Zeitschrift: Mitteilungen aus dem Gebiete der Lebensmitteluntersuchung und Hygiene = Travaux de chimie alimentaire et d'hygiène

Herausgeber: Bundesamt für Gesundheit

Band: 88 (1997)

Heft: 2

Artikel: Food and waterborne viral gastroenteritis : a review of agents and their epidemiology

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DOI: https://doi.org/10.5169/seals-982317

Mitt. Gebiete Lebensm. Hyg. 88, 119–150 (1997)
Received 14 October 1996. Accepted 20 December 1996

Food and Waterborne viral Gastroenteritis: a Review of Agents and their Epidemiology

Key words: Viral gastroenteritis, Food, Water, Epidemiology, Review

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Introduction

Diarrheal diseases affect millions of people world-wide, having the greatest impact among children, especially in developing countries. They are also of public health importance in developed countries and are associated with considerably morbidity and a substantial number of hospitalisations among children and the elderly (1). In these countries the estimated median percentage of diarrheal episodes in children associated with specific agents was given by Bern et al. (1) as approximately 30% caused by rotaviruses, 15% by bacteria, and 15% by other viruses. However, in about 40% of the episodes an agent was not recognised.

Until 25 years ago the causes of acute non-bacterial gastroenteritis were unknown, even though John Zahorsky, an American paediatrician, described a syndrome which he named winter vomiting disease in 1929 (2). A viral agent was first described by *Kapikian* et al. in 1972 (3) to be the etiological agent of the syndrome following an outbreak in Norwalk Ohio (4) in 1969.

Two patterns of disease exists endemic and epidemic non-bacterial gastroenteritis. Food and water seem to play an important role in epidemics. Foodborne or waterborne diseases, defined by WHO as «a disease of an infectious or toxic nature caused by, or thought to be caused by, the consumption of food or water» (5), are an important burden of communicable diseases in developed countries. The Centres for Disease Control and Prevention (CDC) in Atlanta, USA, estimate that contaminated food causes 6.6 million acute illnesses and 9000 associated deaths annually in the US alone. Unlike many other communicable diseases, foodborne illness is largely preventable in developed countries (6). Those most at risk are usually infant, the very old or those debilitated by pre-existing conditions such as AIDS (7). Although episodes of diarrhoea usually are of acute character, studies

suggest that there is also a chronic component in about 1% of affected people who may develop long-term sequelae (7).

Foodborne viral gastroenteritis is of emerging importance (7) and several viruses have been identified as etiological agents. The WHO defines a foodborne outbreak as «compromising two or more people having a similar illness after eating the same food and on the whole, some level of epidemiological evidence indicating the implicated food as a common factor to those ill, or isolation of the disease-causing agent from the food, is required» (8). Transmission by food or water has been documented for astroviruses, caliciviruses, rotaviruses and a group defined as «small round structured viruses» (SRSVs), also known as Norwalk-like viruses (9). However, the diagnosis of viral gastroenteritis is far from routine, and the etiological agents not always easily identified. In this article the possible agents of foodborne and waterborne viral gastroenteritis are reviewed.

Astrovirus

Classification

Astroviruses were first described in 1975 (10). The genome organisation lead to the establishment of the family of Astroviridae (11, 12) with human astrovirus 1 (HAstV-1) as type species (13). Seven serotypes of human astroviruses were reported (13–16).

Virology

Astroviruses are single stranded RNA viruses of 28–30 nm, non-enveloped and of cubic symmetry (fig. 1). The particles have a characteristic morphology of round smooth edges with multiple triangular electron-lucent areas and an electron dense centre, which results in a star-like appearance (17).

Endemic disease

Astroviruses are distributed world-wide. Infections occur throughout the year but peaks during winter (15) and spring (14) are recognised. The illness is most common among one to three year old infants (14). An antibody prevalence survey of children in Oxfordshire, UK showed a rise from 4% in 6–12 month old to 64% in three to four year olds, and 87% in five to ten year olds (18). A study into the prevalence of astroviruses was undertaken in the same area and involved the serotyping of 291 astrovirus positive stools collected between 1976 and 1992 and showed 64.9% were serotype 1. Other serotypes varied in frequency between 1%–7% (14, 15). The infections were also more frequent in the last quarter of the

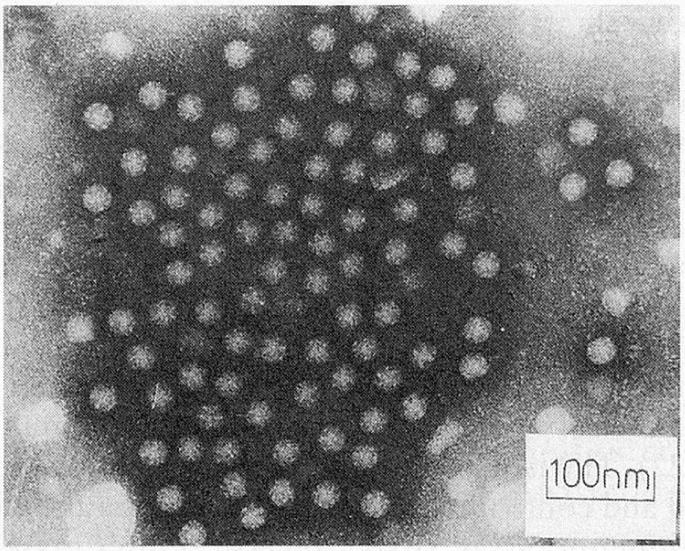

Fig. 1. Astroviruses (Kindly submitted by Dr. E.O. Caul, Public Health Laboratory Bristol, UK)

year. During the last five years of the study serotype 1 occurred with greater frequency in alternate years (16).

