



Selected Viruses Detected on and in our Food

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Published online: 21 March 2018

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Abstract

Purpose of Review The purpose of this review is to provide an update on recent literature and findings concerning selected foodborne viruses. Two groups of viruses were selected: (a) the most important viruses contaminating food, based on numbers of publications in the last 5 years and (b) viruses infecting sources of food that might have an impact on human health.

Recent Findings Important foodborne viruses such as norovirus, hepatitis A and rotavirus are usually “only” contaminating food and are detected on the surface of foodstuffs. However, they are threats to human public health and make up for the majority of cases. In contrast, the meaning of viruses born from within the food such as natural animal and plant viruses is still in many cases unknown. An exception is Hepatitis E virus that is endemic in pigs, transmitted via pork meat and is recognised as an emerging zoonosis in industrialised countries.

Summary Even though the clinical meaning of “new” foodborne viruses, often detected by next generation sequencing, still needs clarification, the method has great potential to enhance surveillance and detection particularly in view of an increasingly globalised food trade.

Keywords Foodborne viruses · Emerging viruses · Zoonosis · Hepatitis E · Next generation sequencing

Introduction

Every form of live harbours its own range of viruses [1]. No wonder, they are also present on and in our food, being it of animal or vegetable origin, and are consumed on a regular basis [2]. Considering this fact, only relatively few outbreaks or cases of disease due to foodborne viruses are reported—in contrast to bacterial infections [3]. This may be largely due to inability of these viruses to infect humans and/or inactivation during food processing. However, there are also several reasons that hamper recognition and reporting. Foodborne viruses are highly diverse but the clinical signs they cause are usually not specific for the single virus and often rather general such as diarrhoea and malaise making diagnosis challenging and tedious. In addition, in case of human-to-human transmission after uptake of the virus, the initial foodborne origin may not be recognisable anymore if it is not extremely

obvious. Furthermore, lacking awareness of clinicians [4] and a limitation of concerted surveillance programmes for foodborne viruses may contribute to underreporting [5].

Interestingly, the most important foodborne viruses regarding case numbers and economic impact are not really borne from within sources of food but are contaminating the surface of foodstuffs. Examples are large outbreaks of Hepatitis A from frozen berries or norovirus present on salad and vegetables [6, 7]. Often, the people handling and processing food as well as contaminated water play a key role in transmitting viruses onto food [8]. On the other hand, our foodstuffs originate from living organisms that carry their own set of viruses. Hence, there is also a spectrum of viruses present within our food. The role of these viruses on our health is less studied and many viruses have only recently been detected by next generation sequencing (NGS).

New diagnostic methods may improve detection of foodborne viruses dramatically, allowing for more efficient surveillance programmes and enhancing our knowledge on the importance of viruses in food [9]. In contrast to traditional diagnostic methods, metagenomic approaches by NGS are untargeted and require no specific knowledge of the viral genome. For bacteria, conserved genetic markers such as 16S rRNA allow for amplicon sequencing and subsequent taxonomic analysis resulting in an efficient representation of the

This article is part of the Topical Collection on *Foodborne Pathogens*

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bacterial abundance in a sample [10]. Since there are no conserved genetic markers present in different virus families, metagenomic analysis of viral populations is based on untargeted shotgun sequencing. Basically, all nucleic acid present in a sample is sequenced concurrently and comparison of the resulting nucleotide or deduced protein sequence to existing databases allows identification of all viruses that are somewhat similar to existing database entries.

Thanks to NGS, the range of foodborne viruses detected on and in food is constantly increasing. However, a fully comprehensive overview is beyond the scope of this article. Therefore, a selection had to be made. Due to the lack of systematic surveillance on most foodborne viruses, it was not possible to use case numbers as selective parameter. Therefore, the number of PubMed entries in the last 5 years was taken as selective criterion (status on the 7th December 2017).

