieve a reduction of over 3.2 log.

Ultraviolet light (UVC) can inactivate HAV, feline calicivirus and AiV on lettuce and green onion with log reductions between 2.5 and 5.6 (Fino and Kniel 2008), and can only marginally reduce bacteriophage MS2 on lettuce (up to 2 log) (Xie et al. 2016). For water, lettuce and green onion, ozone inactivation has been observed to be effective on MNV and Feline calicivirus (Hirneisen et al. 2011) or RV (Hirneisen et al. 2011; Khadre and Yousef 2002).

Heat inactivation studies of HAV in cockles showed a 4 log reduction of infectious viruses after heating to internal temperatures of 85-90°C for 1 min (Millard et al. 1987). Traditionally, thermal inactivation of viruses is a reliable process for food decontamination. Though, the process may be time consuming (Hirneisen et al. 2010) and may not be suitable for all surfaces in industrial or health care facility settings or for inactivation of viruses on fresh produce without compromising the quality of food (Berk 2009). Thermal processing of food can reduce the quality of the product visually by altering the texture, flavour, colour or appearance (Oliveira 2004), as well as compromising the nutritional value of food by for example destroying heat-labile vitamins (Awuah et al. 2007). Overall more research is needed into effective mitigation strategies.

5. Conclusions

- The issue of foodborne viruses in our food supply is recognized as an important food safety priority.
- The present report is a contribution to the foodborne virus risk profile being developed by the Danish Veterinary and Food Administration (Fødevarestyrelsen) and includes a review of the current knowledge about the biology of relevant viruses, contamination pathways and product relationships, detection methods and the efficacy of mitigation methods to reduce foodborne viruses.

- Human norovirus (NoV) and hepatitis A virus (HAV) are by far the predominant pathogenic foodborne viruses, with hepatitis E virus (HEV) recently having attained attention as an important contributor to foodborne illnesses.
- Common contamination routes for food are via infected food handlers and/or exposure to contaminated water and materials during primary production of bivalve shellfish, lettuce, fresh or frozen fruits and vegetables, and products of pork and wild boar meat.
- Efficient surveillance and virus control measures are required throughout the food production chain from “farm to fork”. Improved surface surveillance and control after cleaning of kitchen environments may for example reduce food handler transmitted virus outbreaks.
- Research is needed to devise better virus detection methods and mitigation strategies including methods to properly validate the effect of interventions. This would allow for the development of better risk assessments and more targeted control in food production and processing.

6. References

Aggarwal, R., & Naik, S. (2009). Epidemiology of hepatitis E: current status. *Journal of Gastroenterology and Hepatology*, *24*(9), 1484–93. doi:10.1111/j.1440-1746.2009.05933.x

Ahmed, S. M., Hall, A. J., Robinson, A. E., Verhoef, L., Premkumar, P., Parashar, U. D., et al. (2014). Global prevalence of norovirus in cases of gastroenteritis: a systematic review and meta-analysis. *The Lancet. Infectious Diseases*, *14*(8), 725–730. doi:10.1016/S1473-3099(14)70767-4

Alegbeleye, O. O., Singleton, I., Sant'Ana, A. S., & Sant'Ana, A. S. (2018). Sources and contamination routes of microbial pathogens to fresh produce during field cultivation: A review. *Food Microbiology*, *73*, 177–208. doi:10.1016/j.fm.2018.01.003

Alfano-Sobsey, E., Sweat, D., Hall, A., Breedlove, F., Rodriguez, R., Greene, S., et al. (2012). Norovirus outbreak associated with undercooked oysters and secondary household transmission. *Epidemiology and Infection*, *140*(2), 276–282. doi:10.1017/S0950268811000665

Althof, N., Trojnar, E., Böhm, T., Burkhardt, S., Carl, A., Contzen, M., et al. (2019). Interlaboratory validation of a method for Hepatitis E Virus RNA detection in meat and meat products. *Food and Environmental Virology*, *11*(1), 1–8. doi:10.1007/s12560-018-9360-6

Anderson-Coughlin, B. L., & Kniel, K. E. (2019). Recovery and detection of enteric viruses from non-traditional irrigation water sources. *Methods and Protocols*, *2*(3), 55. doi:10.3390/mps2030055

Anderson, A. D., Garrett, V. D., Sobel, J., Monroe, S. S., Fankhauser, R. L., Schwab, K. J., et al. (2001). Multistate outbreak of Norwalk-like virus gastroenteritis associated with a common caterer. *American Journal of Epidemiology*, *154*(11), 1013–9. doi:10.1093/aje/154.11.1013

Anty, R., Ollier, L., Péron, J. M., Nicand, E., Cannavo, I., Bongain, A., et al. (2012). First case report of an acute genotype 3 hepatitis E infected pregnant woman living in South-Eastern France. *Journal of Clinical Virology*, *54*(1), 76–78. doi:10.1016/j.jcv.2012.01.016

Ao, Y., Cong, X., Jin, M., Sun, X., Wei, X., Wang, J., et al. (2018). Genetic analysis of reemerging GII.P16-GII.2 noroviruses in 2016-2017 in China. *The Journal of Infectious Diseases*, *218*(1), 133–143. doi:10.1093/infdis/jiy182

Appleton, H., Palmer, S. R., & Gilbert, R. J. (1981). Foodborne gastroenteritis of unknown aetiology: a virus infection? *British Medical Journal (Clinical research ed.)*, *282*(6278), 1801–2. http://www.ncbi.nlm.nih.gov/pubmed/6786630. Accessed 10 February 2020

Appleton, H., & Pereira, M. S. (1977). A possible virus aetiology in outbreaks of food-poisoning from cockles. *Lancet (London, England)*, *1*(8015), 780–1. doi:10.1016/s0140-6736(77)92960-9

Arias, C., & DuBois, R. (2017). The Astrovirus Capsid: A Review. *Viruses*, *9*(1), 15. doi:10.3390/v9010015

Atmar, R. L. (2010). Noroviruses - State of the Art. *Food and Environmental Virology*, *2*(3), 117–126. doi:10.1007/s12560-010-9038-1

Atmar, R. L., Opekun, A. R., Gilger, M. A., Estes, M. K., Crawford, S. E., Neill, F. H., et al. (2014). Determination of the 50% human infectious dose for Norwalk virus. *The Journal of Infectious Diseases*, *209*(7), 1016–22. doi:10.1093/infdis/jit620

Atmar, R. L., Opekun, A. R., Gilger, M. A., Estes, M. K., Crawford, S. E., Neill, F. H., & Graham, D. Y. (2008). Norwalk virus shedding after experimental human infection. *Emerging Infectious Diseases*, *14*(10), 1553–1557. doi:10.3201/eid1410.080117

Awuah, G. B., Ramaswamy, H. S., & Economides, A. (2007). Thermal processing and quality: Principles and overview. *Chemical Engineering and Processing: Process Intensification*, *46*(6), 584–602. doi:10.1016/j.cep.2006.08.004

Baert, L., Debevere, J., & Uyttendaele, M. (2009). The efficacy of preservation methods to inactivate foodborne viruses. *International Journal of Food Microbiology*, *131*(2–3), 83–94. doi:10.1016/j.ijfoodmicro.2009.03.007

Baker, K., Morris, J., McCarthy, N., Saldana, L., Lowther, J., Collinson, A., & Young, M. (2011). An outbreak of norovirus infection linked to oyster consumption at a UK restaurant, February 2010. *Journal of Public*

Health, *33*(2), 205–211. doi:10.1093/pubmed/fdq089

Balayan, M. S., Andjaparidze, A. G., Savinskaya, S. S., Ketiladze, E. S., Braginsky, D. M., Savinov, A. P., & Poleschuk, V. F. (1983). Evidence for a virus in non-A, non-B hepatitis transmitted via the fecal-oral route. *Intervirology*, *20*(1), 23–31. doi:10.1159/000149370

Bank-Wolf, B. R., König, M., & Thiel, H.-J. (2010). Zoonotic aspects of infections with noroviruses and sapoviruses. *Veterinary Microbiology*, *140*(3–4), 204–12. doi:10.1016/j.vetmic.2009.08.021

Barker, J., Stevens, D., & Bloomfield, S. F. (2001). Spread and prevention of some common viral infections in community facilities and domestic homes. *Journal of Applied Microbiology*, *91*(1), 7–21. doi:10.1046/j.1365-2672.2001.01364.x

Barker, J., Vipond, I. B., & Bloomfield, S. F. (2004). Effects of cleaning and disinfection in reducing the spread of Norovirus contamination via environmental surfaces. *Journal of Hospital Infection*, *58*(1), 42–49. doi:10.1016/j.jhin.2004.04.021

Barker, S., O'Toole, J., Sinclair, M., Leder, K., Malawaraarachchi, M., & Hamilton, A. (2013). A probabilistic model of norovirus disease burden associated with greywater irrigation of home-produced lettuce in Melbourne, Australia. *Water Research*, *47*(3), 1421–32. doi:10.1016/j.watres.2012.12.012

Bartsch, C., Szabo, K., Dinh-Thanh, M., Schrader, C., Trojnar, E., & Johne, R. (2016). Comparison and optimization of detection methods for noroviruses in frozen strawberries containing different amounts of RT-PCR inhibitors. *Food Microbiology*, *60*, 124–130. doi:10.1016/j.fm.2016.07.005

Beauté, J., Spiteri, G., Warns-Petit, E., & Zeller, H. (2018). Tick-borne encephalitis in Europe, 2012 to 2016. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *23*(45). doi:10.2807/1560-7917.ES.2018.23.45.1800201

Bellou, M., Kokkinos, P., & Vantarakis, A. (2013). Shellfish-borne viral outbreaks: a systematic review. *Food and Environmental Virology*, *5*(1), 13–23. doi:10.1007/s12560-012-9097-6

Berk, Z. (2009). *Food Process Engineering and Technology*. Elsevier. doi:10.1016/B978-0-12-373660-4.X0001-4

Bernard, H., Faber, M., Wilking, H., Haller, S., Höhle, M., Schielke, A., et al. (2014). Large multistate outbreak of norovirus gastroenteritis associated with frozen strawberries, Germany, 2012. *Eurosurveillance*, *19*(8). doi:10.2807/1560-7917.ES2014.19.8.20719

Berto, A., Martelli, F., Grierson, S., & Banks, M. (2012). Hepatitis E virus in pork food chain, United Kingdom, 2009-2010. *Emerging Infectious Diseases*, *18*(8), 1358–60. doi:10.3201/eid1808.111647

Beuchat, L. (1996). Pathogenic microorganisms associated with fresh produce. *Journal of Food Protection*, *59*(2), 204–216. doi:10.4315/0362-028X-59.2.204

Beuchat, L., & Ryu, J. (1997). Produce handling and processing practices. *Emerging Infectious Diseases*, *3*(4), 459–65. doi:10.3201/eid0304.970407

Bidawid, S., Farber, J. M., & Sattar, S. A. (2000). Contamination of foods by food handlers: Experiments on hepatitis A virus transfer to food and its interruption. *Applied and Environmental Microbiology*, *66*(7), 2759–2763. doi:10.1128/AEM.66.7.2759-2763.2000

Bidawid, S., Malik, N., Adegbunrin, O., Sattar, S. A., & Farber, J. M. (2004). Norovirus cross-contamination during food handling and interruption of virus transfer by hand antisepsis: Experiments with feline Calicivirus as a surrogate. *Journal of Food Protection*, *67*(1), 103–109. doi:10.4315/0362-028X-67.1.103

Bitler, E. J., MATTHEWS, J. E., DICKEY, B. W., EISENBERG, J. N. S., & LEON, J. S. (2013). Norovirus outbreaks: a systematic review of commonly implicated transmission routes and vehicles. *Epidemiology and Infection*, *141*(08), 1563–1571. doi:10.1017/S095026881300006X

Bogovic, P., & Strle, F. (2015). Tick-borne encephalitis: A review of epidemiology, clinical characteristics, and management. *World Journal of Clinical Cases*, *3*(5), 430–41. doi:10.12998/wjcc.v3.i5.430

Boone, S. A., & Gerba, C. P. (2007). Significance of fomites in the spread of respiratory and enteric viral disease. *Applied and Environmental Microbiology*, *73*(6), 1687–1696. doi:10.1128/AEM.02051-06

Bosch, A., Gkogka, E., Le Guyader, F. S., Loisy-Hamon, F., Lee, A., van Lieshout, L., et al. (2018). Foodborne viruses: Detection, risk assessment, and control options in food processing. *International Journal of Food Microbiology*, *285*(June 2018), 110–128. doi:10.1016/j.ijfoodmicro.2018.06.001

Bosch, A., Pintó, R. M., & Guix, S. (2014). Human astroviruses. *Clinical Microbiology Reviews*, *27*(4), 1048–74. doi:10.1128/CMR.00013-14

Bouwknegt, M, Engel, B., Herremans, M. M. P. T., Widdowson, M. A., Worm, H. C., Koopmans, M. P. G., et al. (2008). Bayesian estimation of hepatitis E virus seroprevalence for populations with different exposure levels to swine in The Netherlands. *Epidemiology and Infection*, *136*(4), 567–76. doi:10.1017/S0950268807008941

Bouwknegt, Martijn, Verhaelen, K., Rzeżutka, A., Kozyra, I., Maunula, L., von Bonsdorff, C.-H., et al. (2015). Quantitative farm-to-fork risk assessment model for norovirus and hepatitis A virus in European leafy green vegetable and berry fruit supply chains. *International Journal of Food Microbiology*, *198*, 50–58. doi:10.1016/j.ijfoodmicro.2014.12.013

Boxman, I. L. A., Tilburg, J. J. H. C., te Loeke, N. A. J. M., Vennema, H., de Boer, E., & Koopmans, M. (2007). An efficient and rapid method for recovery of norovirus from food associated with outbreaks of gastroenteritis. *Journal of Food Protection*, *70*(2), 504–8. doi:10.4315/0362-028x-70.2.504

Boxman, I. L. A., Verhoef, L., Vennema, H., Ngui, S.-L., Friesema, I. H. M., Whiteside, C., et al. (2016). International linkage of two food-borne hepatitis A clusters through traceback of mussels, the Netherlands, 2012. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *21*(3), 30113. doi:10.2807/1560-7917.ES.2016.21.3.30113

BOXMAN, I., TILBURG, J., TELOEKE, N., VENNEMA, H., JONKER, K., DEBOER, E., & KOOPMANS, M. (2006). Detection of noroviruses in shellfish in the Netherlands. *International Journal of Food Microbiology*, *108*(3), 391–396. doi:10.1016/j.ijfoodmicro.2006.01.002

Brockmann, S. O., Oehme, R., Buckenmaier, T., Beer, M., Jeffery-Smith, A., Spannenkrebs, M., et al. (2018). A cluster of two human cases of tick-borne encephalitis (TBE) transmitted by unpasteurised goat milk and cheese in Germany, May 2016. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *23*(15). doi:10.2807/1560-7917.ES.2018.23.15.17-00336

Bucardo, F., Kindberg, E., Paniagua, M., Grahn, A., Larson, G., Vildevall, M., & Svensson, L. (2009). Genetic susceptibility to symptomatic norovirus infection in Nicaragua. *Journal of Medical Virology*, *81*(4), 728–35. doi:10.1002/jmv.21426

Bull, R. A., & White, P. A. (2011). Mechanisms of GII.4 norovirus evolution. *Trends in Microbiology*, *19*(5), 233–40. doi:10.1016/j.tim.2011.01.002

Burkhardt, W., & Calci, K. R. (2000). Selective accumulation may account for shellfish-associated viral illness. *Applied and Environmental Microbiology*, *66*(4), 1375–1378. doi:10.1128/AEM.66.4.1375-1378.2000

Burkhardt, W., Watkins, W. D., & Rippey, S. R. (1992). Seasonal effects on accumulation of microbial indicator organisms by *Mercenaria mercenaria*. *Applied and Environmental Microbiology*, *58*(3), 826–31. http://www.ncbi.nlm.nih.gov/pubmed/1575484. Accessed 10 February 2020

Caini, S., Szomor, K., Ferenczi, E., Szekelyne Gaspar, A., Csohan, A., Krisztalovics, K., et al. (2012). Tick-borne encephalitis transmitted by unpasteurised cow milk in western Hungary, September to October 2011. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *17*(12). http://www.ncbi.nlm.nih.gov/pubmed/22490310. Accessed 30 September 2019