Astroviruses appear to be the most common causes of diarrhoea in immunocompromised adults with human immunodeficiency virus infection (HIV) (19).

Clinical syndrome

The incubation period is between three to four days (14, 15, 17), however, CDC reports an incubation period of 24 to 36 hours (20). Other authors describe incubation periods of 1 to 4 days (21). The main symptoms are fever ≥37 °C, headache, malaise, anorexia, nausea, abdominal pain (20), occasionally vomiting occurs (15); within 24 hours of systemic symptoms the diarrhoea begins, typically unformed or watery with two to six episodes per day, which may last two to 14 days (14, 15). Virus excretion usually continues for the duration of the diarrhoea (15), but chronic infections in the immunocompromised have been reported (14). Complications following astrovirus infections are temporary monosaccharide intolerance for one to two weeks and in very rare cases intolerance to cow's milk protein for 10 to 16 months (15).

Outbreak characteristics

Outbreaks mainly occur in the family, nurseries and in paediatric wards. Others are associated with eating oysters or drinking contaminated water (14). *Kurtz* describes an outbreak in an old peoples home with astrovirus type 1 with an attack rate of 80% among residents, and 44% among staff (14). Adults are rarely affected (14), and only a few food associated outbreaks are reported in the UK (14). One of the first foodborne outbreaks described was associated with eating oysters which

were infected by Norwalk viruses and astroviruses simultaneously. Contamination with both viruses lead to characteristic symptoms after the specific incubation periods of 24 hours and four days respectively. Mixed infections within one outbreak are quite common, especially in seafood (14). Food and waterborne outbreaks are rare (15) but in 1994 a large outbreak of acute gastroenteritis associated with astrovirus type 6 among students and teachers in Osaka, Japan, was reported. This outbreak affected more than 4700 people and lasted for five days and was believed to be linked to a common supplier, although no specific epidemiological investigation was undertaken. Attack rates were not calculated because the denominator was missing. In an outbreak in a kindergarten an attack rate of 50% was reported with secondary transmission of the illness to families occurring in one third of the cases (22). The isolates of the Osaka outbreak caused by astroviruses have been identified and confirmed with solid phase immune electron microscopy (SPIEM), enzyme immuno assay (EIA), reverse transcriptase polymerase chain reaction (RT-PCR), and virus isolation in CaCo-2 cells. The illness was reported to be relatively mild but with a high attack rate, contrary to volunteer studies. The outbreak was widespread and abrupt throughout the school system. This outbreak was the largest viral gastroenteritis outbreak associated to astrovirus (23).

Management of foodborne/waterborne outbreaks

Basically all viral gastroenteritis may be managed the same way to prevent further spread. The measures given for Norwalk virus may be principally used for astroviruses also.

Mode of transmission

The mode of transmission in astrovirus infections may be via the faecal-oral route directly or indirectly via fomites, food, and water. Another route is person-to-person spread in families, nurseries, and paediatric wards where infections may be endemic (14). Recently astrovirus has been associated with bathing waters (24). The risks to windsurfers and yachtsmen of virus infections was described in an age matched study, 93% of surfers had serological evidence of exposure to astrovirus type 4, compared with 22% of the controls who did not bathe in the sea. All the surfers had suffered diarrheal illness in the previous 12 month, whereas only 39% of the controls reported a similar event.

Consumption of contaminated water and shellfish have given rise to outbreaks in the UK (14).

Diagnosis

Electron microscopy is the method of choice. Astroviruses may be seen from one day before the onset of diarrhoea and may persist in faeces for two to four days

(15). Only about 10% of particles show the star like appearance, which results in an underestimation of astrovirus incidences, because these particles will be labelled as small round structured viruses (SRSV) (15). Astrovirus does not grow in conventional tissue cultures.

Environment

Astroviruses are found in different animals but no cross reaction between the different astroviruses from animal sources and human astrovirus is described (13, 15). Astroviruses are acid stable (pH 3) for one hour, and do survive at 50 °C for 30 minutes, at 60 °C the concentration of viruses drops three log in five minutes and six log in 15 minutes. Additionally they resist inactivation with alcohols, and are stable to lipid solvents (14, 15).

Immunity

High titres in most developed countries (14) are found and 75% of British children for example have acquired antibody by the age of ten years (18).

Conclusions

Astrovirus is an important cause of outbreaks of diarrhoea among children attending day care centres. More frequently younger children are infected, and often asymptomatic infections occur (25). The viruses are distributed world-wide and are associated with about 2–8% of acute nonbacterial gastroenteritis in children. The predominant feature of the infection in humans is a selflimiting gastroenteritis (13). The role of foodborne and waterborne outbreaks seems to be anecdotal and rare. Nevertheless such outbreaks do occur as exemplified by the Osaka outbreak (23). Other routes of infections via the environment for example water for recreational purposes are under discussion.