The Classics—Viruses Contaminating Food (Table 1)

Norovirus

Of the 558 articles matching to the search terms “foodborne” and “virus”, 272 comply with “foodborne” and “norovirus”. Undoubtedly, norovirus (NoV) ranks top among the most important causes of acute gastroenteritis in humans worldwide. Impressive annual numbers of up to 21 million illnesses, 71,000 hospitalisation and 800,000 deaths that are accounted to NoV in the USA alone show the importance of this virus for human public health [11•]. *Norovirus* is a genus within the family of *Caliciviridae*. Virus particles are 27–37 nm in diameter and unenveloped which accounts for the high tenacity and resistance to disinfection. The genome is a single-stranded positive-sensed RNA of 7.5–7.7 kb length and contains three open reading frames (ORF) [12]. Propagation of NoV in cell culture is notoriously difficult. Successful cultivation requires for example the addition of enteric bacteria expressing strain-suitable histo-blood group antigen (HBGA) [13] or stem cell-derived, nontransformed human intestinal enteroid monolayer cultures with addition of bile [14]. Due to these difficulties, the

recently published ISO standard method for NoV in food is based on quantitative RT-PCR [15]. Beside of humans, several mammal species were shown to harbour noroviruses, such as pigs, cattle, rodents, dogs, cats, bats and even sea mammals such as harbour porpoises and sea lions [16]. While NoV are mostly species-specific, human noroviruses were detected in pigs and cattle in Canada [17] and some porcine NoV isolates are genetically closely related to human NoV [18]. Zoonotic transmission may hence be possible. However, due to the high contagiousity, the most important mode of transmission is directly from human-to-human or indirectly via the contaminated environment. Particularly vulnerable are people on cruise ships, schools and other situations of dense clustering, even if hygiene standards are high. Based on genotype profiles, only 14% of all NoV outbreaks seem to be attributed to contaminated food [19]. The most relevant source of food contamination with NoV seems to be infected humans handling food rather than environmental contamination [20, 21]. However, outbreaks due to contaminated fruit (e.g. raspberries and strawberries [22, 23]), leafy vegetables [24] and particularly oysters [25] show that the combination of faecally contaminated water and uncooked foods is particularly dangerous. Thanks to molecular tracing of outbreaks and the acquired knowledge on sources and ways of transmission measures such as efficient disinfection and water treatment are increasingly taken to reduce the risk of foodborne NoV infections [26].

Hepatitis A Virus

The second most frequently reported foodborne virus in PubMed is hepatitis A virus (95 reports in the last 5 years). However, in contrast to NoV infection, hepatitis A (HAV) is a vaccineable disease. HAV is a member of the family *Picornaviridae* and belongs to the genus *Hepatovirus*. The virus particles come in two versions: naked, unenveloped icosahedral virions of 27 nm diameter that are shed in faeces and pseudo-enveloped virions that are found in the blood of infected people and in cell cultures [27]. The WHO estimates that hepatitis A virus (HAV) accounted for 14 million foodborne illnesses and 27.731 death in 2010 [28••]. However, the

Table 1 Selected viruses contaminating food

Virus	Family	Transmission	Clinical signs	Reservoir/host
Norovirus	Caliciviridae	Direct, water, environment, food	Gastroenteritis	Humans
Hepatitis A virus	Picornaviridae	Direct, water, environment, food	Hepatitis	Humans
Hepatitis E virus genotypes 1 and 2	Hepeviridae	Direct, water, environment, food	Hepatitis	Humans
Rotavirus A	Reoviridae	Direct, water, environment, food	Gastroenteritis	Humans (mainly children)
Adenovirus	Adenoviridae	Direct, water, environment, food	Gastroenteritis, respiratory, conjunctivitis	Humans (mainly children)
Sapovirus	Caliciviridae	Direct, water, environment, food	Gastroenteritis	Humans (mainly children)

prevalence and incidence vary significantly around the world. Based on the level of anti-HAV antibodies, endemicity is grouped into low (< 15%), intermediate (15–50%) and high (> 50%). Particularly high endemicity is observed in sub-Saharan Africa and India, while Western Europe, USA and Australia have low levels [29]. However, the disease burden in high endemicity regions is comparably low [30]. This “paradox of hepatitis A risk” is due to the fact that in endemic areas children are infected at early age, e.g. in sub-Saharan Africa, 90% of the 10-year-olds are antibody positive [31] but the infection in young children is often asymptomatic or atypical and triggers a robust immunity [32]. In contrast, in regions with low endemicity, an increase in more severe clinical outbreaks can be observed due to a high degree of susceptible, non-vaccinated and older people. Population movements and globalised markets play an important additional role [32]. For example, in 2013/2014, HAV-contaminated imported frozen berries led to the largest hepatitis A outbreak ever reported in Europe [6•]. As a result and to enhance comparability, the HAV laboratory network (HAVNET) recommended sequencing protocols in May 2013 to enable molecular tracing on an international basis [6•].