Cao, Y.-F., Tao, H., Hu, Y.-M., Shi, C.-B., Wu, X., Liang, Q., et al. (2017). A phase 1 randomized open-label clinical study to evaluate the safety and tolerability of a novel recombinant hepatitis E vaccine. *Vaccine*, *35*(37), 5073–5080. doi:10.1016/j.vaccine.2017.05.072

Carver, C. E. A., & Mallet, A. L. (1990). Estimating the carrying capacity of a coastal inlet for mussel culture. *Aquaculture*, *88*(1), 39–53. doi:10.1016/0044-8486(90)90317-G

Castanys-Muñoz, E., Martin, M. J., & Prieto, P. A. (2013). 2'-fucosyllactose: an abundant, genetically determined soluble glycan present in human milk. *Nutrition Reviews*, *71*(12), 773–89. doi:10.1111/nure.12079

Casteel, M. J., Schmidt, C. E., & Sobsey, M. D. (2008). Chlorine disinfection of produce to inactivate hepatitis A virus and coliphage MS2. *International Journal of Food Microbiology*, *125*(3), 267–273. doi:10.1016/J.IJFOODMICRO.2008.04.015

CDC. (2016). Outbreak of hepatitis A in Hawaii linked to raw scallops. https://www.cdc.gov/hepatitis/outbreaks/2016/hav-hawaii.htm. Accessed 10 February 2020

Chalupa, P., Vasickova, P., Pavlik, I., & Holub, M. (2014). Endemic Hepatitis E in the Czech Republic. *Clinical Infectious Diseases*, *58*(4), 509–516. doi:10.1093/cid/cit782

Cheesbrough, J. S., Green, J., Gallimore, C. I., Wright, P. A., & Brown, D. W. (2000). Widespread environmental contamination with Norwalk-like viruses (NLV) detected in a prolonged hotel outbreak of gastroenteritis. *Epidemiology and Infection*, *125*(1), 93–8. doi:10.1017/s095026889900432x

Chen, M.-Y., Chen, W.-C., Chen, P.-C., Hsu, S.-W., & Lo, Y.-C. (2016). An outbreak of norovirus gastroenteritis associated with asymptomatic food handlers in Kinmen, Taiwan. *BMC Public Health*, *16*(1), 372. doi:10.1186/s12889-016-3046-5

Chen, Shih-Yen, Tsai, C., Lai, M., Chen, C., Lin, K., Lin, T., & Chiu, C. (2009). Norovirus infection as a cause of diarrhea-associated benign infantile seizures. *Clinical Infectious Diseases*, *48*(7), 849–855. doi:10.1086/597256

Chen, Shu, Zhou, Z., Wei, F.-X., Huang, S.-J., Tan, Z., Fang, Y., et al. (2015). Modeling the long-term antibody response of a hepatitis E vaccine. *Vaccine*, *33*(33), 4124–9. doi:10.1016/j.vaccine.2015.06.050

Chironna, M., Lopalco, P., Prato, R., Germinario, C., Barbuti, S., & Quarto, M. (2004). Outbreak of infection with hepatitis A virus (HAV) associated with a foodhandler and confirmed by sequence analysis reveals a new HAV genotype IB variant. *Journal of Clinical Microbiology*, *42*(6), 2825–8. doi:10.1128/JCM.42.6.2825-2828.2004

Cho, H. G., Lee, S. G., Lee, M. Y., Hur, E. S., Lee, J. S., Park, P. H., et al. (2016). An outbreak of norovirus infection associated with fermented oyster consumption in South Korea, 2013. *Epidemiology and Infection*, *144*(13), 2759–2764. doi:10.1017/S0950268816000170

Christensen, P. B., Engle, R. E., Hjort, C., Homburg, K. M., Vach, W., Georgsen, J., & Purcell, R. H. (2008). Time trend of the prevalence of Hepatitis E antibodies among farmers and blood Donors: A potential zoonosis in Denmark. *Clinical Infectious Diseases*, *47*(8), 1026–1031. doi:10.1086/591970

Chuchaona, W., Khamrin, P., Yodmeeklin, A., Kumthip, K., Saikruang, W., Thongprachum, A., et al. (2017). Detection and characterization of Aichi virus 1 in pediatric patients with diarrhea in Thailand. *Journal of Medical Virology*, *89*(2), 234–238. doi:10.1002/jmv.24630

Cisak, E., Wójcik-Fatla, A., Zając, V., Sroka, J., Buczek, A., & Dutkiewicz, J. (2010). Prevalence of tick-borne encephalitis virus (TBEV) in samples of raw milk taken randomly from cows, goats and sheep in eastern Poland. *Annals of Agricultural and Environmental Medicine : AAEM*, *17*(2), 283–6. http://www.ncbi.nlm.nih.gov/pubmed/21186771. Accessed 9 February 2020

Clay, S., Maherchandani, S., Malik, Y. S., & Goyal, S. M. (2006). Survival on uncommon fomites of feline calicivirus, a surrogate of noroviruses. *American Journal of Infection Control*, *34*(1), 41–43. doi:10.1016/j.ajic.2005.05.013

Clemente-Casares, P., Ramos-Romero, C., Ramirez-Gonzalez, E., & Mas, A. (2016). Hepatitis E virus in industrialized countries: The silent threat. *BioMed Research International*, *2016*, 9838041. doi:10.1155/2016/9838041

Collier, M. G., Khudyakov, Y. E., Selvage, D., Adams-Cameron, M., Epson, E., Cronquist, A., et al. (2014). Outbreak of hepatitis A in the USA associated with frozen pomegranate arils imported from Turkey: an epidemiological case study. *The Lancet Infectious Diseases*, *14*(10), 976–981. doi:10.1016/S1473-3099(14)70883-7

Colson, P., Romanet, P., Moal, V., Borentain, P., Purgus, R., Benezech, A., et al. (2012). Autochthonous infections with hepatitis E virus genotype 4, France. *Emerging Infectious Diseases*, *18*(8), 1361–4. doi:10.3201/eid1808.111827

Cook, N., & van der Poel, W. H. M. M. (2015). Survival and elimination of Hepatitis E virus: A review. *Food and Environmental Virology*, *7*(3), 189–194. doi:10.1007/s12560-015-9196-2

Cossaboom, C. M., Heffron, C. L., Cao, D., Yugo, D. M., Houk-Miles, A. E., Lindsay, D. S., et al. (2016). Risk factors and sources of foodborne hepatitis E virus infection in the United States. *Journal of Medical Virology*, *88*(9), 1641–1645. doi:10.1002/jmv.24497

Costafreda, M. I., Bosch, A., & Pintó, R. M. (2006). Development, evaluation, and standardization of a real-time TaqMan reverse transcription-PCR assay for quantification of hepatitis A virus in clinical and shellfish

samples. *Applied and Environmental Microbiology*, *72*(6), 3846–55. doi:10.1128/AEM.02660-05

Coutts, S., Sturge, K., Lalor, K., Marshall, J., Bruggink, L., Subasinghe, N., & Easton, M. (2017). An outbreak of foodborne norovirus gastroenteritis linked to a restaurant in Melbourne, Australia, 2014. *Western Pacific Surveillance and Response Journal*, *8*(2), 12–16. doi:10.5365/wpsar.2017.8.1.008

Crance, J. M., Gantzer, C., Schwartzbrod, L., & Deloince, R. (1998). Effect of temperature on the survival of hepatitis A virus and its capsidal antigen in synthetic seawater. *Environmental Toxicology and Water Quality*, *13*(1), 89–92. doi:10.1002/(SICI)1098-2256(1998)13:1<89::AID-TOX7>3.0.CO;2-3

Crawford, S. E., Ramani, S., Tate, J. E., Parashar, U. D., Svensson, L., Hagbom, M., et al. (2017). Rotavirus infection. *Nature Reviews. Disease Primers*, *3*, 17083. doi:10.1038/nrdp.2017.83

D'Souza, D. H. (2015). Update on foodborne viruses: types, concentration and sampling methods. In *Advances in Microbial Food Safety* (Vol. 2, pp. 102–116). Elsevier. doi:10.1533/9781782421153.1.102

D'Souza, D. H., Sair, A., Williams, K., Papafragkou, E., Jean, J., Moore, C., & Jaykus, L. (2006). Persistence of caliciviruses on environmental surfaces and their transfer to food. *International Journal of Food Microbiology*, *108*(1), 84–91. doi:10.1016/j.ijfoodmicro.2005.10.024

Daniels, N. A., Bergmire-Sweat, D. A., Schwab, K. J., Hendricks, K. A., Reddy, S., Rowe, S. M., et al. (2000). A foodborne outbreak of gastroenteritis associated with Norwalk-like viruses: first molecular traceback to deli sandwiches contaminated during preparation. *The Journal of Infectious Diseases*, *181*(4), 1467–70. doi:10.1086/315365

de Graaf, M, van Beek, J., Vennema, H., Podkolzin, A., Hewitt, J., Bucardo, F., et al. (2015). Emergence of a novel GII.17 norovirus – End of the GII.4 era? *Eurosurveillance*, *20*(26), 21178. doi:10.2807/1560-7917.ES2015.20.26.21178

de Graaf, Miranda, van Beek, J., & Koopmans, M. P. G. (2016). Human norovirus transmission and evolution in a changing world. *Nature Reviews. Microbiology*, *14*(7), 421–33. doi:10.1038/nrmicro.2016.48

de Roda Husman, A. M., Lodder, W. J., Rutjes, S. A., Schijven, J. F., & Teunis, P. F. M. (2009). Long-term inactivation study of three enteroviruses in artificial surface and groundwaters, using PCR and cell culture. *Applied and Environmental Microbiology*, *75*(4), 1050–1057. doi:10.1128/AEM.01750-08

de Wit, M. A. S., Widdowson, M. A., Vennema, H., de Bruin, E., Fernandes, T., & Koopmans, M. (2007). Large outbreak of norovirus: the baker who should have known better. *The Journal of Infection*, *55*(2), 188–93. doi:10.1016/j.jinf.2007.04.005

Demina, T. V, Dzhioev, Y. P., Verkhozina, M. M., Kozlova, I. V, Tkachev, S. E., Plyusnin, A., et al. (2010). Genotyping and characterization of the geographical distribution of tick-borne encephalitis virus variants with a set of molecular probes. *Journal of Medical Virology*, *82*(6), 965–76. doi:10.1002/jmv.21765

Dentinger, C. M., Bower, W. A., Nainan, O. V., Cotter, S. M., Myers, G., Dubusky, L. M., et al. (2001). An outbreak of Hepatitis A associated with green onions. *The Journal of Infectious Diseases*, *183*(8), 1273–1276. doi:10.1086/319688

Di Bartolo, I., Diez-Valcarce, M., Vasickova, P., Kralik, P., Hernandez, M., Angeloni, G., et al. (2012). Hepatitis E virus in pork production chain in Czech Republic, Italy, and Spain, 2010. *Emerging Infectious Diseases*, *18*(8), 1282–9. doi:10.3201/eid1808.111783

Di Martino, B., Di Profio, F., Ceci, C., Di Felice, E., & Marsilio, F. (2013). Molecular detection of Aichi virus in raw sewage in Italy. *Archives of Virology*, *158*(9), 2001–5. doi:10.1007/s00705-013-1694-7

Diez-Valcarce, M., Kokkinos, P., Söderberg, K., Bouwknegt, M., Willems, K., de Roda-Husman, A. M., et al. (2012). Occurrence of human enteric viruses in commercial mussels at retail level in three European countries. *Food and Environmental Virology*, *4*(2), 73–80. doi:10.1007/s12560-012-9078-9

Disease Outbreak Control Division. (2017). Hepatitis A outbreak 2016:Working together to control infectious diseases. https://health.hawaii.gov/docd/hepatitis-a-outbreak-2016/. Accessed 10 February 2020

Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, C. for D. C. and P. (2011). *Updated norovirus outbreak management and disease prevention guidelines. MMWR. Recommendations and reports : Morbidity and Mortality Weekly Report.* (Vol. 60). http://www.ncbi.nlm.nih.gov/pubmed/21368741. Accessed 9 February 2020

Dobler, G. (2010). Zoonotic tick-borne flaviviruses. *Veterinary Microbiology*, *140*(3–4), 221–8. doi:10.1016/j.vetmic.2009.08.024

Dolin, R., Blacklow, N. R., DuPont, H., Buscho, R. F., Wyatt, R. G., Kasel, J. A., et al. (1972). Biological properties of Norwalk agent of acute infectious nonbacterial gastroenteritis. *Proceedings of the Society for Experimental Biology and Medicine. Society for Experimental Biology and Medicine (New York, N.Y.)*, *140*(2), 578–83. doi:10.3181/00379727-140-36508

Dolin, R., Blacklow, N. R., DuPont, H., Formal, S., Buscho, R. F., Kasel, J. A., et al. (1971). Transmission of acute infectious nonbacterial gastroenteritis to volunteers by oral administration of stool filtrates. *The Journal of Infectious Diseases*, *123*(3), 307–12. doi:10.1093/infdis/123.3.307

Donnan, E. J., Fielding, J. E., Gregory, J. E., Lalor, K., Rowe, S., Goldsmith, P., et al. (2012). A multistate outbreak of Hepatitis A associated with semidried tomatoes in Australia, 2009. *Clinical Infectious Diseases*, *54*(6), 775–781. doi:10.1093/cid/cir949

Dorko, E., Hockicko, J., Rimárová, K., Bušová, A., Popaďák, P., Popaďáková, J., & Schréter, I. (2018). Milk outbreaks of tick-borne encephalitis in Slovakia, 2012-2016. *Central European Journal of Public Health*, *26 Suppl*(Supplement), S47–S50. doi:10.21101/cejph.a5272

Doudier, B., Verrot, D., Serratrice, C., Poucel, C., Auguste, R., & Colson, P. (2015). Fatal outcome of autochthonous hepatitis E in a patient with B cell lymphoma in Southeastern France. *Journal of Clinical Microbiology*, *53*(1), 339–42. doi:10.1128/JCM.02009-14

Drobeniuc, J., Favorov, M. O., Shapiro, C. N., Bell, B. P., Mast, E. E., Dadu, A., et al. (2001). Hepatitis E virus antibody prevalence among persons who work with swine. *The Journal of Infectious Diseases*, *184*(12), 1594–7. doi:10.1086/324566

Duizer, E., Bijkerk, P., Rockx, B., De Groot, A., Twisk, F., & Koopmans, M. (2004). Inactivation of caliciviruses. *Applied and Environmental Microbiology*, *70*(8), 4538–43. doi:10.1128/AEM.70.8.4538-4543.2004

Duizer, Erwin, Schwab, K. J., Neill, F. H., Atmar, R. L., Koopmans, M. P. G., & Estes, M. K. (2004). Laboratory efforts to cultivate noroviruses. *Journal of General Virology*, *85*(1), 79–87. doi:10.1099/vir.0.19478-0

Dumpis, U., Crook, D., & Oksi, J. (1999). Tick-Borne Encephalitis. *Clinical Infectious Diseases*, *28*(4), 882–890. doi:10.1086/515195

ECDC. (2016). *Hepatitis A virus in the EU/EEA, 1975–2014*. *ECDC*. Stockholm: ECDC. doi:10.2900/60930

EFSA Panel on Biological Hazards (BIOHAZ). (2011). Scientific opinion on an update on the present knowledge on the occurrence and control of foodborne viruses. *EFSA Journal*, *9*(7), 2190. doi:10.2903/j.efsa.2011.2190

EFSA Panel on Biological Hazards (BIOHAZ). (2012). Scientific opinion on Norovirus (NoV) in oysters: methods, limits and control options. *EFSA Journal*, *10*(1), 2500. doi:10.2903/j.efsa.2012.2500

EFSA Panel on Biological Hazards (BIOHAZ). (2014a). *Tracing of food items in connection to the multinational hepatitis A virus outbreak in Europe*. *EFSA Journal* (Vol. 12). doi:10.2903/j.efsa.2014.3821

EFSA Panel on Biological Hazards (BIOHAZ). (2014b). Scientific opinion on the risk posed by pathogens in food of non-animal origin. Part 2 (*Salmonella* and Norovirus in berries). *EFSA Journal*, *12*(6), 3706. doi:10.2903/j.efsa.2014.3706

EFSA Panel on Biological Hazards (BIOHAZ), Ricci, A., Allende, A., Bolton, D., Chemaly, M., Davies, R., et al. (2017). *Public health risks associated with hepatitis E virus (HEV) as a food-borne pathogen*. *EFSA Journal* (Vol. 15). John Wiley & Sons, Ltd. doi:10.2903/j.efsa.2017.4886

Emerson, S. U., & Purcell, R. H. (2013). Hepatitis E Virus. In D. M. Knipe & P. Howley (Eds.), *Fields virology: Sixth edition* (6th ed., pp. 2242–2258). Wolters Kluwer Health Adis (ESP).