Human calicivirus (HuCV)

Classification

The first description of the HuCV was in 1976 (26). Immuno-electron microscopy (IEM) studies have shown that there are at least five strains of HuCV (27). Early nomenclature describes the agent as «classical caliciviruses» (28) with the serotypes UK1–UK4 (29).

Virology

Caliciviruses have a characteristic surface morphology and are single stranded RNA viruses of 30–40 nm (28). They are non-enveloped and of spherical symmetry. The particles have a characteristic morphology (fig. 2) when viewed along their two-(four hallows), three- (Star of David), and five fold (ten-spiked sphere) axes. They contain of 32 cups (*calices*) on the surface which are used to describe the family (30).

Endemic disease

Surveys in different countries of children with gastroenteritis have been performed and the prevalence of children excreting HuCV was 1.3% (Norway), 1.8% (UK), 1.2% (Japan), 0.5% (Australia), 0.3% (USA) and 1.5% (China) (30). Based on antibody-prevalence studies of pooled immunoglobulin and serum samples of different areas of the world, most people appear to be infected by the age of 12 years (20). The peaks of acquisition are found between six months and two years (30). A seasonality is not yet known (20).

Clinical syndrome

The predominance of various symptoms varies between different outbreaks. In adults, nausea, malaise, aching limbs, and headache in combination with diarrhoea and vomiting are often reported (20, 30). These symptoms are indistinguishable from those caused by Norwalk virus, or Norwalk-like viruses, and often are described as «gastric flu» (30). Volunteer studies have reported the following features: Incubation period: 12–72 hours with mild symptoms of 1–11 days duration

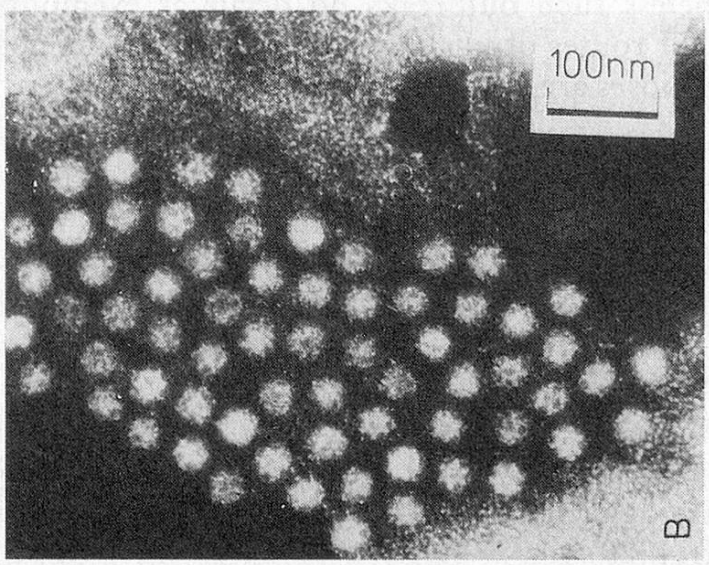

Fig. 2. Caliciviruses (Kindly submitted by Dr. E.O. Caul, Public Health Laboratory Bristol, UK)

with a mean of 3.6 days ± 1.9 days (29). The CDC describes incubation periods of one to three days, with illness lasting on average for four days (20). Upper respiratory tract symptoms (20) are believed to be caused by co-infection with other viruses such as echoviruses and adenoviruses (30).

Outbreak characteristic

The reported calicivirus outbreaks occurred mainly in institutional settings (20). Cross-infection within hospitals, day-care centres, and homes for the elderly is common (30). Attack rates vary with age. However, outbreaks with elderly persons result in higher rates (nearly 100%) than adults (>30%) or children (24–66%). The clinical symptoms vary with age. Most dominant are vomiting, diarrhoea, abdominal pain. Fever is not often reported (30). Asymptomatic persons may also occur and may serve as an important reservoir of infection. Two quite different epidemiological patterns exist. The HuCV UK4 viruses have been associated with large foodborne outbreaks due to cold foods, or shellfish harvested from contaminated water. In these outbreaks high attack rates among all age groups are reported. On the other hand, outbreaks caused by the type UK1 or UK2 particularly affect children and are mainly spread by person-to-person, although nurses and parents in close contact with sick children remained well (31).

Management of foodborne/waterborne outbreaks

Basically all viral gastroenteritis may be managed the same way to prevent further spread. The description given for Norwalk virus may be used for HuCV also.

Mode of transmission

Human caliciviruses are spread by four different routes (1) direct or indirect faecal oral route via contamination of surfaces or hands (2), primary contaminated food or water (e.g. oysters, clams, mussels, and water contaminated at source) (3) secondary contaminated food by food handler (e.g. sandwiches, salads etc.) and (4) by the airborne route through inhalation of aerosols of vomites or faeces (20, 30, 31).

Diagnosis

Diagnosis of the HuCV is almost entirely dependent on the use of electron microscopy.

Environment

The infectious dose of HuCV is believed to be as low as 10–100 virus particles. Caliciviruses can additionally remain infectious for several years (30).

Immunity

In some reported outbreaks of HuCV among children, mothers were rarely infected, which suggests that young adults retain effective immunity from previous exposures. But as mentioned above the epidemiological pattern of the different strains remains unclear. In elderly people this immunity may wane (20).