Hepatitis E Virus Genotypes 1 and 2

On the third place of the most frequently reported foodborne viruses is Hepatitis E virus (HEV) with 65 publications. HEV has gained a lot of attention in recent years. Hepatitis E may clinically be indistinguishable from Hepatitis A but Hepatitis E virus (HEV) is taxonomically unrelated to HAV. HEV is the most important member of the family *Hepeviridae* and the genus *Orthohepevirus*. Interestingly, similar to HAV, hepatitis E virus particles are unenveloped when excreted in faeces but pseudo-enveloped in blood and cell culture [33]. HEV viruses infecting humans belong to the species *Orthohepevirus A*, whereas B, C and D infect birds, rodents and bats respectively [34]. Hepatitis E viruses of the *Orthohepevirus A* species are further divided into the genotypes 1–8. Only the genotypes 1 and 2 are considered primary human pathogens that are transmitted by faecal–oral route. The genotypes 3 and 4 that are recognised as important zoonotic viruses are discussed in the second part of the review. The unenveloped viruses show high tenacity and can be detected in sewage and waste water [35]. Even though the main route of transmission is considered direct contact or faecal contamination of drinking water, HEV-1 and 2 strains may also be foodborne pathogens in developing countries with limited access to sanitation, hygiene and health systems. While the infections are usually self-limiting and often subclinical in immunocompetent people, these figures may rise to 10–30% in pregnant women and immunocompromised individuals [36]. Insufficient immune response to the infection may lead to chronic disease and virus

shedding [37]. However, in Western Europe, infection with HEV-1 or 2 is usually considered an imported or travel disease [36].

Rotavirus A

The fourth foodborne virus to be mentioned (36 entries) is rotavirus. Named after the wheel-like appearance they show on the electron microscope, rotaviruses (RV) are particularly dangerous for young animals and humans. The most important RV infecting mammals is the serogroup A. The WHO estimates that globally 215,000 children under 5 years died in 2013 due to rotavirus infection; nearly half of them in India, Nigeria, Pakistan and the Democratic Republic of the Congo [38]. However, this figure was up to 528,000 in the year 2000. A vaccine against rotavirus is on the market since 2006 and has significantly reduced the death rates due to rotavirus in children, e.g. by 65% in Mexico [39]. Rotaviruses belong to the family *Reoviridae* and form an own genus. They are genetically highly diverse, forming up to eight serogroups [40]. RVA can be detected in many animal species and is an economically important pathogen in suckling pigs and calves but is usually species-specific. Reports of zoonotic transmissions exist but the most important sources of human infection are humans [41, 42]. Foodborne transmission is mainly a problem in developing countries where also water contamination is frequent. In a recent surveillance study in Columbia, 20% of analysed municipal drinking water samples were RV-contaminated [43]. However, RV have also been detected in 13% of mussels in Southern Italy 2014–2015 [44].

Human Adenovirus

Human adenoviruses (HAdV), on the fifth place with 19 reports, are often involved in gastroenteritis (GE) in children, where they are considered the second most frequent cause of GE after rotaviruses [45]. However, they may also cause respiratory signs and eye infections. HAdVs belong to the genus *Mastadenovirus* within the family *Adenoviridae*. To date, there are seven species of human adenoviruses known (human mastadenovirus A–G) (ICTV 9th Report (2011)). The genus is non-segmented, linear double-stranded DNA of 35–36 kb length and the approximately 90 nm large virions are unenveloped, making them very resistant to environmental impacts [46]. Spread may be directly from person to person or via the faecal–oral route. Contaminated recreational and irrigation water seems to be a frequent source of infection [45]. Contaminated water may also lead to contamination of food. For example, human adenoviruses were recently detected on fresh parsley using a metagenomic approach [47] and are often contaminating shellfish [48]. No zoonotic transmission has been reported as adenoviruses are usually species-specific [49].