Enkirch, T., Eriksson, R., Persson, S., Schmid, D., Aberle, S. W., Löf, E., et al. (2018). Hepatitis A outbreak linked to imported frozen strawberries by sequencing, Sweden and Austria, June to September 2018. *Eurosurveillance*, *23*(41). doi:10.2807/1560-7917.ES.2018.23.41.1800528

Enriquez, C. (1995). Survival of the enteric adenoviruses 40 and 41 in tap, sea, and waste water. *Water Research*, *29*(11), 2548–2553. doi:10.1016/0043-1354(95)00070-2

Esposito, S., Ascolese, B., Senatore, L., & Codecà, C. (2014). Pediatric norovirus infection. *European Journal of*

Clinical Microbiology & Infectious Diseases, *33*(3), 285–90. doi:10.1007/s10096-013-1967-9

Estes, M. K., & Greenberg, H. B. (2013). Rotaviruses. In D. M. Knipe & P. Howley (Eds.), *Fields virology: Sixth edition* (6th ed.). Wolters Kluwer Health Adis (ESP).

Estes, M. K., Prasad, B. V., & Atmar, R. L. (2006). Noroviruses everywhere: has something changed? *Current Opinion in Infectious Diseases*, *19*(5), 467–474. doi:10.1097/01.qco.0000244053.69253.3d

Ethelberg, S., Lisby, M., Bottiger, B., Schultz, A. C., Villif, A., Jensen, T., et al. (2010). Outbreaks of gastroenteritis linked to lettuce, Denmark, January 2010. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *15*(6), 19484. doi:10.2807/ese.15.06.19484-en

Ettayebi, K., Crawford, S. E., Murakami, K., Broughman, J. R., Karandikar, U., Tenge, V. R., et al. (2016). Replication of human noroviruses in stem cell-derived human enteroids. *Science*, *5211*(August). doi:10.1126/science.aaf5211

EU. Community Guide to the Principles of Good Practice for the Microbiological Classification and Monitoring of Bivalve Mollusc Production and Relaying Areas with regard to Regulation 854/2004 (2017).

European Communities. (2004). Regulation (EC) No 854/2004 of the European Parliament and of the Council of 29 April 2004 laying down specific rules for the organisation of official controls on products of animal origin intended for human consumption. *Off. J. Eur. Communities L 226*.

European Communities. (2005). Commission Regulation (EC) No 2073/2005 on microbiological criteria for foodstuffs. *Off. J. Eur. Communities L338*.

Evans, M. R., Meldrum, R., Lane, W., Gardner, D., Ribeiro, C. D., Gallimore, C. I., & Westmoreland, D. (2002). An outbreak of viral gastroenteritis following environmental contamination at a concert hall. *Epidemiology and infection*, *129*(2), 355–60. doi:10.1017/s0950268802007446

Fankhauser, R. L., Monroe, S. S., Noel, J. S., Humphrey, C. D., Bresee, J. S., Parashar, U. D., et al. (2002). Epidemiologic and molecular trends of "Norwalk-like Viruses" associated with outbreaks of gastroenteritis in the United States. *The Journal of Infectious Diseases*, *186*(1), 1–7. doi:10.1086/341085

FAO/WHO. (2008a). *Microbiological hazards in fresh leafy vegetables and herbs: Meeting Report. Microbiological Risk Assessment Series No. 14.* Rome. https://www.who.int/foodsafety/publications/micro/Viruses_in_food_MRA.pdf

FAO/WHO. (2008b). *Microbiological hazards in fresh leafy vegetables and herbs: Meeting Report. Microbiological Risk Assessment Series No. 14.* Rome. http://www.who.int/foodsafety/publications/micro/Viruses_in_food_MRA.pdf. Accessed 20 July 2017

Farkas, T., Zhong, W. M., Jing, Y., Huang, P. W., Espinosa, S. M., Martinez, N., et al. (2004). Genetic diversity among sapoviruses. *Archives of Virology*, *149*(7), 1309–23. doi:10.1007/s00705-004-0296-9

Feagins, A. R., Opriessnig, T., Guenette, D. K., Halbur, P. G., & Meng, X.-J. (2007). Detection and characterization of infectious Hepatitis E virus from commercial pig livers sold in local grocery stores in the USA. *The Journal of General Virology*, *88*(Pt 3), 912–7. doi:10.1099/vir.0.82613-0

Fino, V. R., & Kniel, K. E. (2008). UV light inactivation of Hepatitis A virus, Aichi virus, and feline Calicivirus on strawberries, green onions, and lettuce. *Journal of Food Protection*, *71*(5), 908–913. https://jfoodprotection-org.proxy.findit.dtu.dk/doi/pdf/10.4315/0362-028X-71.5.908. Accessed 18 July 2019

Fiore, A. E. (2004). Hepatitis A transmitted by food. *Clinical Infectious Diseases*, *38*(5), 705–715. doi:10.1086/381671

Fraisse, A., Temmam, S., Deboosere, N., Guillier, L., Delobel, A., Maris, P., et al. (2011). Comparison of chlorine and peroxyacetic-based disinfectant to inactivate Feline calicivirus, Murine norovirus and Hepatitis A virus on lettuce. *International Journal of Food Microbiology*, *151*(1), 98–104. doi:10.1016/j.ijfoodmicro.2011.08.011

Franck, K. T., Lisby, M., Fonager, J., Schultz, A. C., Böttiger, B., Villif, A., et al. (2015). Sources of Calicivirus contamination in foodborne outbreaks in Denmark, 2005-2011--the role of the asymptomatic food handler. *The Journal of Infectious Diseases*, *211*(4), 563–70. doi:10.1093/infdis/jiu479

Free, R. J., Buss, B. F., Koirala, S., Ulses, M., Carlson, A., Loeck, B., & Safranek, T. (2019). Successive Norovirus

outbreaks at an event center - Nebraska, October-November, 2017. *MMWR. Morbidity and mortality weekly report*, *68*(28), 627–630. doi:10.15585/mmwr.mm6828a2

Fretz, R., Svoboda, P., Lüthi, T. M., Tanner, M., & Baumgartner, A. (2005). Outbreaks of gastroenteritis due to infections with Norovirus in Switzerland, 2001–2003. *Epidemiology and Infection*, *133*(3), 429–437. doi:10.1017/S0950268804003619

Fu, J., Shi, C., Xu, C., Lin, Q., Zhang, J., Yi, Q., et al. (2017). Outbreaks of acute gastroenteritis associated with a re-emerging GII.P16-GII.2 norovirus in the spring of 2017 in Jiangsu, China. *PLOS ONE*, *12*(12), e0186090. doi:10.1371/journal.pone.0186090

Fujioka, R. S., & Yoneyama, B. S. (2002). Sunlight inactivation of human enteric viruses and fecal bacteria. *Water Science and Technology : a Journal of the International Association on Water Pollution Research*, *46*(11–12), 291–5. http://www.ncbi.nlm.nih.gov/pubmed/12523768. Accessed 9 February 2020

Fusco, G., Di Bartolo, I., Cioffi, B., Ianiro, G., Palermo, P., Monini, M., & Amoroso, M. G. (2017). Prevalence of foodborne viruses in mussels in Southern Italy. *Food and Environmental Virology*, *9*(2), 187–194. doi:10.1007/s12560-016-9277-x

Gallot, C., Grout, L., Roque-Afonso, A.-M., Couturier, E., Carrillo-Santisteve, P., Pouey, J., et al. (2011). Hepatitis A associated with semidried tomatoes, France, 2010. *Emerging Infectious Diseases*, *17*(3), 566–567. doi:10.3201/eid1703.101479

Garson, J. A., Ferns, R. B., Grant, P. R., Ijaz, S., Nastouli, E., Szypulska, R., & Tedder, R. S. (2012). Minor groove binder modification of widely used TaqMan probe for hepatitis E virus reduces risk of false negative real-time PCR results. *Journal of Virological Methods*, *186*(1–2), 157–60. doi:10.1016/j.jviromet.2012.07.027

Girard, M., Mattison, K., Fliss, I., & Jean, J. (2016). Efficacy of oxidizing disinfectants at inactivating murine norovirus on ready-to-eat foods. *International Journal of Food Microbiology*, *219*, 7–11. doi:10.1016/j.ijfoodmicro.2015.11.015

GIRARD, M., NGAZOA, S., MATTISON, K., & JEAN, J. (2010). Attachment of noroviruses to stainless steel and their inactivation, using household disinfectants. *Journal of Food Protection*, *73*(2), 400–404. doi:10.4315/0362-028X-73.2.400

Glass, R. I., Parashar, U. D., & Estes, M. K. (2009). Norovirus gastroenteritis. *New England Journal of Medicine*, *361*(18), 1776–1785. doi:10.1056/NEJMra0804575

Glikson, M., Galun, E., Oren, R., Tur-Kaspa, R., & Shouval, D. (1992). Relapsing Hepatitis A review of 14 cases and literature survey. *Medicine*, *71*(1), 14–23.

Godoy, P., Izcara, J., Bartolomé, R., Bach, P., Escobar, A., Pal, M., et al. (2005). Outbreak of food-borne Norovirus associated with the consumption of sandwiches. *Medicina Clinica*, *124*(5), 161–4. doi:10.1157/13071479

Goller, J. L., Dimitriadis, A., Tan, A., Kelly, H., & Marshall, J. A. (2004). Long-term features of norovirus gastroenteritis in the elderly. *Journal of Hospital Infection*, *58*(4), 286–291. doi:10.1016/j.jhin.2004.07.001

Green, K. Y. (2013). Caliciviridae: The Noroviruses. In D. M. Knipe & P. M. Howley (Eds.), *Fields virology: Sixth edition* (6th ed., Vol. 1, pp. 583–604). Wolters Kluwer Health Adis (ESP). http://findit.dtu.dk/en/catalog/2306146779. Accessed 24 July 2017

Green, K. Y., Belliot, G., Taylor, J. L., Valdesuso, J., Lew, J. F., Kapikian, A. Z., & Lin, F.-Y. C. (2002). A predominant role for Norwalk-like viruses as agents of epidemic gastroenteritis in Maryland nursing homes for the elderly. *The Journal of Infectious Diseases*, *185*(2), 133–46. doi:10.1086/338365

Greer, A. L., Drews, S. J., & Fisman, D. N. (2009). Why "winter" vomiting disease? Seasonality, hydrology, and Norovirus epidemiology in Toronto, Canada. *EcoHealth*, *6*(2), 192–9. doi:10.1007/s10393-009-0247-8

Gresíková-kohútová, M. (1959). *Effect of pH on Infectivity of the Tick-Borne Encephalitis Virus. Acta Virologica* (Vol. 3). Academia, Pub. House of the Czechoslovak Academy of Sciences. https://www.cabdirect.org/cabdirect/abstract/19592704748. Accessed 9 February 2020

Gresíková, M., Havranek, I., & Görner, F. (1961). The effect of pasteurisation on the infectivity of tick-borne encephalitis virus. *Acta Virologica*, *5*(1), 31–6.

Griffin, D. W., Donaldson, K. A., Paul, J. H., & Rose, J. B. (2003). Pathogenic human viruses in coastal waters. *Clinical Microbiology Reviews*, *16*(1), 129–43. doi:10.1128/cmr.16.1.129-143.2003

Guillois-Bécel, Y., Couturier, E., Le Saux, J. C., Roque-Afonso, A. M., Le Guyader, F. S., Le Goas, A., et al. (2009). An oyster-associated hepatitis A outbreak in France in 2007. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *14*(10). http://www.ncbi.nlm.nih.gov/pubmed/19317985. Accessed 28 August 2019

Guillois, Y., Abravanel, F., Miura, T., Pavio, N., Vaillant, V., Lhomme, S., et al. (2016). High Proportion of asymptomatic infections in an outbreak of Hepatitis E associated with a spit-roasted piglet, France, 2013. *Clinical Infectious Diseases*, *62*(3), 351–357. doi:10.1093/cid/civ862

Hagbom, M., Istrate, C., Engblom, D., Karlsson, T., Rodriguez-Diaz, J., Buesa, J., et al. (2011). Rotavirus stimulates release of serotonin (5-HT) from human enterochromaffin cells and activates brain structures involved in nausea and vomiting. *PLoS Pathogens*, *7*(7), e1002115. doi:10.1371/journal.ppat.1002115

Hakim, M. S., Wang, W., Bramer, W. M., Geng, J., Huang, F., de Man, R. A., et al. (2017). The global burden of hepatitis E outbreaks: a systematic review. *Liver International : official journal of the International Association for the Study of the Liver*, *37*(1), 19–31. doi:10.1111/liv.13237

Hall, A. J., Eisenbart, V. G., Etingüe, A. L., Gould, L. H., Lopman, B. A., & Parashar, U. D. (2012). Epidemiology of foodborne norovirus outbreaks, United States, 2001-2008. *Emerging Infectious Diseases*, *18*(10), 1566–73. doi:10.3201/eid1810.120833

Hall, A. J., Lopman, B. A., Payne, D. C., Patel, M. M., Gastañaduy, P. A., Vinjé, J., & Parashar, U. D. (2013). Norovirus disease in the United States. *Emerging Infectious Diseases*, *19*(8), 1198–205. doi:10.3201/eid1908.130465

Hall, A. J., Wikswo, M. E., Manikonda, K., Roberts, V. A., Yoder, J. S., & Gould, L. H. (2013). Acute gastroenteritis surveillance through the national outbreak reporting system, United States. *Emerging Infectious Diseases*, *19*(8), 1305–1309. doi:10.3201/eid1908.130482

Hansman, G. S., Ishida, S., Yoshizumi, S., Miyoshi, M., Ikeda, T., Oka, T., & Takeda, N. (2007). Recombinant sapovirus gastroenteritis, Japan. *Emerging Infectious Diseases*, *13*(5), 786–8. doi:10.3201/eid1305.070049

Hansman, G. S., Oka, T., Katayama, K., & Takeda, N. (2007). Human sapoviruses: genetic diversity, recombination, and classification. *Reviews in Medical Virology*, *17*(2), 133–41. doi:10.1002/rmv.533

Hansman, G. S., Oka, T., Li, T.-C., Nishio, O., Noda, M., & Takeda, N. (2008). Detection of human enteric viruses in Japanese clams. *Journal of Food Protection*, *71*(8), 1689–95. doi:10.4315/0362-028x-71.8.1689

Hansman, G. S., Oka, T., Okamoto, R., Nishida, T., Toda, S., Noda, M., et al. (2007). Human sapovirus in clams, Japan. *Emerging Infectious Diseases*, *13*(4), 620–2. doi:10.3201/eid1304.061390

Hansman, G. S., Saito, H., Shibata, C., Ishizuka, S., Oseto, M., Oka, T., & Takeda, N. (2007). Outbreak of gastroenteritis due to sapovirus. *Journal of Clinical Microbiology*, *45*(4), 1347–9. doi:10.1128/JCM.01854-06

Hansson, M. E. A., Orvell, C., Engman, M.-L., Wide, K., Lindquist, L., Lidefelt, K.-J., & Sundin, M. (2011). Tick-borne encephalitis in childhood: rare or missed? *The Pediatric Infectious Disease Journal*, *30*(4), 355–7. doi:10.1097/INF.0b013e3181fe3b5a

Haramoto, E., & Kitajima, M. (2017). Quantification and genotyping of Aichi virus 1 in water samples in the Kathmandu Valley, Nepal. *Food and Environmental Virology*, *9*(3), 350–353. doi:10.1007/s12560-017-9283-7

Hardstaff, J. L., Clough, H. E., Lutje, V., McIntyre, K. M., Harris, J. P., Garner, P., & O'Brien, S. J. (2018). Foodborne and food-handler Norovirus outbreaks: A systematic review. *Foodborne Pathogens and Disease*, *15*(10), 589–597. doi:10.1089/fpd.2018.2452

Harrach, B., Benkö, M., Both, G. W., Brown, M., Davison, A. J., Echavarría, M., et al. (2012). Family Adenoviridae. In A. M. Q. King, M. J. Adams, E. B. Carstens, & E. J. Lefkowitz (Eds.), *Virus Taxonomy : Classification and Nomenclature of Viruses* (9th ed., pp. 125–141). Elsevier.