Conclusion

HuCV and other caliciviruses play an important role in viral gastroenteritis. Also the food and waterborne routes seems to be quite common. Together with other caliciviruses (SRSV) as described below, this genus is the most important in respect to food or waterborne outbreaks.

Norwalk Virus and Norwalk-like Viruses

Classification

The classification of Norwalk and Norwalk-like viruses is not easy as this group cannot be cultured. Without sufficient antigens a classification of these viruses remained difficult. As a result the viruses in this group have been given different labels related with their place of isolation, or description by different authors. Historically American authors defined viruses according to the first isolation (e.g. Norwalk (4), Hawaii agent (32), Snow Mountain agent (33), Montgomery County virus (34) etc.).

In 1982 *Caul* and *Appelton* proposed an interim scheme for the classification of this group of viruses (fig. 3). Criteria selected were the size, the buoyant density (BD) and the morphological feature for the grouping. Following this scheme viruses with a size range between 30–35 nm, BD of 1.36–1.41 g/ml and amorphous surface and ragged outline were described as small round structured viruses (SRSV) (35). Therefore Norwalk and Norwalk-like viruses (e.g. Montgomery county, Hawaii agent, Southampton, Taunton, Desert shield etc.) are classified within this group. For practical reasons this scheme is useful and used to describe the epidemiological situation of viral gastroenteritis in the UK.

Japanese authors on the other hand described their isolates as SRSV1 to SRSV9 (36). Later, British groups described four groups designated as SRSV UK1 (Taunton

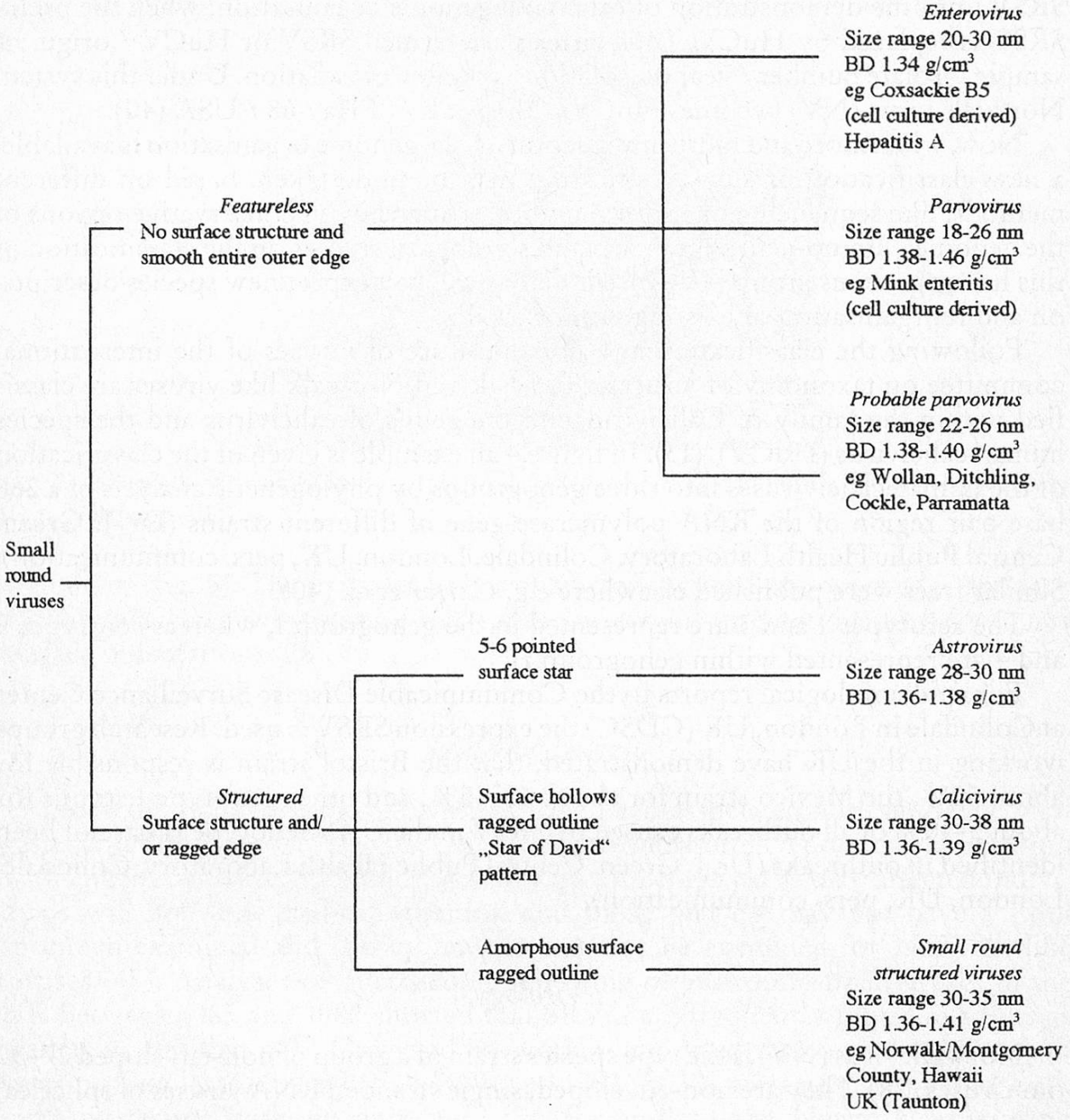

Fig. 3. Interims classification scheme for small round viruses (35). BD: Buoyant Density.

agent), SRSV UK2 (Norwalk agent), SRSV UK3 (Hawaii agent), and SRSV UK4 (Snow mountain agent), which also was correlated to SRSV9, the Japanese grouping (37) or as Serotype 1 (Norwalk), serotype 2 (Hawaii), Serotype 3 (Snow mountain) and Serotype 4 (Taunton) (38). American research groups classified Norwalk-like viruses recently into six antigenic groups: the four types (UK1 to UK4) previously defined in the UK and the Oklahoma agent described in their study (39).