Sapovirus

The last virus showing over ten PubMed entries related to “foodborne” in the last 5 years is the human sapovirus (12 publications). Belonging to the *Caliciviridae* family (like NoV) and forming an own genus, it is a small (27–40 nm) unenveloped RNA virus. Similar to NoV, sapoviruses (SaV) which were only detected in 1977 are highly resistant to unfavourable environmental conditions. Currently, human and animal SaVs are classified into 15 genogroups based on the VP1 protein [50]. As HAdVs, sapovirus outbreaks are often reported in kindergartens, nurseries and schools. The outbreaks are of sporadic nature and are reported world-wide but particularly many reports are from Japan, where the virus was first studied and named after the city of origin of the first type strain: Sapporo [51]. Transmission is mainly direct faecal-oral or via contaminated environmental surfaces. However, several reports show food as source of infection such as catered box lunches in a junior high school or food served at a wedding hall in Japan [52]. Even though porcine SaV are regularly detected in porcine faeces, transmission to humans and zoonotic outbreaks have not been reported to date [53]. However, inter-genogroup recombination events of SaV in pigs have been reported and highlight the high genetic diversity and evolution rate of SaV [54].

Other Food-Contaminating Viruses

Other potentially foodborne viruses that may cause disease in humans but have lower numbers of publications are human astroviruses (*Astroviridae*), Aichivirus/human kobuvirus (*Picornaviridae*) and enteroviruses (*Picornaviridae*) [55•]. Astroviruses were even the most frequently detected viruses in mussels in Southern Italy [44]. However, the clinical importance of these viruses is not completely clear, and literature is controversial. They show worldwide spread and are detected in faeces of healthy individuals and may hence be part of the normal flora of the gastrointestinal tract [56, 57]. However, there are also reports of severe outbreaks of acute gastrointestinal disease, often in children under 5 years [58, 59]. Enteroviruses in particular are frequently detected in environmental samples and waste water used for irrigation [60]. It seems that most mammal species harbour their own astro-, entero- and kobuviruses [56, 61]. While interspecies transmissions seem to occur [56, 62], their frequency and consequences for human health require further investigations.

The “Newbies”—Viruses Intrinsicly Present in Food (Table 2)

The vast majority of humans rely on plants as major source of food. Metagenomic analysis of romaine and iceberg lettuce

has shown the presence of wide range of plant and animal/human viruses already on the field [63•]. It has also been shown that NoV can be internalised by some plants such as lettuce and strawberries through the root system and can therefore be present inside the plant and fruits rather than just contaminating the surface [64, 65]; similar to the internalisation and retention of acid resistant viruses in water filtering molluscs [66]. Even though being internalised, NoV, such as most animal and human viruses, is not able to infect or replicate in plant cells [67]. However, there are numerous viruses specifically infecting plants. Plant viruses are frequently detected in human and animal stool samples [68], but even though some virus families, like *Bunyaviridae*, *Rhabdoviridae* and *Reoviridae*, contain plant-, animal- and human viruses, no plant virus is known to be a human pathogen [69]. However, a report on the detection of antibodies against Pepper mild mottle virus (PMMoV) in patients with abdominal pains and virus positive stool samples points to interaction of the human immune system with this plant virus [70•]. Furthermore, some plant viruses are known to infect and persist in insect-vectors and one of them, Tomato spotted wilt virus, a member of the genus *Tospovirus* of the *Bunyaviridae* family, was even shown to replicate in human cell lines [71]. Due to the high genetic elasticity of their RNA genome and the broad (plant-) host range, tospoviruses are indeed discussed to have the potential to cross the kingdom-barrier [69].

In contrast to crossing the barrier between the plant and animal kingdom, it is far easier for viruses to cross species barriers. Exposure to animal viruses, mainly of other mammals, represents therefore a greater risk for human health. Since viruses are heat sensitive, raw or undercooked foodstuffs such as meat, milk and dairy products are the most likely sources for uptake of infectious animal viruses. Only recently, the range of viruses intrinsicly present in these products is being studied, mainly using NGS, and has revealed several “new” viruses.