Harris, J. P., Edmunds, W. J., Pebody, R., Brown, D. W., & Lopman, B. A. (2008). Deaths from Norovirus among the elderly, England and Wales. *Emerging Infectious Diseases*, *14*(10), 1546–1552. doi:10.3201/eid1410.080188

Hasing, M. E., Lee, B. E., Preiksaitis, J. K., Tellier, R., Honish, L., Senthilselvan, A., & Pang, X. L. (2013). Emergence of a new norovirus GII.4 variant and changes in the historical biennial pattern of norovirus outbreak activity

in Alberta, Canada, from 2008 to 2013. *Journal of Clinical Microbiology*, *51*(7), 2204–11. doi:10.1128/JCM.00663-13

Havelaar, A. H., Kirk, M. D., Torgerson, P. R., Gibb, H. J., Hald, T., Lake, R. J., et al. (2015). World Health Organization global estimates and regional comparisons of the burden of foodborne disease in 2010. *PLOS Medicine*, *12*(12), e1001923. doi:10.1371/journal.pmed.1001923

Hellenbrand, W., Kreusch, T., Böhmer, M. M., Wagner-Wiening, C., Dobler, G., Wichmann, O., & Altmann, D. (2019). Epidemiology of Tick-Borne Encephalitis (TBE) in Germany, 2001–2018. *Pathogens (Basel, Switzerland)*, *8*(2). doi:10.3390/pathogens8020042

Hellmér, M. (2018). *Viral Metagenomics to Assess the Microbial Quality of Reused Wastewater*. Technical University of Denmark, Kgs. Lyngby. Retrieved from https://orbit.dtu.dk/en/publications/viral-metagenomics-to-assess-the-microbial-quality-of-reused-wast

Herremans, M., Bakker, J., Duizer, E., Vennema, H., & Koopmans, M. P. G. (2007). Use of serological assays for diagnosis of hepatitis E virus genotype 1 and 3 infections in a setting of low endemicity. *Clinical and Vaccine Immunology : CVI*, *14*(5), 562–8. doi:10.1128/CVI.00231-06

Hewitt, J., Bell, D., Simmons, G. C., Rivera-Aban, M., Wolf, S., & Greening, G. E. (2007). Gastroenteritis outbreak caused by waterborne norovirus at a New Zealand ski resort. *Applied and Environmental Microbiology*, *73*(24), 7853–7. doi:10.1128/AEM.00718-07

Hirneisen, K. A., Markland, S. M., & Kniel, K. E. (2011). Ozone inactivation of norovirus surrogates on fresh produce. *Journal of Food Protection*, *74*(5), 836–839. doi:10.4315/0362-028X.JFP-10-438

Hirneisen, Kirsten A, Black, E. P., Cascarino, J. L., Fino, V. R., Hoover, D. G., & Kniel, K. E. (2010). Viral inactivation in foods: A review of traditional and novel food-processing technologies. *Comprehensive Reviews in Food Science and Food Safety*, *9*(1), 3–20. doi:10.1111/j.1541-4337.2009.00092.x

Hollinger, F. B., & Martin, A. (2013). Hepatitis A Virus. In D. M. Knipe & P. Howley (Eds.), *Fields Virology: Sixth Edition* (6th ed., pp. 551–577). Wolters Kluwer Health Adis (ESP).

Holm, D. K., Moessner, B. K., Engle, R. E., Zaaijer, H. L., Georgsen, J., Purcell, R. H., & Christensen, P. B. (2015). Declining prevalence of hepatitis E antibodies among Danish blood donors. *Transfusion*, *55*(7), 1662–1667. doi:10.1111/trf.13028

Holzmann, H., Aberle, S. W., Stiasny, K., Werner, P., Mischak, A., Zainer, B., et al. (2009). Tick-borne Encephalitis from eating goat cheese in a mountain Region of Austria. *Emerging Infectious Diseases*, *15*(10), 1671–1673. doi:10.3201/eid1510.090743

Hoofnagle, J. H., Nelson, K. E., & Purcell, R. H. (2012). Hepatitis E. *New England Journal of Medicine*, *367*(13), 1237–1244. doi:10.1056/NEJMra1204512

Hubálek, Z., & Rudolf, I. (2012). Tick-borne viruses in Europe. *Parasitology Research*, *111*(1), 9–36. doi:10.1007/s00436-012-2910-1

Hudopisk, N., Korva, M., Janet, E., Simetinger, M., Grgič-Vitek, M., Gubenšek, J., et al. (2013). Tick-borne Encephalitis associated with consumption of raw goat milk, Slovenia, 2012. *Emerging Infectious Diseases*, *19*(5). doi:10.3201/eid1905.121442

Hurst, C. J., & Gerba, C. P. (1980). Stability of simian rotavirus in fresh and estuarine water. *Applied and Environmental Microbiology*, *39*(1), 1–5. http://www.ncbi.nlm.nih.gov/pubmed/6243899. Accessed 9 February 2020

Huynen, P., Mauroy, A., Martin, C., Savadogo, L. G. B., Boreux, R., Thiry, E., et al. (2013). Molecular epidemiology of norovirus infections in symptomatic and asymptomatic children from Bobo Dioulasso, Burkina Faso. *Journal of Clinical Virology : the official publication of the Pan American Society for Clinical Virology*, *58*(3), 515–21. doi:10.1016/j.jcv.2013.08.013

International Dairy Foods Association. (2016). Pasteurization | International Dairy Foods Association. https://www.idfa.org/news-views/media-kits/milk/pasteurization. Accessed 9 February 2020

Iorio, N., & John, S. (2018). *Hepatitis A*. *StatPearls*. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/pubmed/29083664. Accessed 9 May 2018

ISO. (2017). ISO 15216-1:2017. Microbiology of the food chain — Horizontal method for determination of

hepatitis A virus and norovirus using real-time RT-PCR — Part 1: Method for quantification. https://www.iso.org/obp/ui/#iso:std:iso:15216:-1:ed-1:v1:en. Accessed 7 July 2019

Iturriza-Gómara, M., Kang, G., & Gray, J. (2004). Rotavirus genotyping: keeping up with an evolving population of human rotaviruses. *Journal of Clinical Virology*, *31*(4), 259–265. doi:10.1016/j.jcv.2004.04.009

Jacobsen, K. H. (2010). The global prevalence of hepatitis A virus infection and susceptibility : a systematic review. *World Health Organization*, *WHO/IVB/10*. https://apps.who.int/iris/handle/10665/70513

Jacobsen, K. H., & Wiersma, S. T. (2010). Hepatitis A virus seroprevalence by age and world region, 1990 and 2005. *Vaccine*, *28*(41), 6653–6657. doi:10.1016/j.vaccine.2010.08.037

Jean, J., Vachon, J. F., Moroni, O., Darveau, A., Kukavica-Ibrulj, I., & Fliss, I. (2003). Effectiveness of commercial disinfectants for inactivating hepatitis A virus on agri-food surfaces. *Journal of Food Protection*, *66*(1), 115–9. https://jfoodprotection.org/doi/pdf/10.4315/0362-028X-66.1.115. Accessed 15 July 2019

Jeong, S.-H., & Lee, H.-S. (2010). Hepatitis A: Clinical manifestations and management. *Intervirology*, *53*(1), 15–19. doi:10.1159/000252779

Jimenez, L., & Chiang, M. (2006). Virucidal activity of a quaternary ammonium compound disinfectant against feline calicivirus: A surrogate for norovirus. *American Journal of Infection Control*, *34*(5), 269–273. doi:10.1016/j.ajic.2005.11.009

Johansson, P. J. H., Bergentoft, K., Larsson, P. A., Magnusson, G., Widell, A., Thorhagen, M., & Hedlund, K.-O. (2005). A nosocomial sapovirus-associated outbreak of gastroenteritis in adults. *Scandinavian Journal of Infectious Diseases*, *37*(3), 200–4. doi:10.1080/00365540410020974

John, D. E., & Rose, J. B. (2005). Review of factors affecting microbial survival in groundwater. *Environmental Science & Technology*, *39*(19), 7345–7356. doi:10.1021/es047995w

Johne, R., Trojnar, E., Filter, M., & Hofmann, J. (2016). Thermal stability of Hepatitis E virus as estimated by a cell culture Method. *Applied and Environmental Microbiology*, *82*(14), 4225–4231. doi:10.1128/AEM.00951-16

Johnsen, C. K., Midgley, S., & Böttiger, B. (2009). Genetic diversity of sapovirus infections in Danish children 2005-2007. *Journal of Clinical Virology : the official publication of the Pan American Society for Clinical Virology*, *46*(3), 265–9. doi:10.1016/j.jcv.2009.07.008

Johnson, C., Hargest, V., Cortez, V., Meliopoulos, V. A., & Schultz-Cherry, S. (2017). Astrovirus pathogenesis. *Viruses*, *9*(1). doi:10.3390/v9010022

Jones, M. K., Watanabe, M., Zhu, S., Graves, C. L., Keyes, L. R., Grau, K. R., et al. (2014). Enteric bacteria promote human and mouse norovirus infection of B cells. *Science*, *346*(6210), 755–9. doi:10.1126/science.1257147

Jothikumar, N., Cromeans, T. L., Robertson, B. H., Meng, X. J., & Hill, V. R. (2006). A broadly reactive one-step real-time RT-PCR assay for rapid and sensitive detection of hepatitis E virus. *Journal of Virological Methods*, *131*(1), 65–71. doi:10.1016/j.jviromet.2005.07.004

Kagning Tsinda, E., Malasao, R., Furuse, Y., Gilman, R. H., Liu, X., Apaza, S., et al. (2017). Complete coding genome sequences of uncommon GII.8 Sapovirus strains identified in diarrhea samples collected from Peruvian children. *Genome Announcements*, *5*(43). doi:10.1128/genomeA.01137-17

Kaiser, R. (2016). Frühsommermeningoenzephalitis. *Der Nervenarzt*, *87*(6), 667–680. doi:10.1007/s00115-016-0134-9

Kamar, N., Bendall, R., Legrand-Abravanel, F., Xia, N.-S., Ijaz, S., Izopet, J., & Dalton, H. R. (2012). Hepatitis E. *Lancet (London, England)*, *379*(9835), 2477–2488. doi:10.1016/S0140-6736(11)61849-7

Kang, G., Kelkar, S. D., Chitambar, S. D., Ray, P., & Naik, T. (2005). Epidemiological profile of rotaviral infection in India: Challenges for the 21st Century. *The Journal of Infectious Diseases*, *192*(s1), S120–S126. doi:10.1086/431496

Kaplan, J. E., Feldman, R., Campbell, D. S., Lookabaugh, C., & Gary, G. W. (1982). The frequency of a Norwalk-like pattern of illness in outbreaks of acute gastroenteritis. *American Journal of Public Health*, *72*(12), 1329–32. doi:10.2105/ajph.72.12.1329

Karst, S. M., & Baric, R. S. (2015). What is the reservoir of emergent human norovirus strains? *Journal of Virology*, *89*(11), 5756–9. doi:10.1128/JVI.03063-14

Karst, S. M., Wobus, C. E., Goodfellow, I. G., Green, K. Y., & Virgin, H. W. (2014). Advances in norovirus biology. *Cell Host & Microbe*, *15*(6), 668–80. doi:10.1016/j.chom.2014.05.015

Kaufman, S. S., Green, K. Y., & Korba, B. E. (2014). Treatment of norovirus infections: moving antivirals from the bench to the bedside. *Antiviral Research*, *105*, 80–91. doi:10.1016/j.antiviral.2014.02.012

Kendall, M. E., Mody, R. K., Mahon, B. E., Doyle, M. P., Herman, K. M., & Tauxe, R. V. (2013). Emergence of salsa and guacamole as frequent vehicles of foodborne disease outbreaks in the United States, 1973-2008. *Foodborne Pathogens and Disease*, *10*(4), 316–22. doi:10.1089/fpd.2012.1328

Kerbo, N., Donchenko, I., Kutsar, K., & Vasilenko, V. (2005). Tickborne encephalitis outbreak in Estonia linked to raw goat milk, May-June 2005. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *10*(6), E050623.2. doi:10.2807/esw.10.25.02730-en

Keswick, B. H., Satterwhite, T. K., Johnson, P. C., DuPont, H. L., Secor, S. L., Bitsura, J. A., et al. (1985). Inactivation of Norwalk virus in drinking water by chlorine. *Applied and Environmental microbiology*, *50*(2), 261–4. http://www.ncbi.nlm.nih.gov/pubmed/2996421. Accessed 9 February 2020

Khadre, M. A., & Yousef, A. E. (2002). Susceptibility of human rotavirus to ozone, high pressure, and pulsed electric field. *Journal of Food Protection*, *65*(9), 1441–1446. doi:10.4315/0362-028X-65.9.1441

Khamrin, P., Maneekarn, N., Peerakome, S., Tonusin, S., Malasao, R., Mizuguchi, M., et al. (2007). Genetic diversity of noroviruses and sapoviruses in children hospitalized with acute gastroenteritis in Chiang Mai, Thailand. *Journal of Medical Virology*, *79*(12), 1921–1926. doi:10.1002/jmv.21004

Khan, R. R., Lawson, A. D., Minnich, L. L., Martin, K., Nasir, A., Emmett, M. K., et al. (2009). Gastrointestinal norovirus infection associated with exacerbation of inflammatory bowel disease. *Journal of Pediatric Gastroenterology and Nutrition*, *48*(3), 328–333. doi:10.1097/MPG.0b013e31818255cc

Khuroo, M. S., Kamili, S., Dar, M. Y., Moecklii, R., & Jameel, S. (1993). Hepatitis E and long-term antibody status. *Lancet (London, England)*, *341*(8856), 1355. http://www.ncbi.nlm.nih.gov/pubmed/8098491. Accessed 27 September 2019

Kitajima, M., & Gerba, C. P. (2015). Aichi virus 1: environmental occurrence and behavior. *Pathogens (Basel, Switzerland)*, *4*(2), 256–68. doi:10.3390/pathogens4020256

Kokkinos, P., Kozyra, I., Lazic, S., Bouwknegt, M., Rutjes, S., Willems, K., et al. (2012). Harmonised investigation of the occurrence of human enteric viruses in the leafy green vegetable supply chain in three European countries. *Food and Environmental Virology*, *4*(4), 179–91. doi:10.1007/s12560-012-9087-8

Koo, H. L., Ajami, N., Atmar, R. L., & DuPont, H. L. (2010). Noroviruses: The leading cause of gastroenteritis worldwide. *Discovery Medicine*, *10*(50), 61–70. http://www.ncbi.nlm.nih.gov/pubmed/20670600. Accessed 8 February 2020

Koopmans, M., & Duizer, E. (2004). Foodborne viruses: an emerging problem. *International Journal of Food Microbiology*, *90*(1), 23–41. doi:10.1016/S0168-1605(03)00169-7

Krajden, M., Brown, M., Petrasek, A., & Middleton, P. J. (1990). Clinical features of adenovirus enteritis: a review of 127 cases. *The Pediatric Infectious Disease Journal*, *9*(9), 636–41. http://www.ncbi.nlm.nih.gov/pubmed/2235188. Accessed 22 December 2019

Kríz, B., Benes, C., & Daniel, M. (2009). Alimentary transmission of tick-borne encephalitis in the Czech Republic (1997-2008). *Epidemiologie, mikrobiologie, imunologie : casopis Spolecnosti pro epidemiologii a mikrobiologii Ceske lekarske spolecnosti J.E. Purkyne*, *58*(2), 98–103. https://findit.dtu.dk/en/catalog/2269734809. Accessed 27 August 2019

Krog, J. S., Larsen, L. E., & Schultz, A. C. (2014). Enteric porcine viruses in farmed shellfish in Denmark. *International Journal of Food Microbiology*, *186*, 105–109. doi:10.1016/j.ijfoodmicro.2014.06.012

Krog, Jesper S., Forslund, A., Larsen, L. E., Dalsgaard, A., Kjaer, J., Olsen, P., & Schultz, A. C. (2017). Leaching of viruses and other microorganisms naturally occurring in pig slurry to tile drains on a well-structured loamy field in Denmark. *Hydrogeology Journal*, *25*(4), 1045–1062. doi:10.1007/s10040-016-1530-8