Several different descriptions of these viruses were and are used in the literature. Today, when first observed under the electronmicroscop, viruses are named human caliciviruses (HuCV) or small round structured viruses SRSV by their morphology. If this is typically caliciviral, membership of this family is likely. Viruses are named

SRSV until the demonstration of caliciviral genome organisation, when the prefix SRSV is replaced by HuCV. Thus viruses are termed SRSV or HuCV / origin of sample / isolate number / year of isolation / country of isolation. Under this system Norwalk-virus (NV) becomes HuCV / Norwalk / 8FIIa / 68 / USA (40).

Now, when more and more information on the genome organisation is available, a new classification or sub-classification may be undertaken, based on different methods, like sequencing of entire genomes, sequencing of conservative regions of the genomes, amino-acid alignments and serological studies on the classification of this heterogeneous group (41–47). Therefore we may expect new species description and reorganisation of existing groups.

Following the classification and nomenclature of viruses of the international committee on taxonomy of viruses, Norwalk and Norwalk like viruses are classified within the family of Caliciviridae in the genus of calicivirus and the species human calicivirus (HuCV), (13). In figure 4 an example is given of the classification of the human caliciviruses into three genogroups by phylogenetic analysis of a 266 base pair region of the RNA polymerase gene of different strains (Dr. J. Green, Central Public Health Laboratory, Colindale, London, UK, pers. communication). Similar trees were published elsewhere e.g. *Carter* et al. (40).

The serotypes 1 and 3 are represented in the genogroup I, whereas serotypes 2 and 4 are represented within genogroup II.

For epidemiological reports to the Communicable Disease Surveillance Center at Colindale in London, UK (CDSC) the expression SRSV is used. Research groups working in the UK have demonstrated, that the Bristol strain is responsible for about 50%, the Mexico strain for about 40–45%, and other genotype I strains for about 5–10% of all outbreaks caused by SRSV in the UK. Genotype II has not been identified in outbreaks (Dr. J. Green, Central Public Health Laboratory, Colindale, London, UK, pers. communication).

Virology

Norwalk virus (NV) is the type species strain of a group of non-enveloped 27–32 nm viruses (28). They are non-enveloped, single stranded RNA viruses of spherical

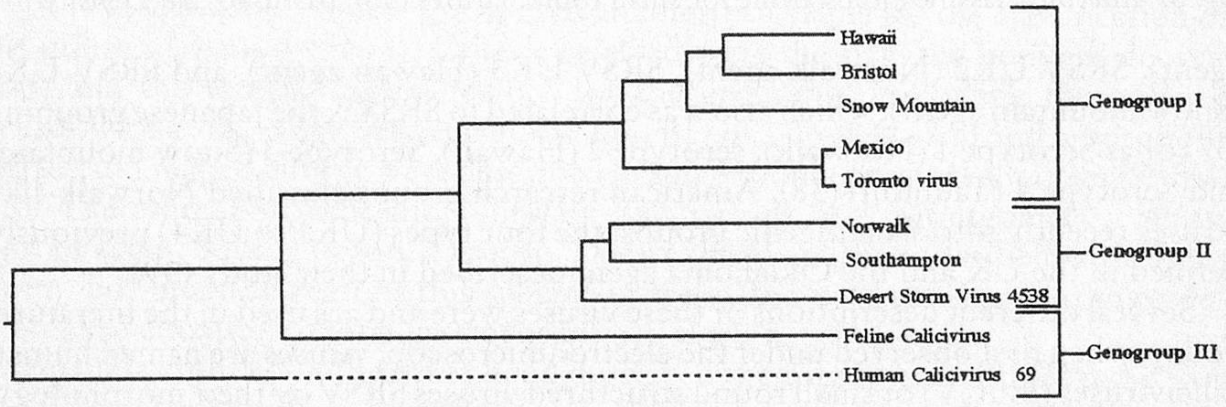

Fig. 4. Phylogenetic tree of Human Caliciviruses (HuCV), Reference see text.