Hepatitis E Virus Genotypes 3 and 4

The most emerging zoonotic foodborne viruses in third world countries may well belong to the Hepatitis E genotypes 3 and 4. HEV-3 and 4 strains infect humans, but the reservoir is thought to be in several animal species, whereof the pig plays the most important role for foodborne transmission. HEV-3 is distributed worldwide and represents the predominating genotype in Europe while HEV-4 is mainly reported from China, Japan, India and Indonesia [74•] but sporadic cases and virus detection have also occurred in Italy [75], France [76] and Belgium [77]. With seroprevalence rates of 46–100% in many countries, HEV seems to be endemic in piggeries and is also present in wild boar [74•]. In pigs, the virus causes only a subclinical disease with mild mostly microscopic lesions in the liver. Virus is shed for 3–7 weeks in faeces and

Table 2 Selected viruses detected within food

Virus	Family	Transmission	Clinical signs	Reservoir/host
Hepatitis E virus genotypes 3 and 4	Hepeviridae	Undercooked/raw pork, venison	Hepatitis	Porcine species, deer, rabbits
Tick-borne encephalitis virus	Flaviviridae	Unpasteurized goat milk	Meningoencephalitis	Ticks, infected mammals
Porcine parvovirus	Parvoviridae	Pork, Beef	None described	Pigs
Torque teno virus	Anelloviridae	Pork, Beef	None described	Pigs, cattle
Porcine circovirus	Circoviridae	Pork	None described	Pigs
Gyrovirus, chicken anaemia virus	Circoviridae	Poultry	None described	Chicken
Bovine polyomavirus	Polyomaviridae	Beef	Colorectal cancer hypothesised [72]	Cattle
Bovine leukaemia virus	Retroviridae	Beef, milk	Breast cancer hypothesised [73]	Cattle
Pepper mild mottle virus	Virgaviridae	Peppers, chillis	Gastroenteritis hypothesised [70•]	<i>Capsicum</i> spp.

transmission between animals is via the faecal–oral route [78]. The first foodborne transmission of HEV was observed in Japan where identical virus sequences were found in a diseased patient and in sika deer meat [79]. Additional reports, linking human cases to grilled wild boar meat in Japan and pig meat in Spain supported the initial finding. Salines et al. (2017) [80•] have summarised the reports of HEV contaminations in meat products and found highest virus prevalence in pork liver pâtés (47% in Canada and 36% in Brazil) and dry-cured sausages containing pig liver such as the figatelli from Corsica in France (30%). Other sources of infection for humans are game meat (deer and probably rabbit) and food potentially contaminated by pig/wild boar faeces such as wild herbs [81]. Human-to-human transmission may occur but seems to be rare; however, blood transfusion has been reported as a transmission pathway [82]. In humans, most infections seem to be subclinical; the most severe clinical signs are observed in older males and patients with pre-existing liver diseases or increased alcohol consumption [83, 84]. A meta-analysis of 432 studies on the HEV seroprevalence in humans in Europe from 2003 to 2015 showed a wide range from 0.6 to 52.5%. Contact to swine/wild animals had a significant influence as well as the type of assay used and the geographical area with highest mean values in France (32%) and lowest in Italy (7.5%) [85•]. The surveillance report of the European Centre for Disease Control (ECDC) that includes data of 22 EU/EEA member states (accounting for >90% of the total EU/EEA population) provides data on confirmed cases of HEV for 2005–2015 and shows an annual three-fold increase in the number of annual cases between 2011 and 2015 [86•]. However, HEV-3 was already present in German wild boars as early as 1995/1996 [87] and in India in 1988 [88] as the analysis of archived samples has shown. Therefore, it may well be that the disease and its zoonotic aspect has been largely overlooked for decades and acute cases regarded as hepatitis A. Only recently, routine diagnostic tools are available

and awareness in clinicians has grown. Similar to HAVNET for hepatitis A, HEVNET which was initiated 2017 aims at concerting and harmonising HEV surveillance in Europe [86•] and governs a HEV sequencing repository for molecular tracing of outbreaks as well as a public HEV online typing tool (<http://www.rivm.nl/mpf/typingtool/hev/>). However, while research and surveillance of the disease in humans is increasing, many aspects of the virus life cycle and epidemiology in pigs are still unknown. Due to the lack of clinical signs, HEV has not been of veterinary importance so far. However, in order to fully understand and counteract the disease in humans, this gap needs to be closed.