Krog, Jesper S, Breum, S. Ø., Jensen, T. H., & Larsen, L. E. (2013). Hepatitis E virus variant in farmed mink, Denmark. *Emerging Infectious Diseases*, *19*(12), 2028–30. doi:10.3201/eid1912.130614

Kroneman, A., Verhoef, L., Harris, J., Vennema, H., Duizer, E., van Duynhoven, Y., et al. (2008). Analysis of

integrated virological and epidemiological reports of norovirus outbreaks collected within the Foodborne Viruses in Europe network from 1 July 2001 to 30 June 2006. *Journal of Clinical Microbiology*, *46*(9), 2959–65. doi:10.1128/JCM.00499-08

Kroneman, Annelies, Vega, E., Vennema, H., Vinjé, J., White, P. A., Hansman, G., et al. (2013). Proposal for a unified norovirus nomenclature and genotyping. *Archives of Virology*, *158*(10), 2059–68. doi:10.1007/s00705-013-1708-5

Kulkarni, S. P., Thanapati, S., Arankalle, V. A., & Tripathy, A. S. (2016). Specific memory B cell response and participation of CD4+ central and effector memory T cells in mice immunized with liposome encapsulated recombinant NE protein based Hepatitis E vaccine candidate. *Vaccine*, *34*(48), 5895–5902. doi:10.1016/j.vaccine.2016.10.046

Kumazaki, M., & Usuku, S. (2016). Norovirus genotype distribution in outbreaks of acute gastroenteritis among children and older people: an 8-year study. *BMC Infectious Diseases*, *16*(1), 643. doi:10.1186/s12879-016-1999-8

Kumthip, K., Khamrin, P., Ushijima, H., & Maneekarn, N. (2019). Enteric and non-enteric adenoviruses associated with acute gastroenteritis in pediatric patients in Thailand, 2011 to 2017. *PloS one*, *14*(8), e0220263. doi:10.1371/journal.pone.0220263

Kuo, H.-W., Schmid, D., Jelovcan, S., Pichler, A.-M., Magnet, E., Reichart, S., & Allerberger, F. (2009). A foodborne outbreak due to norovirus in Austria, 2007. *Journal of Food Protection*, *72*(1), 193–6. doi:10.4315/0362-028x-72.1.193

Kusumi, E., Tanimoto, T., Hosoda, K., Tsubokura, M., Hamaki, T., Takahashi, K., & Kami, M. (2017). Multiple norovirus outbreaks due to shredded, dried, laver seaweed in Japan. *Infection Control & Hospital Epidemiology*, *38*(7), 885–886. doi:10.1017/ice.2017.70

Kuusi, M., Nuorti, J. P., Maunula, L., Minh Tran, N. N., Ratia, M., Karlsson, J., & von Bonsdorff, C. H. (2002). A prolonged outbreak of Norwalk-like calicivirus (NLV) gastroenteritis in a rehabilitation centre due to environmental contamination. *Epidemiology and Infection*, *129*(1), 133–8. doi:10.1017/s0950268802007276

Kwan, H. S., Chan, P. K. S., & Chan, M. C. W. (2017). Overview of norovirus as a foodborne pathogen. In *The Norovirus: Features, Detection, and Prevention of Foodborne Disease* (pp. 21–30). Academic Press. doi:10.1016/B978-0-12-804177-2.00002-6

Lamhoujeb, S., Fliss, I., Ngazoa, S. E., & Jean, J. (2009). Molecular study of the persistence of infectious human norovirus on food-contact surfaces. *Food and Environmental Virology*, *1*(2), 51–56. doi:10.1007/s12560-009-9010-0

Lamhoujeb, Safaa, Fliss, I., Ngazoa, S. E., & Jean, J. (2008). Evaluation of the persistence of infectious human noroviruses on food surfaces by using real-time nucleic acid sequence-based amplification. *Applied and Environmental Microbiology*, *74*(11), 3349–3355. doi:10.1128/AEM.02878-07

Lassen, G. S., Soborg, B., Midgley, S. E., Steens, A., Vold, L., Stene-Johansen, K., et al. (2013). Ongoing multi-strain food-borne hepatitis A outbreak with frozen berries as suspected vehicle: four Nordic countries affected, October 2012 to April 2013. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *18*(17), 20467. doi:10.2807/ese.18.17.20467-en

Lau, C.-S., Wong, D. A., Tong, L. K. L., Lo, J. Y. C., Ma, A. M. C., Cheng, P. K. C., & Lim, W. W. L. (2004). High rate and changing molecular epidemiology pattern of norovirus infections in sporadic cases and outbreaks of gastroenteritis in Hong Kong. *Journal of Medical Virology*, *73*(1), 113–7. doi:10.1002/jmv.20066

Le Guyader, F. S., Atmar, R. L., & Le Pendu, J. (2012). Transmission of viruses through shellfish: when specific ligands come into play. *Current Opinion in Virology*, *2*(1), 103–10. doi:10.1016/j.coviro.2011.10.029

Le Pendu, J., Ruvoën-Clouet, N., Kindberg, E., & Svensson, L. (2006). Mendelian resistance to human norovirus infections. *Seminars in Immunology*, *18*(6), 375–86. doi:10.1016/j.smim.2006.07.009

Lednar, W. M., Lemon, S. M., Kirkpatrick, J. W., Redfield, R. R., Fields, M. L., & Kelley, P. W. (1985). Frequency of illness associated with epidemic Hepatitis E virus infections in adults. *American Journal of Epidemiology*, *122*(2), 226–233. doi:10.1093/oxfordjournals.aje.a114093

Lee, R. M., Lessler, J., Lee, R. A., Rudolph, K. E., Reich, N. G., Perl, T. M., & Cummings, D. A. T. (2013). Incubation

periods of viral gastroenteritis: a systematic review. *BMC Infectious Diseases*, *13*(1), 446. doi:10.1186/1471-2334-13-446

Lees, D. (2000). Viruses and bivalve shellfish. *International Journal of Food Microbiology*, *59*(1–2), 81–116. doi:10.1016/S0168-1605(00)00248-8

Lemes, L. G. N., Corrêa, T. S., Fiaccadori, F. S., Cardoso, D. das D. de P., Arantes, A. de M., Souza, K. M. C., & Souza, M. (2014). Prospective study on Norovirus infection among allogeneic stem cell transplant recipients: Prolonged viral excretion and viral RNA in the blood. *Journal of Clinical Virology*, *61*(3), 329–333. doi:10.1016/j.jcv.2014.08.004

León-Félix, J., Martínez-Bustillos, R. A., Báez-Sañudo, M., Peraza-Garay, F., & Chaidez, C. (2010). Norovirus contamination of bell pepper from handling during harvesting and packing. *Food and Environmental Virology*, *2*(4), 211–217. doi:10.1007/s12560-010-9048-z

Leung, A. K. C., & Robson, W. L. M. (2007). Acute gastroenteritis in children: role of anti-emetic medication for gastroenteritis-related vomiting. *Paediatric Drugs*, *9*(3), 175–84. doi:10.2165/00148581-200709030-00006

Li, J., Gao, X., Ye, Y.-L., Wan, T., Zang, H., Mo, P.-H., & Song, C.-L. (2018). An acute gastroenteritis outbreak associated with person-to-person transmission in a primary school in Shanghai: first report of a GI.5 norovirus outbreak in China. *BMC Infectious Diseases*, *18*(1), 316. doi:10.1186/s12879-018-3224-4

Li, L.-L., Liu, N., Yu, J., Ao, Y., Li, S., Stine, O. C., & Duan, Z. (2017). Analysis of Aichi virus and Saffold virus association with pediatric acute gastroenteritis. *Journal of Clinical Virology : the official publication of the Pan American Society for Clinical Virology*, *87*, 37–42. doi:10.1016/j.jcv.2016.12.003

Li, L., Pesavento, P. A., Shan, T., Leutenegger, C. M., Wang, C., & Delwart, E. (2011). Viruses in diarrhoeic dogs include novel kobuviruses and sapoviruses. *The Journal of General Virology*, *92*(Pt 11), 2534–41. doi:10.1099/vir.0.034611-0

Li, T.-C., Chijiwa, K., Sera, N., Ishibashi, T., Etoh, Y., Shinohara, Y., et al. (2005). Hepatitis E virus transmission from wild boar meat. *Emerging Infectious Diseases*, *11*(12), 1958–1960. doi:10.3201/eid1112.051041

Lian, Y., Wu, S., Luo, L., Lv, B., Liao, Q., Li, Z., et al. (2019). Epidemiology of Norovirus outbreaks reported to the Public Health Emergency Event Surveillance System, China, 2014–2017. *Viruses*, *11*(4). doi:10.3390/v11040342

Linder, K. A., & Malani, P. N. (2017). Hepatitis A. *JAMA*, *318*(23), 2393. doi:10.1001/jama.2017.17244

Lindesmith, L. C., Donaldson, E. F., & Baric, R. S. (2011). Norovirus GII.4 strain antigenic variation. *Journal of virology*, *85*(1), 231–42. doi:10.1128/JVI.01364-10

Lindquist, L. (2014). Tick-borne encephalitis. *Handbook of Clinical Neurology*, *123*, 531–59. doi:10.1016/B978-0-444-53488-0.00025-0

Lindquist, L., & Vapalahti, O. (2008). Tick-borne encephalitis. *Lancet (London, England)*, *371*(9627), 1861–71. doi:10.1016/S0140-6736(08)60800-4

Lisa, Lindesmith, Moe, C., Marionneau, S., Ruvoen, N., Jiang, X., et al. (2003). Human susceptibility and resistance to Norwalk virus infection. *Nature Medicine*, *9*(5), 548–53. doi:10.1038/nm860

Lodder, W. J., Rutjes, S. A., Takumi, K., & Husman, A. M. de R. (2013). Aichi Virus in sewage and surface water, the Netherlands. *Emerging Infectious Diseases*, *19*(8), 1222–1230. doi:10.3201/eid1908.130312

Lodo, K. L., Veitch, M. G., & Green, M. L. (2014). An outbreak of norovirus linked to oysters in Tasmania. *Communicable diseases intelligence quarterly report*, *38*(1), E16-19. https://www1.health.gov.au/internet/main/publishing.nsf/Content/cda-cdi3801-pdf-cnt.htm/$FILE/cdi3801d.pdf

Lopes-João, A., Mesquita, J. R., de Sousa, R., Oleastro, M., Penha-Gonçalves, C., & Nascimento, M. S. J. (2019). Simultaneous norovirus outbreak in three Portuguese army bases in the Lisbon region, December 2017. *Journal of the Royal Army Medical Corps*, jramc-2019-001242. doi:10.1136/jramc-2019-001242

Lopman, B. A., Hall, A. J., Curns, A. T., & Parashar, U. D. (2011). Increasing rates of gastroenteritis hospital discharges in US adults and the contribution of Norovirus, 1996–2007. *Clinical Infectious Diseases*, *52*(4), 466–474. doi:10.1093/cid/ciq163

Lopman, B., Vennema, H., Kohli, E., Pothier, P., Sanchez, A., Negredo, A., et al. (2004). Increase in viral gastroenteritis outbreaks in Europe and epidemic spread of new norovirus variant. *Lancet (London, England)*, *363*(9410), 682–8. doi:10.1016/S0140-6736(04)15641-9

Lowther, J. A., Gustar, N. E., Powell, A. L., Hartnell, R. E., & Lees, D. N. (2012). Two-year systematic study to assess norovirus contamination in oysters from commercial harvesting areas in the United Kingdom. *Applied and Environmental Microbiology*, *78*(16), 5812–7. doi:10.1128/AEM.01046-12

Lu, L., Li, C., & Hagedorn, C. H. (2006). Phylogenetic analysis of global hepatitis E virus sequences: genetic diversity, subtypes and zoonosis. *Reviews in Medical Virology*, *16*(1), 5–36. doi:10.1002/rmv.482

Lunestad, B. T., Maage, A., Roiha, I. S., Myrmel, M., Svanevik, C. S., & Duinker, A. (2016). An outbreak of norovirus infection from shellfish soup due to unforeseen insufficient heating during preparation. *Food and Environmental Virology*, *8*(4), 231–234. doi:10.1007/s12560-016-9245-5

Lytle, C. D., & Sagripanti, J.-L. (2005). Predicted inactivation of viruses of relevance to biodefense by solar radiation. *Journal of Virology*, *79*(22), 14244–52. doi:10.1128/JVI.79.22.14244-14252.2005

Maalouf, H., Schaeffer, J., Parnaudeau, S., Le Pendu, J., Atmar, R. L., Crawford, S. E., & Le Guyader, F. S. (2011). Strain-dependent norovirus bioaccumulation in oysters. *Applied and Environmental Microbiology*, *77*(10), 3189–96. doi:10.1128/AEM.03010-10

Maalouf, H., Zakhour, M., Le Pendu, J., Le Saux, J.-C., Atmar, R. L., & Le Guyader, F. S. (2010). Distribution in tissue and seasonal variation of norovirus genogroup I and II ligands in oysters. *Applied and Environmental Microbiology*, *76*(16), 5621–30. doi:10.1128/AEM.00148-10

Macori, G., Gilardi, G., Bellio, A., Bianchi, D. M., Gallina, S., Vitale, N., et al. (2018). Microbiological parameters in the primary production of berries: A pilot study. *Foods*, *7*(7), 105. doi:10.3390/foods7070105

Mäde, D., Irmscher, H.-M., Helmecke, C., Ketteritzsch, K., Schwarzer, U., Teige, A., et al. (2016). Norovirus outbreak in a restaurant: investigation of the path of infection by sequence analysis of food and human samples. *Journal für Verbraucherschutz und Lebensmittelsicherheit*, *11*(4), 345–351. doi:10.1007/s00003-016-1048-y

Mäde, D., Trübner, K., Neubert, E., Höhne, M., & Johne, R. (2013). Detection and typing of norovirus from frozen strawberries involved in a large-scale gastroenteritis outbreak in Germany. *Food and Environmental Virology*, *5*(3), 162–168. doi:10.1007/s12560-013-9118-0

Mandl, C. W., Heinz, F. X., Holzmann, H., Kunz, C., & Ecker, M. (1997). Infectious cDNA clones of tick-borne encephalitis virus European subtype prototypic strain Neudoerfl and high virulence strain Hypr. *Journal of General Virology*, *78*(5), 1049–1057. doi:10.1099/0022-1317-78-5-1049

Mansfield, K. L., Johnson, N., Phipps, L. P., Stephenson, J. R., Fooks, A. R., & Solomon, T. (2009). Tick-borne encephalitis virus - a review of an emerging zoonosis. *The Journal of General Virology*, *90*(Pt 8), 1781–94. doi:10.1099/vir.0.011437-0

Manso, C. F., & Romalde, J. L. (2013). Detection and characterization of hepatitis A virus and norovirus in mussels from Galicia (NW Spain). *Food and Environmental Virology*, *5*(2), 110–118. doi:10.1007/s12560-013-9108-2

Markovinović, L., Kosanović Ličina, M. L., Tešić, V., Vojvodić, D., Vladušić Lucić, I., Kniewald, T., et al. (2016). An outbreak of tick-borne encephalitis associated with raw goat milk and cheese consumption, Croatia, 2015. *Infection*, *44*(5), 661–5. doi:10.1007/s15010-016-0917-8

Martínez, A., Broner, S., Sala, M. R., Manzanares-Laya, S., Godoy, P., Planas, C., et al. (2015). Changes in the epidemiology of hepatitis A outbreaks 13 years after the introduction of a mass vaccination program. *Human Vaccines & Immunotherapeutics*, *11*(1), 192–7. doi:10.4161/hv.35861

Massoudi, M. S., Bell, B. P., Paredes, V., Insko, J., Evans, K., & Shapiro, C. N. (1999). An outbreak of hepatitis a associated with an infected foodhandler. *Public Health Reports*, *114*(2), 157–164. doi:10.1093/phr/114.2.157

MASUDA, J., YANO, K., TAMADA, Y., TAKII, Y., ITO, M., OMAGARI, K., & KOHNO, S. (2005). Acute hepatitis E of a man who consumed wild boar meat prior to the onset of illness in Nagasaki, Japan. *Hepatology Research*, *31*(3), 178–183. doi:10.1016/j.hepres.2005.01.008