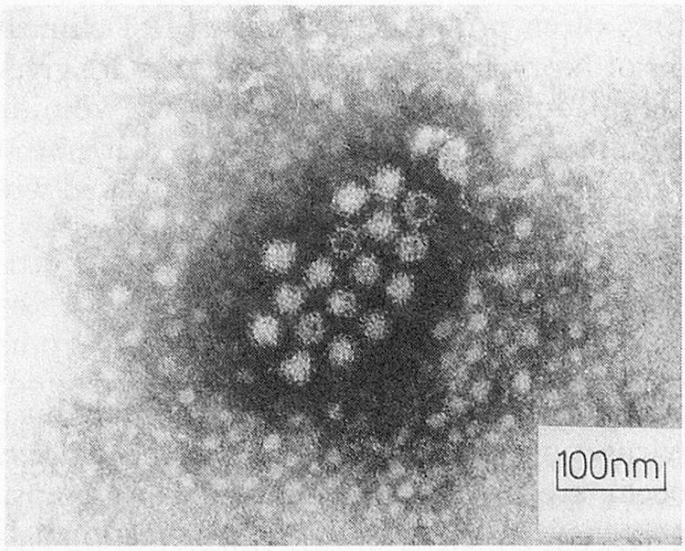

Fig. 5. Norwalk viruses (Kindly submitted by Dr. E.O. Caul, Public Health Laboratory Bristol, UK)

symmetry (fig. 5). The particles have a characteristic feathery outer edge and lack a definite surface substructure but appear in certain orientations to have minor surface indentations (28).

Endemic Disease

Norwalk and Norwalk-like viruses have been associated with epidemic viral gastroenteritis in the USA. In the UK, SRSVs are more often reported in connection with endemic disease. Sporadic cases may go unrecognised as may affected individuals will not seek medical attention and those that do may not have a stool specimen examined and if they have it may not be examined for Norwalk-like viruses (48). Analyses of microscopic reporting of gastrointestinal viruses in the UK between 1985 and 1987 showed that SRSVs are frequently found in adults as well as in children (49). Gray and co-workers reported that out of 3,250 serum specimens collected in England in 1991 and 1992, 73.3% were positive for Norwalk virus by testing with an indirect ELISA for antibody to Norwalk virus using baculovirus-expressed capsid antigen. The prevalence of Norwalk virus antibody differed with age and region. Adults older than 60 years being antibody positive. The titers rise with age. Similar results were found in different countries (50). The less developed a country the earlier in age individuals acquire antibodies.

Clinical Syndrome

The clinical features of Norwalk virus and Norwalk-like agents have been studied in outbreaks and also in volunteers. Outbreaks caused by these agents are characterised by median incubation periods of 24 to 48 hours, median duration of 12 to 60 hours, and a high percentage of patients with diarrhoea, nausea, abdominal

cramps, and vomiting, often projectile (51). In table 1 clinical characteristics for confirmed outbreaks of Norwalk virus gastroenteritis are given (9, 51).

Children and young adults are likely to experience vomiting more frequently than diarrhoea, but adults experience higher rates of diarrhoea than vomiting (4, 9, 51). Diarrhoea induced by Norwalk virus is also associated with malabsorption of D-xylose and fat (52).

Outbreak characteristic

Numerous reports have described the course of outbreaks caused by Norwalk and Norwalk-like viruses usually involving adults and older children. The places where outbreaks occur are diverse and involve cruise ships, geriatric facilities, hospital wards, emergency rooms, restaurants, recreational facilities, swimming pools, hotels, restaurants, cafeterias, canteens, air craft carriers etc. (20, 51).

Norwalk and Norwalk-like agents induce a low background level of immunity within a community. However, if an infected individual contaminates a common source (food, water etc.) an explosive outbreak can occur (20). Additionally secondary person-to-person transmission seems to be a characteristic feature of outbreaks with Norwalk-like viruses. Although secondary cases increase the number of affected individuals and extend the duration of the outbreak, outbreaks are generally limited to one to two weeks unless transmission is facilitated by a closed environment (e.g. elderly peoples home) or prolonged by re-entry of successive new and susceptible individuals (e.g. new set of passengers on a cruise ship) (20), or overlapping cohorts of guests in a hotel (90).

The combination of incubation period, duration of illness, and relative frequency of reported symptoms is unlike those associated with outbreaks of bacterial infection or intoxication and is believed by *Kaplan* et al. (51), *Hedberg* et al. (9) and *Lüthi* et al. (53) to be of descriptive value. Person-to-person transmission precipitating outbreaks is believed to be the most common transmission route (54).

Table 1. Clinical features of confirmed Norwalk outbreaks (9,51)

	Median % (range)	
Characteristic	1976–1980 (n = 38)	1980–1989 (n = 23)
Nausea	79 (51–100)	78 (33–99)
Vomiting	69 (25–100)	57 (16–81)
Diarrhoea	66 (21–100)	78 (9–96)
Abdominal Cramps	71 (17– 90)	60 (37–87)
Fever	37 (13– 71)	31 (3–52)

The first aspect of managing a foodborne or waterborne outbreak must be to prevent any further spread. Usually person-to-person transmission is the most likely ongoing transmission route. A typical example was presented in the publication of *Stevenson* et al. (55).

Especially in settings with susceptible individuals living close together (e.g. elderly homes, cruise ships, hotels etc.) the importance of personal hygiene must be stressed. The removal of any potentially contaminated food and cleaning of contaminated environments (e.g. toilet facilities, kitchen environment) is absolutely essential. As soon as possible the source of the outbreak has to be traced, whether it is primary foodborne, secondary foodborne or person-to-person spread. Interviewing the kitchen staff about their health status (and their relatives and close contacts e.g. children), and analysing the food eaten by whom it was prepared and identifying possible risks (e.g. no heat process) can help to trace the source.

Primary contaminated food (e.g. oysters) must be traced back to their origin and steps to withdraw the same batch of products from the market considered. Secondary contamination of food must be investigated by identifying hygiene failure. Critical control point analysis (HACCP) (56) can identify high risk areas and practices which can be addressed to prevent future outbreaks.