Tick-borne Encephalitis Virus in Milk

Another animal product that may contain viruses is milk. While it is well known that several important bacterial diseases can be attained by consuming raw milk or dairy products such as brucellosis, tuberculosis and listeriosis, not so much is known about transmission of zoonotic viruses by milk. An exception is the confirmed transmission of tick-borne encephalitis virus (TBEV) via goat milk leading to human infection [89, 90]. A study in a high TBE risk region in Poland showed 22.2% of sheep milk positive for TBEV by RT-PCR followed by goat milk (20.7%) and cow milk (11.1%) [91]. Importantly, even though TBEV and other related tick-borne flaviviruses, being enveloped RNA viruses, are not generally considered particularly resistant to environmental influences, they may survive low pH conditions such as present in the stomach. However, while Langat virus, a close relative to TBEV, survived conditions present during cheese production, it was completely inactivated by pasteurisation [92]. Raw milk cheese, particularly of sheep and goats may thus present a source of infection for the potentially lethal TBEV and probably other tick-borne flaviviruses.

Foodborne Animal Viruses with Unclear Zoonotic Potential

While foodborne HEV and TBEV clearly represent a threat for human public health, the role of several other viruses of animal origin detected in food still needs to be assessed. Zhang et al. (2014) [93••] have used NGS to search for viruses present in beef, pork and chicken bought in supermarkets in San Francisco. The muscle tissue they analysed was explicitly taken from the centre, not the surface of the meat pieces. Interestingly, all viruses found were small, unenveloped DNA viruses, mostly of the *Parvoviridae* family. In pork, they found sequences of four different parvovirus species of three parvovirus genera. Parvoviruses are among the smallest DNA viruses (Latin “parvus” = small) with a diameter of only 18–28 nm and are particularly resistant to disinfection and environmental conditions. They are frequently detected in faeces of diverse domesticated and wild animal species and humans, and may range from asymptomatic to highly virulent causing mainly enteric diseases [94]. Even though they are usually species-specific, interspecies transmission is occurring as in the case of canine parvovirus-2 that is thought to originate from cats [95]. Interestingly, porcine parvovirus was also detected in beef which may point to an interspecies transmission [93••].

Other DNA viruses detected in beef and pork are Torque teno viruses (TTV) of the *Anelloviridae* family and members of the *Circoviridae* family (e.g. porcine circovirus-2 in pork) [93••]. For TTV alone, no clear association with disease, but a role in rendering other infections (e.g. by circoviruses) more virulent is discussed in pigs [96]. However, newer studies have not observed a correlation of post-weaning multisystemic wasting syndrome (PMWS) caused by porcine circovirus-2 and the presence of TTV [97]. Interestingly, human and animal TTVs are often detected in sera by NGS, even in healthy individuals [98, 99]; this may also be the reason why they are present in meat. Porcine circovirus-2 (PCV-2) is endemic in pigs and associated with several clinical syndromes. It is also present in skeletal muscle tissue of infected pigs which was shown to be infectious for other pigs after oral uptake [100]. No antibodies against PCV-2 were detected in humans so far but a certain risk for immunocompromised humans after receiving porcine xenotransplants is discussed [101]. PCV-2 as well as parvovirus may also originate from live attenuated vaccines that are routinely used in piggeries [102]. However, even though infectious PCV-1 was detected as a contaminant of a human rotavirus vaccine, no seroconversion was detected in the vaccinated children [103].

In the analysed chicken, sequences matching to six different types of gyroviruses were detected [93••]. They belong to the family of *Circoviridae* but are structurally similar to *Anelloviridae* and are small unenveloped viruses with a circular DNA genome of about 2.3 kb. The most prevalent and world widely distributed representative of this genus is the

chicken anaemia virus (CAV) that infects and induces apoptosis in erythropoietic and lymphatic progenitor cells leading to anaemia and immunosuppression in young chicken. Vaccines against this virus are routinely used in poultry farms [104]. CAV sequences have been detected in faeces of children and cats but due to the low copy numbers it is assumed that they are of dietary origin without infecting human cells [105]. Even though several gyroviruses with high similarity to CAV were detected on the skin, in the blood and in faeces of immunocompromised humans, no antibody response against CAV was observed [106].