Matsushima, Y., Ishikawa, M., Shimizu, T., Komane, A., Kasuo, S., Shinohara, M., et al. (2015). Genetic analyses

of GII.17 norovirus strains in diarrheal disease outbreaks from December 2014 to March 2015 in Japan reveal a novel polymerase sequence and amino acid substitutions in the capsid region. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *20*(26). doi:10.2807/1560-7917.es2015.20.26.21173

Mattioli, M. C., Sassoubre, L. M., Russell, T. L., & Boehm, A. B. (2017). Decay of sewage-sourced microbial source tracking markers and fecal indicator bacteria in marine waters. *Water Research*, *108*, 106–114. doi:10.1016/j.watres.2016.10.066

Mattison, K., Karthikeyan, K., Abebe, M., Malik, N., Sattar, S. A., Farber, J. M., & Bidawid, S. (2007). Survival of calicivirus in foods and on surfaces: experiments with feline calicivirus as a surrogate for norovirus. *Journal of Food Protection*, *70*(2), 500–3. doi:10.4315/0362-028x-70.2.500

Mattner, F., Sohr, D., Heim, A., Gastmeier, P., Vennema, H., & Koopmans, M. (2006). Risk groups for clinical complications of norovirus infections: an outbreak investigation. *Clinical Microbiology and Infection*, *12*(1), 69–74. doi:10.1111/j.1469-0691.2005.01299.x

Maunula, L., Roivainen, M., Keränen, M., Mäkela, S., Söderberg, K., Summa, M., et al. (2009). Detection of human norovirus from frozen raspberries in a cluster of gastroenteritis outbreaks. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *14*(49). doi:doi.org/10.2807/ese.14.49.19435-en

Mayet, A., Andreo, V., Bedubourg, G., Victorion, S., Plantec, J., Soullie, B., et al. (2011). Food-borne outbreak of norovirus infection in a French military parachuting unit, April 2011. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *16*(30), 19930. doi:10.2807/ese.16.30.19930-en

Meng, D., Newburg, D. S., Young, C., Baker, A., Tonkonogy, S. L., Sartor, R. B., et al. (2007). Bacterial symbionts induce a FUT2-dependent fucosylated niche on colonic epithelium via ERK and JNK signaling. *American Journal of Physiology. Gastrointestinal and Liver Physiology*, *293*(4), G780-7. doi:10.1152/ajpgi.00010.2007

Meng, X. J. (2003). Swine hepatitis E virus: cross-species infection and risk in xenotransplantation. *Current Topics in Microbiology and Immunology*, *278*, 185–216. doi:10.1007/978-3-642-55541-1_7

Meng, X. J. (2010). Hepatitis E virus: animal reservoirs and zoonotic risk. *Veterinary Microbiology*, *140*(3–4), 256–65. doi:10.1016/j.vetmic.2009.03.017

Meng, X. J., Wiseman, B., Elvinger, F., Guenette, D. K., Toth, T. E., Engle, R. E., et al. (2002). Prevalence of antibodies to hepatitis E virus in veterinarians working with swine and in normal blood donors in the United States and other countries. *Journal of Clinical Microbiology*, *40*(1), 117–22. doi:10.1128/jcm.40.1.117-122.2002

Menon, V. K., George, S., Ramani, S., Illiayaraja, J., Sarkar, R., Jana, A. K., et al. (2010). Genogroup IIb norovirus infections and association with enteric symptoms in a neonatal nursery in southern India. *Journal of Clinical Microbiology*, *48*(9), 3212–5. doi:10.1128/JCM.02510-09

Meschke, J. S., & Boyle, D. (2007). Shellfish and microbial source tracking. In J. W. S. Domingo & M. J. Sadowasky (Eds.), *Microbial Source Tracking* (pp. 137–179). Washington D.C.: ASM Press.

Mesquita, J. R., Oliveira, D., Rivadulla, E., Abreu-Silva, J., Varela, M. F., Romalde, J. L., & Nascimento, M. S. J. (2016). Hepatitis E virus genotype 3 in mussels (Mytilus galloprovinciallis), Spain. *Food Microbiology*, *58*, 13–5. doi:10.1016/j.fm.2016.03.009

Michelitsch, A., Wernike, K., Klaus, C., Dobler, G., & Beer, M. (2019). Exploring the reservoir hosts of Tick-Borne Encephalitis virus. *Viruses*, *11*(7). doi:10.3390/v11070669

Millard, J., Appleton, H., & Parry, J. V. (1987). Studies on heat inactivation of hepatitis A virus with special reference to shellfish. Part 1. Procedures for infection and recovery of virus from laboratory-maintained cockles. *Epidemiology and Infection*, *98*(3), 397–414. doi:10.1017/s0950268800062166

Miura, T., Sano, D., Suenaga, A., Yoshimura, T., Fuzawa, M., Nakagomi, T., et al. (2013). Histo-blood group antigen-like substances of human enteric bacteria as specific adsorbents for human noroviruses. *Journal of Virology*, *87*(17), 9441–51. doi:10.1128/JVI.01060-13

Moal, V., Gerolami, R., & Colson, P. (2012). First human case of co-infection with two different subtypes of hepatitis E virus. *Intervirology*, *55*(6), 484–7. doi:10.1159/000335664

Mollers, M., Boxman, I. L. A., Vennema, H., Slegers-Fitz-James, I. A., Brandwagt, D., Friesema, I. H., et al. (2018). Successful use of advertisement pictures to assist recall in a food-borne Hepatitis A outbreak in The Netherlands, 2017. *Food and Environmental Virology*. doi:10.1007/s12560-018-9347-3

Monica, B., Ramani, S., Banerjee, I., Primrose, B., Iturriza-Gomara, M., Gallimore, C. I., et al. (2007). Human caliciviruses in symptomatic and asymptomatic infections in children in Vellore, South India. *Journal of Medical Virology*, *79*(5), 544–51. doi:10.1002/jmv.20862

Monini, M., Ostanello, F., Vignolo, E., Pagani, E., Gamper, S., Spertini, S., et al. (2019). Occurrence of two Norovirus outbreaks in the same cafeteria in one week. *The New Microbiologica*, *42*(2). http://www.ncbi.nlm.nih.gov/pubmed/31305934. Accessed 22 July 2019

Moor, D., Liniger, M., Baumgartner, A., & Felleisen, R. (2018). Screening of ready-to-eat meat products for Hepatitis E virus in Switzerland. *Food and Environmental Virology*, *10*(3), 263–271. doi:10.1007/s12560-018-9340-x

Mori, K., Nagano, M., Kimoto, K., Somura, Y., Akiba, T., Hayashi, Y., et al. (2017). Detection of enteric viruses in fecal specimens from nonbacterial foodborne gastroenteritis outbreaks in Tokyo, Japan between 1966 and 1983. *Japanese Journal of Infectious Diseases*, *70*(2), 143–151. doi:10.7883/yoken.JJID.2015.456

Müller, L., Schultz, A. C., Fonager, J., Jensen, T., Lisby, M., Hindsdal, K., et al. (2015). Separate norovirus outbreaks linked to one source of imported frozen raspberries by molecular analysis, Denmark, 2010–2011. *Epidemiology and Infection*, *143*(11), 2299–2307. doi:10.1017/S0950268814003409

Müller, Luise, Rasmussen, L. D., Jensen, T., Schultz, A. C., Kjelsø, C., Barnadas, C., et al. (2016). Series of norovirus outbreaks caused by consumption of green coral lettuce, Denmark, April 2016. *PLoS Currents*, *8*. doi:10.1371/currents.outbreaks.115761d5d6de6a8bc7dd4b41f0f5f142

Muniain-Mujika, I., Calvo, M., Lucena, F., & Girones, R. (2003). Comparative analysis of viral pathogens and potential indicators in shellfish. *International Journal of Food Microbiology*, *83*(1), 75–85. doi:10.1016/s0168-1605(02)00324-0

Mushahwar, I. K. (2008). Hepatitis E virus: Molecular virology, clinical features, diagnosis, transmission, epidemiology, and prevention. *Journal of Medical Virology*, *80*(4), 646–658. doi:10.1002/jmv.21116

Nordic outbreak investigation team, C. (2013). Joint analysis by the Nordic countries of a hepatitis A outbreak, October 2012 to June 2013: frozen strawberries suspected. *Eurosurveillance*, *18*(27), 1–7. doi:10.2807/1560-7917.ES2013.18.27.20520

Offerdahl, D. K., Clancy, N. G., & Bloom, M. E. (2016). Stability of a tick-borne flavivirus in milk. *Frontiers in Bioengineering and Biotechnology*, *4*(MAY), 1–6. doi:10.3389/fbioe.2016.00040

Oka, T., Doan, Y. H., Haga, K., Mori, K., Ogawa, T., & Yamazaki, A. (2017). Genetic characterization of rare genotype GII.5 Sapovirus strain detected from a suspected food-borne gastroenteritis outbreak among adults in Japan in 2010. *Japanese Journal of Infectious Diseases*, *70*(2), 223–224. doi:10.7883/yoken.JJID.2016.468

Oka, T., Wang, Q., Katayama, K., & Saif, L. J. (2015). Comprehensive review of human sapoviruses. *Clinical Microbiology Reviews*, *28*(1), 32–53. doi:10.1128/CMR.00011-14

Okamoto, H. (2013). Culture systems for hepatitis E virus. *Journal of Gastroenterology*, *48*(2), 147–58. doi:10.1007/s00535-012-0682-0

Oliveira, J. C. (2004). Optimising the efficiency and productivity of thermal processing. In P. Richardson (Ed.), *Improving the Thermal Processing of Foods* (pp. 3–31). Woodhead Publishing Limited. https://pdf.sciencedirectassets.com/307626/3-s2.0-C20130178543/3-s2.0-B9781855737303500061/main.pdf?X-Amz-Security-Token=AgoJb3JpZ2luX2VjEBIaCXVzLWVhc3QtMSJIMEYCIQCoIXxQIQMTvo5BhpSd6IDdqj486JY59ySO0RulEDSi0AIhAL3oQq%2BFwFSDOy3l8TKf5LYTG0Yx1pTSE%2FSVOa0qfc. Accessed 31 August 2019

Ozawa, K., Oka, T., Takeda, N., & Hansman, G. S. (2007). Norovirus infections in symptomatic and asymptomatic food handlers in Japan. *Journal of Clinical Microbiology*, *45*(12), 3996–4005. doi:10.1128/JCM.01516-07

Park, S. Bin. (2012). Hepatitis E vaccine debuts. *Nature*, *491*(7422), 21–2. doi:10.1038/491021a

Park, J. H., Jeong, H. S., Lee, J. S., Lee, S. W., Choi, Y. H., CHOI, S. J., et al. (2015). First norovirus outbreaks associated with consumption of green seaweed (Enteromorpha spp.) in South Korea. *Epidemiology and*

Infection, *143*(3), 515–521. doi:10.1017/S0950268814001332

Parrón, I., Álvarez, J., Jané, M., Cornejo Sánchez, T., Razquin, E., Guix, S., et al. (2019). A foodborne norovirus outbreak in a nursing home and spread to staff and their household contacts. *Epidemiology and Infection*, *147*, e225. doi:10.1017/S0950268819001146

Patel, M. M., Hall, A. J., Vinjé, J., & Parashar, U. D. (2009). Noroviruses: a comprehensive review. *Journal of Clinical Virology : the official publication of the Pan American Society for Clinical Virology*, *44*(1), 1–8. doi:10.1016/j.jcv.2008.10.009

Patel, M. M., Widdowson, M.-A., Glass, R. I., Akazawa, K., Vinjé, J., & Parashar, U. D. (2008). Systematic literature review of role of noroviruses in sporadic gastroenteritis. *Emerging Infectious Diseases*, *14*(8), 1224–31. doi:10.3201/eid1408.071114

Paulsen, K. M., Stuen, S., das Neves, C. G., Suhel, F., Gurung, D., Soleng, A., et al. (2019). Tick-borne encephalitis virus in cows and unpasteurized cow milk from Norway. *Zoonoses and Public Health*, *66*(2), 216–222. doi:10.1111/zph.12554

Pavio, N., Doceul, V., Bagdassarian, E., & Johne, R. (2017). Recent knowledge on hepatitis E virus in Suidae reservoirs and transmission routes to human. *Veterinary Research*, *48*(1), 78. doi:10.1186/s13567-017-0483-9

Pavio, N., Meng, X.-J., & Renou, C. (2010). Zoonotic hepatitis E: animal reservoirs and emerging risks. *Veterinary Research*, *41*(6), 46. doi:10.1051/vetres/2010018

Pérot, P., Lecuit, M., & Eloit, M. (2017). Astrovirus diagnostics. *Viruses*, *9*(1). doi:10.3390/v9010010

Perrin, A., Loutreul, J., Boudaud, N., Bertrand, I., & Gantzer, C. (2015). Rapid, simple and efficient method for detection of viral genomes on raspberries. *Journal of Virological Methods*, *224*, 95–101. doi:10.1016/j.jviromet.2015.08.005

Petrignani, M., Harms, M., Verhoef, L., van Hunen, R., Swaan, C., van Steenbergen, J., et al. (2010). Update: a food-borne outbreak of hepatitis A in the Netherlands related to semi-dried tomatoes in oil, January-February 2010. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *15*(20), 1–4. doi:10.2807/ese.15.20.19572-en

Phillips, G., Tam, C. C., Rodrigues, L. C., & Lopman, B. (2010). Prevalence and characteristics of asymptomatic norovirus infection in the community in England. *Epidemiology and Infection*, *138*(10), 1454–8. doi:10.1017/S0950268810000439

Pintó, R. M., Costafreda, M. I., Pérez-Rodriguez, F. J., D'Andrea, L., & Bosch, A. (2010). Hepatitis A Virus: State of the Art. *Food and Environmental Virology*, *2*(3), 127–135. doi:10.1007/s12560-010-9044-3

Pires, S. M., Fischer-Walker, C. L., Lanata, C. F., Devleesschauwer, B., Hall, A. J., Kirk, M. D., et al. (2015). Aetiology-specific estimates of the global and regional incidence and mortality of diarrhoeal diseases commonly transmitted through food. *PloS one*, *10*(12), e0142927. doi:10.1371/journal.pone.0142927

Pol-Hofstad, I. E., Rutjes, S. A., Gerssen, A., Poelman, M., & Linden, A. D. van der. (2014). Evaluation of the sanitary status of the Dutch shellfish production waters over a 7 year period. *Proceedings of the 9th International Conference on Molluscan Shellfish Safety, Sydney, Australia, 17-22 March 2013*, 52–54. https://www.cabdirect.org/cabdirect/abstract/20153057380. Accessed 10 February 2020

Racaniello, V. R. (2013). Picornaviridae: The Viruses and their Replication. In D. M. Knipe & P. Howley (Eds.), *Fields Virology* (6th ed., pp. 454–488). Wolters Kluwer Health Adis (ESP).

Rajiuddin, S. M. (2019). *Development and use of new methods and technologies to study and control foodborne viruses on fruits, greens and surfaces of plastic and steel*. Technical University of Denmark.