Meanwhile non heated food must not be served unless it was produced outside the suspected area. Potentially contaminated food must – when samples have been taken – be destroyed. The decontamination of kitchen surfaces and also toilets must be performed using hot water and general purpose detergent which may be followed by 500 ppm hypochlorite (54).

The most difficult part in managing a foodborne outbreak is to identify infected food handler(s) followed by their exclusion from work until the risk of spreading the virus is minimised. It must not be forgotten that staff must be sent home and must not stay in areas (e.g. common rooms) where other staff may be infected consequently. This includes also managerial staff and not only staff working with food or patients. Exclusion for 48 hours after diarrhoea and/or vomiting has resolved should be mandatory (51).

The guidance of the management of outbreaks of foodborne illness, published by the Department of Health, UK, recommends an exclusion of persons who pose a special risk until 48 hours after clinical recovery and 72 hours for children (57). *Hedberg* and *Osterholm* (9), however, recommended in outbreak settings in Minnesota, USA, exclusion of ill food handlers for 72 hours. When there is evidence of transmission among food handlers and transmission to patrons on multiple days, these authors recommend closure of the restaurant for 72 hours to provide an opportunity for the virus to «burn itself out».

In volunteer studies *Graham* et al. (58) concluded that the peak of viral shedding was between 25 and 72 hours, and virus first appeared in stool at 15 hours after inoculation of the 8FIIa NV strain. Virus was still shed seven days after inoculation.

Haruki and co-workers reported that the faecal shedding of SRSV particles in two adult patients after oyster consumption occurred within five days of illness,

thereafter, the concentration rapidly decreased but still on day eight of illness SRSV was detectable in two patients (59). However, even though highly desirable to exclude food handlers, the financial realities to the catering industry mean that this is unlikely to be achievable routinely (54). Individual solutions have to be found for each outbreak separately balancing all aspects.

To prevent person-to-person spread movement of patients and staff must be restricted. Whenever possible, the infected, and therefore infectious people should be isolated, and social events which lead to crowding avoided. All people should be encouraged to practice good personal hygiene (54).

Outbreaks of viral gastroenteritis which are waterborne demand investigations to identify the source of the contamination and drinking water must be disinfected to prevent further spread within the community. For individual households boiling of water for ten minutes is sufficient to inactivate viral agents of gastroenteritis (20). For mass treatment of water supplies, concentrations of chlorine as high as 10 mg/l are necessary (20).

Mode of transmission

The Norwalk and related viruses are transmitted by the faecal-oral route (28). Contamination of food or ice, aerolisation of vomitus, and direct contact with an infected person and fomites may all contribute to transmission (60). Raw shellfish have been implicated in outbreaks of foodborne viral gastroenteritis. Outbreaks occur following consumption of shellfish harvested from waters contaminated with human sewage. Oysters, clams etc. filter virus particles from contaminated water and accumulate them in their tissue (9). Although shellfish and oysters in particular may be associated with outbreaks of foodborne viral gastroenteritis, transmission from infected symptomatic and asymptomatic food handlers appears to be a common and widespread transmission route (9). Characteristically cold food with manual production steps like sandwiches, desserts, salads etc. are frequently involved.

Outbreaks of waterborne viral gastroenteritis have involved different water sources. Cross contamination of drinking water with human excreta following leakage of septic tanks, overflowing after heavy rain falls etc. are a common feature. Contributing factors in these outbreaks included the absence of filtration and the absence or failure of efficient chlorination of the water supply (9). Outbreaks may be associated with water for recreational purposes and have been associated with swimming in lakes (61) as well as in swimming pools (62). Infected individuals contaminating crowded swimming areas can produce apparent point source outbreaks among exposed groups (9). Airborne transmission has been proposed by different authors and outbreaks involving these transmission routes have been reported (63). However, studies that have suggested «airborne» transmission by inhalation have not definitely excluded hand/mouth transmission from environmental contamination (28, 64).

Diagnosis

One of the major problems involved with SRSV is their inability to grow in tissue cultures. Volunteers have been used to produce sufficient antigen to study and use as reagents in diagnosis. However, a recent breakthrough in diagnostic methods occurred when the Norwalk virus capsid protein was expressed in a baculovirus system to form virus-like particles (65). This antigen was shown to be specific, sensitive, and efficient in a direct ELISA for the detection of serological evidence of NV infection (28). Methods which have been used to detect viruses in outbreaks include electron microscopy (EM), immune electron microscopy (IEM) (9), solid phase immune electron microscopy (SPIEM) (54), Radio immuno assays (RIA) and Enzyme immuno assay (EIA) (9). However at present examination of faeces by electron microscopy remains the only method that is used routinely in the UK, but application of molecular method-based assays like reverse transcriptase polymerase chain reactions (RT-PCR) to investigate outbreaks are described and may eventually become widely available (e.g. 66). «The shortage of diagnostic reagents means that there is no routine service using such techniques in the UK. However, it is likely that, following the sequencing of the Norwalk virus genome this situation will change» (54).