In contrast to gyrovirus, antibodies against an animal polyomavirus (BPyV) have been reported in humans. *Polyomaviridae* are relatively small (50 nm) unenveloped viruses with a circular, double-stranded DNA genome of 5 kb length and consist of the genera *Alpha-*, *Beta-*, *Gamma-*, *Deltapolyomavirus*. Polyomaviruses have shown to persist in the organs of humans and many animal species, usually without causing overt clinical signs. However, in immunocompromised patients, an association with oncogenesis through transformation of infected cells has been proposed [107]. Since this transformation is due to integration of viral DNA into the host genome—particularly in non-permissive infections—the relatively high seroprevalence against bovine polyomavirus (BPyV-1) in people handling cattle such as farmers, vets and abattoir workers was of some concern [108]. Based on epidemiological data, it was also speculated that BPyV in red meat might have an etiological role in the development of colorectal cancer in humans regularly consuming beef [72]. Furthermore, the presence of a novel BPyV-2 in beef was recently shown by metagenomic analysis [93••]. However, while BPyV seems to be highly prevalent in cattle and may be transmitted to humans, no disease has yet been clearly attributable to the infection neither in cattle nor in man [108].

Another virus that is contradictorily discussed regarding its clinical meaning in humans after foodborne transmission is bovine leukaemia virus (BLV). BLV is endemic in cattle in many countries where it causes leukosis in 2–5% of infected animals [109]. Its presence in meat and dairy products has been shown [110] and Buehring et al. (2003) [111] found antibodies against BLV capsid antigen in 74% of human serum samples using immunoblotting. There are also several reports claiming an association of breast or colon cancer with BLV [73, 112]. However, data from a recent study in China did not detect any BLV genome or antibodies against BLV in women with or without breast cancer even though the virus- and antibody prevalences of cows in the analysed regions were high [113]. In addition, being a member of the Retrovirus family, BLV is highly susceptible to inactivation and it is unlikely to survive gastric conditions. However, more data are required to conclude on the foodborne zoonotic potential of BLV.

Non-Oral Transmission of Important Foodborne Zoonotic Viruses

Even viruses prone to inactivation by low gastric pH levels and proteases may cause foodborne infection if uptake occurs via a non-oral route. Occupational groups like abattoir worker, vets and butchers may become infected thorough animal blood, body fluids and excretions via skin lesions, mucous membranes or by inhalation of aerosols [55•]. It is assumed that several important human viruses such as HIV, SARS coronavirus and Ebola were and still are crossing the species barrier not primarily through the consumption of meat but mainly during the butchering process of animals carrying the viruses such as primates and bats [114, 115]. Similarly, live poultry markets and culling of infected birds was shown to be a significant risk factor for human infection with H5N1 influenza virus [116, 117].

Conclusions

The classic foodborne pathogens such as NoV, HAV and Rotavirus make up the majority of clinical cases in humans. These viruses are adapted to humans and are efficiently transmitted between humans, making it often difficult to untangle foodborne and direct human-to-human transmission. Furthermore, in case of relatively “novel” foodborne viruses such as Astroviridae or Sapoviruses, it is often difficult to differentiate between “commensal” viruses, opportunistic pathogens and real threats for human public health. NGS has made it possible to non-specifically screen food for viruses and has shown that many intrinsic plant and animal viruses are also present in food products. The finding of several types of circo- and parvoviruses in beef, pork and poultry shows that also pure muscle tissue of apparently healthy animals harbours a surprising range of viruses [93••]. The high tenacity of these small unenveloped DNA viruses means that they can also be present in processed meat. This is supported by own observations, where NGS sequencing reads obtained from a dry cured pork sausage covered not only the whole genome of HEV [118] but also of porcine circo- and parvoviruses as well a plant virus (Pepino mosaic virus) in high depth (unpublished data). It is not sure if these viruses remained infectious in the sausage. However, the HEV sequence was identical to the virus isolated from a patient with acute hepatitis who consumed this type of sausage [118, 119].

Hence, new diagnostic tools have massively enhanced the possibility to detect foodborne viruses but subsequent virological, clinical and epidemiological studies are necessary to determine the importance of these findings for human health. However, increasing globalisation of the food trade facilitates introduction of new or “exotic” viruses and demands for broad range surveillance tool on an international scale. Therefore,

establishment of suitable protocols for non-specific screening of foods using NGS and endeavours towards concerted molecular tracing such as HAV- and HEVNET are essential tools for the control of foodborne viruses in the future.

Compliance with Ethical Standards

Conflict of Interest The author declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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Recently published papers of particular interest have been highlighted as:

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