RASFF. (2019). RASFF 2019:3003. Rapid Alert System for Food and Feed, Notification 2019.3003 - foodborne outbreak suspected to be caused by norovirus (G II) in frozen seaweed salad from China, via Denmark. https://webgate.ec.europa.eu/rasff-window/portal/?event=notificationDetail&NOTIF_REFERENCE=2019.3003. Accessed 11 November 2019

Rasmussen, L. D., Schultz, A. C., Uhrbrand, K., Jensen, T., & Fischer, T. K. (2016). Molecular Evidence of Oysters as Vehicle of Norovirus GII.P17-GII.17. *Emerging Infectious Diseases*, *22*(11), 2024–2025. doi:10.3201/eid2211.161171

Rein, D. B., Stevens, G. A., Theaker, J., Wittenborn, J. S., & Wiersma, S. T. (2012). The global burden of hepatitis E virus genotypes 1 and 2 in 2005. *Hepatology (Baltimore, Md.)*, *55*(4), 988–97. doi:10.1002/hep.25505

Renou, C., Pariente, A., Cadranel, J.-F., Nicand, E., & Pavio, N. (2011). Clinically silent forms may partly explain the rarity of acute cases of autochthonous genotype 3c hepatitis E infection in France. *Journal of Clinical Virology : the official publication of the Pan American Society for Clinical Virology*, *51*(2), 139–41. doi:10.1016/j.jcv.2011.02.013

Renou, C., Roque-Afonso, A.-M., Afonso, A.-M. R., & Pavio, N. (2014). Foodborne transmission of hepatitis E virus from raw pork liver sausage, France. *Emerging Infectious Diseases*, *20*(11), 1945–7. doi:10.3201/eid2011.140791

Richardson, C., Bargatze, R. F., Goodwin, R., & Mendelman, P. M. (2013). Norovirus virus-like particle vaccines for the prevention of acute gastroenteritis. *Expert Review of Vaccines*, *12*(2), 155–167. doi:10.1586/erv.12.145

RIERA-MONTES, M., BRUS SJÖLANDER, K., ALLESTAM, G., HALLIN, E., HEDLUND, K.-O., & LÖFDAHL, M. (2011). Waterborne norovirus outbreak in a municipal drinking-water supply in Sweden. *Epidemiology and Infection*, *139*(12), 1928–1935. doi:10.1017/S0950268810003146

Robesyn, E., De Schrijver, K., Wollants, E., Top, G., Verbeeck, J., & Van Ranst, M. (2009). An outbreak of hepatitis A associated with the consumption of raw beef. *Journal of Clinical Virology*, *44*(3), 207–210. doi:10.1016/j.jcv.2008.12.012

Robilotti, E., Deresinski, S., & Pinsky, B. A. (2015). Norovirus. *Clinical Microbiology Reviews*, *28*(1), 134–164. doi:10.1128/CMR.00075-14

Rockx, B., De Wit, M., Vennema, H., Vinjé, J., De Bruin, E., Van Duynhoven, Y., & Koopmans, M. (2002). Natural history of human calicivirus infection: a prospective cohort study. *Clinical Infectious Diseases : an official publication of the Infectious Diseases Society of America*, *35*(3), 246–53. doi:10.1086/341408

Rodriguez-Baez, N., O'Brien, R., Qiu, S.-Q., & Bass, D. M. (2002). Astrovirus, adenovirus, and rotavirus in hospitalized children: prevalence and association with gastroenteritis. *Journal of Pediatric Gastroenterology and Nutrition*, *35*(1), 64–8. doi:10.1097/00005176-200207000-00014

Rodríguez-Lázaro, D., Cook, N., Ruggeri, F. M., Sellwood, J., Nasser, A., Nascimento, M. S. J., et al. (2012). Virus hazards from food, water and other contaminated environments. *FEMS Microbiology Reviews*, *36*(4), 786–814. doi:10.1111/j.1574-6976.2011.00306.x

Rohayem, J. (2009). Norovirus seasonality and the potential impact of climate change. *Clinical Microbiology and Infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases*, *15*(6), 524–7. doi:10.1111/j.1469-0691.2009.02846.x

Rossati, A., Bargiacchi, O., Kroumova, V., Nebbiolo, C., Tacca, M. G., Pratillo, S., & Garavelli, P. L. (2017). Outbreak of severe Hepatitis A in Eastern Piedmont, Italy. *Le infezioni in medicina : rivista periodica di eziologia, epidemiologia, diagnostica, clinica e terapia delle patologie infettive*, *25*(4), 344–346. http://www.ncbi.nlm.nih.gov/pubmed/29286013

RUZANTE, J. M., MAJOWICZ, S. E., FAZIL, A., & DAVIDSON, V. J. (2011). Hospitalization and deaths for select enteric illnesses and associated sequelae in Canada, 2001–2004. *Epidemiology and Infection*, *139*(6), 937–945. doi:10.1017/S0950268810001883

Rzezutka, A., Cook, N., Rzeżutka, A., & Cook, N. (2004). Survival of human enteric viruses in the environment and food. *FEMS Microbiology Reviews*, *28*(4), 441–453. doi:10.1016/j.femsre.2004.02.001

Saier, R., Maier, G., Atamer, Z., & Hinrichs, J. (2015). Thermal inactivation of tickborne encephalitis virus in milk. *International Journal of Dairy Technology*, *68*(3), 366–373. doi:10.1111/1471-0307.12230

Sakon, N., Sadamasu, K., Shinkai, T., Hamajima, Y., Yoshitomi, H., Matsushima, Y., et al. (2018). Foodborne outbreaks caused by human norovirus GII.P17-GII.17-contaminated nori, Japan, 2017. *Emerging Infectious Diseases*, *24*(5), 920–923. doi:10.3201/eid2405.171733

Sakon, N., Yamazaki, K., Nakata, K., Kanbayashi, D., Yoda, T., Mantani, M., et al. (2015). Impact of genotype-specific herd immunity on the circulatory dynamism of norovirus: a 10-year longitudinal study of viral acute gastroenteritis. *The Journal of Infectious Diseases*, *211*(6), 879–88. doi:10.1093/infdis/jiu496

Salaheen, S., Chowdhury, N., Hanning, I., & Biswas, D. (2015). Zoonotic bacterial pathogens and mixed crop-

livestock farming. *Poultry Science*, *94*(6), 1398–1410. doi:10.3382/ps/peu055

Salát, J., Formanová, P., Huňady, M., Eyer, L., Palus, M., & Ruzek, D. (2018). Development and testing of a new tick-borne encephalitis virus vaccine candidate for veterinary use. *Vaccine*, *36*(48), 7257–7261. doi:10.1016/j.vaccine.2018.10.034

Sarvikivi, E., Roivainen, M., Maunula, L., Niskanen, T., Korhonen, T., Lappalainen, M., & Kuusi, M. (2012). Multiple norovirus outbreaks linked to imported frozen raspberries. *Epidemiology and Infection*, *140*(2), 260–267. doi:10.1017/S0950268811000379

Scallan, E., Griffin, P. M., Angulo, F. J., Tauxe, R. V., & Hoekstra, R. M. (2011). Foodborne illness acquired in the United States--unspecified agents. *Emerging Infectious Diseases*, *17*(1), 16–22. doi:10.3201/eid1701.091101p2

Schiff, E. R. (1992). Atypical clinical manifestations of hepatitis A. *Vaccine*, *10*, S18–S20. doi:10.1016/0264-410X(92)90534-Q

Schmid, D., Kuo, H.-W., Hell, M., Kasper, S., Lederer, I., Mikula, C., et al. (2011). Foodborne gastroenteritis outbreak in an Austrian healthcare facility caused by asymptomatic, norovirus-excreting kitchen staff. *Journal of Hospital Infection*, *77*(3), 237–241. doi:10.1016/j.jhin.2010.11.015

Schrader, C., Schielke, A., Ellerbroek, L., & Johne, R. (2012). PCR inhibitors - occurrence, properties and removal. *Journal of Applied Microbiology*, *113*(5), 1014–1026. doi:10.1111/j.1365-2672.2012.05384.x

Schwab, K. J., Neill, F. H., Estes, M. K., Metcalf, T. G., & Atmar, R. L. (1998). Distribution of Norwalk virus within shellfish following bioaccumulation and subsequent depuration by detection using RT-PCR. *Journal of Food Protection*, *61*(12), 1674–1680. doi:10.4315/0362-028X-61.12.1674

Seah, E. L., Gunesekere, I. C., Marshall, J. A., & Wright, P. J. (1999). Variation in ORF3 of genogroup 2 Norwalk-like viruses. *Archives of Virology*, *144*(5), 1007–14. doi:10.1007/s007050050563

Severi, E., Verhoef, L., Thornton, L., Guzman-Herrador, B. R., Faber, M., Sundqvist, L., et al. (2015). Large and prolonged food-borne multistate hepatitis A outbreak in Europe associated with consumption of frozen berries, 2013 to 2014. *Eurosurveillance*, *20*(29), 21192. doi:10.2807/1560-7917.ES2015.20.29.21192

Shin, H., Park, H., Seo, D. J., Jung, S., Yeo, D., Wang, Z., et al. (2019). Foodborne viruses detected sporadically in the fresh produce and its production environment in South Korea. *Foodborne Pathogens and Disease*, *16*(6), 411–420. doi:10.1089/fpd.2018.2580

Shrestha, M. P., Scott, R. M., Joshi, D. M., Mammen, M. P., Thapa, G. B., Thapa, N., et al. (2007). Safety and efficacy of a recombinant Hepatitis E vaccine. *New England Journal of Medicine*, *356*(9), 895–903. doi:10.1056/NEJMoa061847

Siebenga, J. J., Beersma, M. F. C., Vennema, H., van Biezen, P., Hartwig, N. J., & Koopmans, M. (2008). High prevalence of prolonged norovirus shedding and illness among hospitalized patients: A model for in vivo molecular evolution. *The Journal of Infectious Diseases*, *198*(7), 994–1001. doi:10.1086/591627

Sjogren, M. H., Tanno, H., Fay, O., Sileoni, S., Cohen, B. D., Burke, D. S., & Feighny, R. J. (1987). Hepatitis A virus in stool during clinical relapse. *Annals of Internal Medicine*, *106*(2), 221–6. doi:10.7326/0003-4819-106-2-221

Slovenia., I. of P. H. of the R. of. (2014). Epidemiological surveillance of infectious diseases in Slovenia in year 2013. *Tick-borne Encephalitis*, 57–59.

Šmit, R., & Postma, M. J. (2015). Review of tick-borne encephalitis and vaccines: clinical and economical aspects. *Expert Review of Vaccines*, *14*(5), 737–47. doi:10.1586/14760584.2015.985661

Smith, A. J., McCarthy, N., Saldana, L., Ihekweazu, C., McPhedran, K., Adak, G. K., et al. (2012). A large foodborne outbreak of norovirus in diners at a restaurant in England between January and February 2009. *Epidemiology and Infection*, *140*(9), 1695–1701. doi:10.1017/S0950268811002305

Sobsey, M., Shields, P., Hauchman, F., Hazard, R., & Caton, L. I. (1989). Survival and transport of hepatitis A virus in soils, groundwater and wastewater. *Water Science and Technology*, (10), 97–106.

Solomon, E. B., Fino, V., Wei, J., & Kniel, K. E. (2009). Comparative susceptibilities of hepatitis A virus, feline calicivirus, bacteriophage MS2 and bacteriophage ΦX-174 to inactivation by quaternary ammonium and oxidative disinfectants. *International Journal of Antimicrobial Agents*, *33*(3), 288–289.

doi:10.1016/j.ijantimicag.2008.09.004

Somura, Y., Kimoto, K., Oda, M., Okutsu, Y., Kato, R., Suzuki, Y., et al. (2017). [Serial Food Poisoning Outbreaks Caused by Norovirus-Contaminated Shredded Dried Laver Seaweed Provided at School Lunch, Tokyo, 2017]. *Shokuhin eiseigaku zasshi. Journal of the Food Hygienic Society of Japan*, *58*(6), 260–267. doi:10.3358/shokueishi.58.260

Springthorpe, V. S., Loh, C. L., Robertson, W. J., & Sattar, S.A. (1993). In situ survival of indicator bacteria, MS-2 phage and human pathogenic viruses in river water. *Water Science and Technology (United Kingdom)*, (27), 413–420. http://agris.fao.org/agris-search/search.do?recordID=GB9609354. Accessed 1 October 2019

Steyer, A., Poljsak-Prijatelj, M., Barlic-Maganja, D., & Marin, J. (2008). Human, porcine and bovine rotaviruses in Slovenia: evidence of interspecies transmission and genome reassortment. *The Journal of General Virology*, *89*(Pt 7), 1690–8. doi:10.1099/vir.0.2008/001206-0

Storch, G. A. (2013). Diagnostic Virology. In D. M. Knipe & P. Howley (Eds.), *Fields Virology* (6th ed., pp. 415–451). Wolters Kluwer Health Adis (ESP).

Stoszek, S. K., Engle, R. E., Abdel-Hamid, M., Mikhail, N., Abdel-Aziz, F., Medhat, A., et al. (2006). Hepatitis E antibody seroconversion without disease in highly endemic rural Egyptian communities. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, *100*(2), 89–94. doi:10.1016/j.trstmh.2005.05.019

Sundkvist, T., Hamilton, G. R., Hourihan, B. M., & Hart, I. J. (2000). Outbreak of hepatitis A spread by contaminated drinking glasses in a public house. *Communicable Disease and Public Health*, *3*(1), 60–2. http://www.ncbi.nlm.nih.gov/pubmed/10743322. Accessed 10 February 2020

Süss, J. (2011). Tick-borne encephalitis 2010: epidemiology, risk areas, and virus strains in Europe and Asia-an overview. *Ticks and Tick-borne Diseases*, *2*(1), 2–15. doi:10.1016/j.ttbdis.2010.10.007

Svraka, S., Vennema, H., van der Veer, B., Hedlund, K.-O., Thorhagen, M., Siebenga, J., et al. (2010). Epidemiology and genotype analysis of emerging Sapovirus-associated infections across Europe. *Journal of Clinical Microbiology*, *48*(6), 2191–2198. doi:10.1128/JCM.02427-09

Taba, P., Schmutzhard, E., Forsberg, P., Lutsar, I., Ljøstad, U., Mygland, Å., et al. (2017). EAN consensus review on prevention, diagnosis and management of tick-borne encephalitis. *European Journal of Neurology*, *24*(10), 1214-e61. doi:10.1111/ene.13356

Taku, A., Gulati, B. R., Allwood, P. B., Palazzi, K., Hedberg, C. W., & Goyal, S. M. (2002). Concentration and detection of Caliciviruses from food contact surfaces. *Journal of Food Protection*, *65*(6), 999–1004. doi:10.4315/0362-028X-65.6.999

Tam, C. C., O'Brien, S. J., Tompkins, D. S., Bolton, F. J., Berry, L., Dodds, J., et al. (2012). Changes in causes of acute gastroenteritis in the United Kingdom over 15 years: microbiologic findings from 2 prospective, population-based studies of infectious intestinal disease. *Clinical Infectious Diseases : an official publication of the Infectious Diseases Society of America*, *54*(9), 1275–86. doi:10.1093/cid/cis028

Tassopoulos, N. C., Papaevangelou, G. J., Ticehurst, J. R., & Purcell, R. H. (1986). Fecal excretion of Greek strains of hepatitis A virus in patients with hepatitis A and in experimentally infected chimpanzees. *The Journal of Infectious Diseases*, *154*(2), 231–7. doi:10.1093/infdis/154.2.231

Tate, J. E., Burton, A. H., Boschi-Pinto, C., Parashar, U. D., & World Health Organization–Coordinated Global Rotavirus Surveillance Network. (2016). Global, regional, and national estimates of Rotavirus mortality in children <5 Years of Age, 2000-2013. *Clinical Infectious Diseases : an official publication of the Infectious Diseases Society of America*, *62 Suppl 2*(suppl 2), S96–S105. doi:10.1093/cid/civ1013

Tate, J. E., Burton, A. H., Boschi-Pinto, C., Steele, A. D., Duque, J., Parashar, U. D., & WHO-coordinated Global Rotavirus Surveillance Network. (2012). 2008 estimate of worldwide rotavirus-associated mortality in children younger than 5 years before the introduction of universal rotavirus vaccination programmes: a systematic review and meta-analysis. *The Lancet. Infectious Diseases*, *12*(2), 136–41. doi:10.1016/S1473-3099(11)70253-5

ter Waarbeek, H. L. G., Dukers-Muijrers, N. H. T. M., Vennema, H., & Hoebe, C. J. P. A. (2010). Waterborne gastroenteritis outbreak at a scouting camp caused by two norovirus genogroups: GI and GII. *Journal of Clinical Virology : the official publication of the Pan American Society for Clinical Virology*, *47*(3), 268–72. doi:10.1016/j.jcv.2009.12.002

Terio, V., Bottaro, M., Di Pinto, A., Fusco, G., Barresi, T., Tantillo, G., & Martella, V. (2018). Occurrence of Aichi virus in retail shellfish in Italy. *Food Microbiology*, *74*, 120–124. doi:10.1016/j.fm.2018.02.013

Tessé, S., Lioure, B., Fornecker, L., Wendling, M.-J., Stoll-Keller, F., Bigaillon, C., & Nicand, E. (2012). Circulation of genotype 4 hepatitis E virus in Europe: first autochthonous hepatitis E infection in France. *Journal of Clinical Virology : the official publication of the Pan American Society for Clinical Virology*, *54*(2), 197–200. doi:10.1016/j.jcv.2012.02.007

Teunis, P. F. M., Moe, C. L., Liu, P., E. Miller, S., Lindesmith, L., Baric, R. S., et al. (2008). Norwalk virus: How infectious is it? *Journal of Medical Virology*, *80*(8), 1468–1476. doi:10.1002/jmv.21237

Todd, E. C. D., Greig, J. D., Bartleson, C. A., & Michaels, B. S. (2007a). Outbreaks where food workers have been implicated in the spread of foodborne disease. Part 2. Description of outbreaks by size, severity, and settings. *Journal of Food Protection*, *70*(8), 1975–93. doi:10.4315/0362-028x-70.8.1975

Todd, E. C. D., Greig, J. D., Bartleson, C. A., & Michaels, B. S. (2007b). Outbreaks where food workers have been implicated in the spread of foodborne disease. Part 3. Factors contributing to outbreaks and description of outbreak categories. *Journal of Food Protection*, *70*(9), 2199–2217. doi:10.4315/0362-028X-70.9.2199

Trmal, J., Pavlík, I., Vasícková, P., Matejícková, L., Simůnková, L., Luks, S., & Pazderková, J. (2012). [Outbreaks of viral hepatitis E in the Czech Republic?]. *Epidemiologie, mikrobiologie, imunologie : casopis Spolecnosti pro epidemiologii a mikrobiologii Ceske lekarske spolecnosti J.E. Purkyne*, *61*(1–2), 15–20. http://www.ncbi.nlm.nih.gov/pubmed/22880260. Accessed 7 February 2020

Tryfinopoulou, K., Kyritsi, M., Mellou, K., Kolokythopoulou, F., Mouchtouri, V. A., Potamiti-Komi, M., et al. (2019). Norovirus waterborne outbreak in Chalkidiki, Greece, 2015: detection of GI.P2_GI.2 and GII.P16_GII.13 unusual strains. *Epidemiology and Infection*, *147*, e227. doi:10.1017/S0950268819000852

Tse, H., Chan, W.-M., Li, K. S. M., Lau, S. K. P., Woo, P. C. Y., & Yuen, K.-Y. (2012). Discovery and genomic characterization of a novel bat Sapovirus with unusual genomic features and phylogenetic position. *PLoS ONE*, *7*(4), e34987. doi:10.1371/journal.pone.0034987

Turcios-Ruiz, R. M., Axelrod, P., St. John, K., Bullitt, E., Donahue, J., Robinson, N., & Friss, H. E. (2008). Outbreak of necrotizing enterocolitis caused by norovirus in a neonatal intensive care unit. *The Journal of Pediatrics*, *153*(3), 339–344. doi:10.1016/j.jpeds.2008.04.015

Uhnoo, I., Svensson, L., & Wadell, G. (1990). Enteric adenoviruses. *Bailliere's clinical gastroenterology*, *4*(3), 627–42. doi:10.1016/0950-3528(90)90053-j

van Alphen, L. B., Dorléans, F., Schultz, A. C., Fonager, J., Ethelberg, S., Dalgaard, C., et al. (2014). The application of new molecular methods in the investigation of a waterborne outbreak of norovirus in Denmark, 2012. *PLoS ONE*, *9*(9), e105053. doi:10.1371/journal.pone.0105053

van Asten, L., Siebenga, J., van den Wijngaard, C., Verheij, R., van Vliet, H., Kretzschmar, M., et al. (2011). Unspecified gastroenteritis illness and deaths in the elderly associated with norovirus epidemics. *Epidemiology*, *22*(3), 336–343. doi:10.1097/EDE.0b013e31821179af

Van der Poel, W. H. M., Dalton, H. R., Johne, R., Pavio, N., Bouwknegt, M., Wu, T., et al. (2018). Knowledge gaps and research priorities in the prevention and control of hepatitis E virus infection. *Transboundary and Emerging Diseases*, *65*, 22–29. doi:10.1111/tbed.12760

Van Duynhoven, Y., De Jager, C., Kortbeek, L., Vennema, H., Koopmans, M., Van Leusden, F., et al. (2005). A one-year intensified study of outbreaks of gastroenteritis in The Netherlands. *Epidemiology and Infection*, *133*(1), 9–21. doi:10.1017/S0950268804002936

Varela, M. F., Hooper, A. S., Rivadulla, E., & Romalde, J. L. (2016). Human Sapovirus in mussels from Ría do Burgo, A Coruña (Spain). *Food and Environmental Virology*, *8*(3), 187–193. doi:10.1007/s12560-016-9242-8

Vega, E., Barclay, L., Gregoricus, N., Shirley, S. H., Lee, D., & Vinje, J. (2014). Genotypic and epidemiologic trends of norovirus outbreaks in the United States, 2009 to 2013. *Journal of Clinical Microbiology*, *52*(1), 147–155. doi:10.1128/JCM.02680-13

Veje, M., Studahl, M., Johansson, M., Johansson, P., Nolskog, P., & Bergström, T. (2018). Diagnosing tick-borne encephalitis: a re-evaluation of notified cases. *European Journal of Clinical Microbiology & Infectious Diseases*, *37*(2), 339–344. doi:10.1007/s10096-017-3139-9

Velázquez, F. R., Matson, D. O., Calva, J. J., Guerrero, M. L., Morrow, A. L., Carter-Campbell, S., et al. (1996).

Rotavirus infection in infants as protection against subsequent infections. *The New England Journal of Medicine*, *335*(14), 1022–8. doi:10.1056/NEJM199610033351404

Velebit, B., Radin, D., & Teodorovic, V. (2015). Transmission of common foodborne viruses by meat products. *Procedia Food Science*, *5*, 304–307. doi:10.1016/j.profoo.2015.09.069

Vinjé, J. (2015). Advances in laboratory methods for detection and typing of norovirus. *Journal of Clinical Microbiology*, *53*(2), 373–381. doi:10.1128/JCM.01535-14

Vinjé, J., Altena, S. A., & Koopmans, M. P. (1997). The incidence and genetic variability of small round-structured viruses in outbreaks of gastroenteritis in The Netherlands. *The Journal of Infectious Diseases*, *176*(5), 1374–8. doi:10.1086/517325

Vu, D.-L., Bosch, A., Pintó, R. M., & Guix, S. (2017). Epidemiology of classic and novel human Astrovirus: gastroenteritis and beyond. *Viruses*, *9*(2). doi:10.3390/v9020033

Wacklin, P., Tuimala, J., Nikkilä, J., Sebastian Tims, Mäkivuokko, H., Alakulppi, N., et al. (2014). Faecal microbiota composition in adults is associated with the FUT2 gene determining the secretor status. *PloS ONE*, *9*(4), e94863. doi:10.1371/journal.pone.0094863

Wadl, M., Scherer, K., Nielsen, S., Diedrich, S., Ellerbroek, L., Frank, C., et al. (2010). Food-borne norovirus-outbreak at a military base, Germany, 2009. *BMC Infectious Diseases*, *10*(1), 30. doi:10.1186/1471-2334-10-30

Wen, J., Behloul, N., Dai, X., Dong, C., Liang, J., Zhang, M., et al. (2016). Immunogenicity difference between two hepatitis E vaccines derived from genotype 1 and 4. *Antiviral Research*, *128*, 36–42. doi:10.1016/j.antiviral.2016.02.002

Werber, D., Michaelis, K., Hausner, M., Sissolak, D., Wenzel, J., Bitzegeio, J., et al. (2017). Ongoing outbreaks of hepatitis A among men who have sex with men (MSM), Berlin, November 2016 to January 2017 – linked to other German cities and European countries. *Eurosurveillance*, *22*(5). doi:10.2807/1560-7917.ES.2017.22.5.30457

Werneck, L. M. C., Vieira, C. B., Fumian, T. M., Caetano, T. B., Emílio dos Santos, J., Ferreira, F. C., et al. (2017). Dissemination of gastroenteric viruses in the production of lettuce in developing countries: a public health concern. *FEMS Microbiology Letters*, *364*(9), 1–7. doi:10.1093/femsle/fnx085

Westrell, T., Dusch, V., Ethelberg, S., Harris, J., Hjertqvist, M., Jourdan-da Silva, N., et al. (2010). Norovirus outbreaks linked to oyster consumption in the United Kingdom, Norway, France, Sweden and Denmark, 2010. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin*, *15*(12), 19524. doi:10.2807/ese.15.12.19524-en

Weststrate, A. C., Knapen, D., Laverman, G. D., Schot, B., Prick, J. J., Spit, S. A., et al. (2017). Increasing evidence of tick-borne encephalitis (TBE) virus transmission, the Netherlands, June 2016. *Eurosurveillance*, *22*(11), 30482. doi:10.2807/1560-7917.ES.2017.22.11.30482

Wheeler, C., Vogt, T. M., Armstrong, G. L., Vaughan, G., Weltman, A., Nainan, O. V., et al. (2005). An outbreak of Hepatitis A associated with green onions. *New England Journal of Medicine*, *353*(9), 890–897. doi:10.1056/NEJMoa050855

Whitehead, K., & McCue, K. A. (2010). Virucidal efficacy of disinfectant actives against feline calicivirus, a surrogate for norovirus, in a short contact time. *American Journal of Infection Control*, *38*(1), 26–30. doi:10.1016/j.ajic.2009.03.015

WHO. (2010). The global prevalence of Hepatitis E virus infection and susceptibility: A systematic review. *World Health Organization*, *WHO/IVB/10*. https://apps.who.int/iris/handle/10665/70513

WHO. (2011). Vaccines against tick-borne encephalitis: WHO position paper. *Weekly epidemiological record / Health Section of the Secretariat of the League of Nations*, *86*(24), 241–256.

WHO. (2015a). *WHO estimates of the global burden of foodborne diseases: foodborne disease burden epidemiology reference group 2007-2015.*

WHO. (2015b). Hepatitis E vaccine: WHO position paper, May 2015. *Releve epidemiologique hebdomadaire*, *90*(18), 185–200. http://www.ncbi.nlm.nih.gov/pubmed/25935931

WHO. (2016). *Global Health Sector Strategy on Viral Hepatitis 2016-2021 : Towards ending viral hepatitis*.

https://www.who.int/hepatitis/strategy2016-2021/ghss-hep/en/

WHO. (2019). Hepatitis E. *WHO*. World Health Organization. https://www.who.int/biologicals/areas/vaccines/Hepatitis_E/en/. Accessed 8 February 2020

Wikswo, M. E., Hall, A. J., & Centers for Disease Control and Prevention. (2012). Outbreaks of acute gastroenteritis transmitted by person-to-person contact--United States, 2009-2010. *Morbidity and mortality weekly report. Surveillance summaries (Washington, D.C.: 2002)*, *61*(9), 1–12. http://www.ncbi.nlm.nih.gov/pubmed/23235338. Accessed 9 February 2020

Williams, R. A., & Zorn, D. J. (1997). Hazard analysis and critical control point systems applied to public health risks: the example of seafood. *Revue Scientifique et Technique (International Office of Epizootics)*, *16*(2), 349–58. doi:10.20506/rst.16.2.1028

Winter, J. E. (1973). The filtration rate of *Mytilus edulis* and its dependence on algal concentration, measured by a continuous automatic recording apparatus. *Marine Biology*, *22*(4), 317–328. doi:10.1007/BF00391388

Wold, W. S. M., & Ison, M. G. (2013). Adenoviruses. In D. M. Knipe & P. Howley (Eds.), *Fields virology: Sixth edition* (6th ed., pp. 1734–1767). Wolters Kluwer Health Adis (ESP).

Wood, D. J. (1988). Adenovirus gastroenteritis. *British Medical Journal (Clinical research ed.)*, *296*(6617), 229–30. doi:10.1136/bmj.296.6617.229-a

Wu, F.-T., Chen, H.-C., Yen, C., Wu, C.-Y., Katayama, K., Park, Y., et al. (2015). Epidemiology and molecular characteristics of norovirus GII.4 Sydney outbreaks in Taiwan, January 2012-December 2013. *Journal of Medical Virology*, *87*(9), 1462–70. doi:10.1002/jmv.24208

Wu, H. M., Fornek, M., Schwab, K. J., Chapin, A. R., Gibson, K., Schwab, E., et al. (2005). A Norovirus outbreak at a long-term-care facility: The role of environmental surface contamination. *Infection Control & Hospital Epidemiology*, *26*(10), 802–810. doi:10.1086/502497

Wu, T., Zhu, F.-C., Huang, S.-J., Zhang, X.-F., Wang, Z.-Z., Zhang, J., & Xia, N.-S. (2012). Safety of the hepatitis E vaccine for pregnant women: A preliminary analysis. *Hepatology*, *55*(6), 2038–2038. doi:10.1002/hep.25522

Xia, M., Wei, C., Wang, L., Cao, D., Meng, X.-J., Jiang, X., & Tan, M. (2016). Development and evaluation of two subunit vaccine candidates containing antigens of hepatitis E virus, rotavirus, and astrovirus. *Scientific Reports*, *6*(1), 25735. doi:10.1038/srep25735

Xie, Y., Hajdok, C., Mittal, G. S., & Warriner, K. (2016). Inactivation of MS2 F(+) coliphage on lettuce by a combination of UV light and hydrogen peroxide. *Journal of Food Protection*, *71*(5), 903–907. doi:10.4315/0362-028x-71.5.903

Yamashita, T., Ito, M., Tsuzuki, H., & Sakae, K. (2001). Identification of Aichi virus infection by measurement of immunoglobulin responses in an enzyme-linked immunosorbent assay. *Journal of Clinical Microbiology*, *39*(11), 4178–80. doi:10.1128/JCM.39.11.4178-4180.2001

Yamashita, T., Sakae, K., Tsuzuki, H., Suzuki, Y., Ishikawa, N., Takeda, N., et al. (1998). Complete nucleotide sequence and genetic organization of Aichi virus, a distinct member of the Picornaviridae associated with acute gastroenteritis in humans. *Journal of Virology*, *72*(10), 8408–12. http://www.ncbi.nlm.nih.gov/pubmed/9733894. Accessed 10 December 2019

Yamashita, Y., Ootsuka, Y., Kondo, R., Oseto, M., Doi, M., Miyamoto, T., et al. (2010). Molecular characterization of Sapovirus detected in a gastroenteritis outbreak at a wedding hall. *Journal of Medical Virology*, *82*(4), 720–6. doi:10.1002/jmv.21646

Yazaki, Y., Mizuo, H., Takahashi, M., Nishizawa, T., Sasaki, N., Gotanda, Y., & Okamoto, H. (2003). Sporadic acute or fulminant hepatitis E in Hokkaido, Japan, may be food-borne, as suggested by the presence of hepatitis E virus in pig liver as food. *The Journal of General Virology*, *84*(Pt 9), 2351–7. doi:10.1099/vir.0.19242-0

Yeh, H.-Y., Hwang, Y.-C., Yates, M. V., Mulchandani, A., & Chen, W. (2008). Detection of hepatitis a virus by using a combined cell culture-molecular beacon assay. *Applied and Environmental microbiology*, *74*(7), 2239–43. doi:10.1128/AEM.00259-08

Zhang, J., Shih, J. W.-K., & Xia, N.-S. (2015). Long-term efficacy of a hepatitis E vaccine. *The New England Journal of Medicine*, *372*(23), 2265–6. doi:10.1056/NEJMc1504302

Zheng, D.-P., Ando, T., Fankhauser, R. L., Beard, R. S., Glass, R. I., & Monroe, S. S. (2006). Norovirus classification and proposed strain nomenclature. *Virology*, *346*(2), 312–323. doi:10.1016/j.virol.2005.11.015

Zhou, X., de Man, R. A., de Knegt, R. J., Metselaar, H. J., Peppelenbosch, M. P., & Pan, Q. (2013). Epidemiology and management of chronic hepatitis E infection in solid organ transplantation: a comprehensive literature review. *Reviews in Medical Virology*, *23*(5), 295–304. doi:10.1002/rmv.1751

Zhou, Y.-H., Purcell, R. H., & Emerson, S. U. (2004). An ELISA for putative neutralizing antibodies to hepatitis E virus detects antibodies to genotypes 1, 2, 3, and 4. *Vaccine*, *22*(20), 2578–85. doi:10.1016/j.vaccine.2003.12.017

Zhu, F.-C., Zhang, J., Zhang, X.-F., Zhou, C., Wang, Z.-Z., Huang, S.-J., et al. (2010). Efficacy and safety of a recombinant hepatitis E vaccine in healthy adults: a large-scale, randomised, double-blind placebo-controlled, phase 3 trial. *Lancet (London, England)*, *376*(9744), 895–902. doi:10.1016/S0140-6736(10)61030-6