Food microbiology

Public health controls for molluscan shellfish are hampered by the absence of methods for the detection in shellfish of the viral pathogens. At present bacterial indicator organisms are used to estimate the risk of viral contamination with SRSVs. However, there is a poor correlation between levels of bacterial contamination and the likelihood of viral contamination (54). Recently methods have been reported to detect SRSV in artificially (67) and natural contaminated shellfish (68) using RT-PCR. The main problem is to overcome inhibitors of the polymerase chain reaction which are present in food (Dr. J. Green, Central Public Health Laboratory (CPHL), pers. communication). Therefore procedures are necessary to purify the virus and nucleic acid prior to the PCR reaction to remove potential inhibitors present in shellfish which makes the technique a time consuming and costly procedure.

At present the strategy for identification of SRSVs in shellfish associated with outbreaks at the Enteric and Respiratory Virus Lab at the Central Public Health Lab in Colindale, London, UK, is a three step procedure. First, stool or preferable samples of vomit, of affected people is used to identify the genotype of the responsible agent by performing a reverse transcriptase polymerase chain reaction. The optimum primer pair is then selected and used to carry out a nested RT-PCR on the suspected food. Finally the amplification product – a region of the RNA-Polymerase – will be sequenced to determine the position of the infectious agent within the known strains to develop phylogenetic trees for further epidemiological

investigations (Dr. J. Green, Central Public Health Laboratory (CPHL), pers. communication).

Environment

Norwalk-like viruses are resistant to ether and relatively resistant to acid (pH 2.7) at room temperature and are also relatively heat stable. Viral suspensions heated to 60 °C for 30 minutes remained infectious in volunteers (48). In the environment Norwalk-like viruses seem to be fairly stable. *Hedberg* and *Osterholm* (9) propose three days for closure of an infected area to provide an opportunity for the virus to «burn itself out», therefore one must assume that these viruses are stable on surfaces, tools etc. for at least several hours. However, no concrete data were found in the literature.

Immunity

Immunity to SRSV was mainly studied using human volunteers. However, the nature of immunity to this viruses «remains an enigma» (28). Studies of volunteers have documented the paradox that persons with the highest titres against NV before challenge are also more likely to develop symptomatic infection (20). These early findings, that pre-existing serum antibody was not associated with protection, have been confirmed recently in a multiple-challenge study in volunteers (28). Contrary to the above findings, other authors report that acutely elevated antibody levels appear to correlate with resistance to infection (20).

When volunteers were challenged with Norwalk virus and seven to 15 weeks later were challenged with a different strain (e.g. Hawaii agent) they became ill. Moreover, Norwalk infection appeared to protect against Montgomery county agent, although Montgomery county infection may not protect against Norwalk infection (48).

Conclusion

Outbreaks of foodborne or waterborne viral gastroenteritis have become an increasing problem. In the United States, Norwalk virus appears to be the major cause of outbreaks of viral gastroenteritis and has been identified as the cause of 32–42% of such outbreaks (9). In contrast to national surveillance data, state-wide surveillance data in Minnesota suggested that outbreaks of viral gastroenteritis were more common than outbreaks due to *salmonella*, *shigella*, and *campylobacter spp.* In the period from 1984 to 1991, viral gastroenteritis was the most common foodborne illness in Minnesota (9).

In the UK SRSV's «are the commonest cause of epidemic gastrointestinal infection» (69, 54). Between 1989 and 1991 twenty-nine outbreaks of foodborne

SRSV gastroenteritis were reported (69), and between 1992 and 1994 forty-one outbreaks of foodborne SRSV gastroenteritis were reported (70).

The role of foodborne and waterborne outbreaks on the one hand and person-to-person spread on the other hand seems to be an artificial distinction. In outbreak situations both transmission routes often occur at the same time, as is shown by the existence of high secondary attack rates. The role of other routes, like airborne, or via contaminated surfaces, remain difficult to confirm but in terms of outbreak management may play an important role and must not be forgotten.

The diagnosis of SRSV in food remains a major problem in respect to costs and timeliness. Routine screening of food (e.g. oysters) seems to be very difficult and not cost effective. At present only the strategy of optimising the food microbiological methods (e.g. optimised primer pairs) after having identified the agents in clinical specimens will be successful to isolate and identify the virus at much lower concentrations from suspected food. The combined effort of epidemiological, medical microbiological and food microbiological methods is necessary for successful identifications of both transmission routes and outbreaks. To describe the epidemiology of SRSV infections the classification has to be standardised on a local, national and also international level to identify distinct pattern of viruses responsible for foodborne and waterborne gastroenteritis clustered in space and time.

Rotavirus

Classification

Rotaviruses belong to the family Reoviridae. Until now six distinct antigenic different groups have been recognised, which are designated A to F (71). Only group A, B and C have been shown to infect humans. Most human rotavirus infections in both the young and the elderly in North America and Europe are caused by group A virus (48). However, infections with group A occur mainly in young children up to two years of age (71). Although, group B and C have been reported to be etiological agents of foodborne or waterborne viral gastroenteritis (9). Whereas group B rotaviruses were found during waterborne outbreaks mainly in China (72), group C rotaviruses were found in Japan and elsewhere (9).

Virology

Rotaviruses measure approximately 70 nm in diameter and contain a double stranded RNA, which is separated in 11 segments (9). The name is derived from the Latin word *rota* (wheel), which describes the appearance of the virus on negative-contrast electron microscopy (fig. 6) (71). Rotaviruses are non enveloped and consist of an outer capsid and core (73).

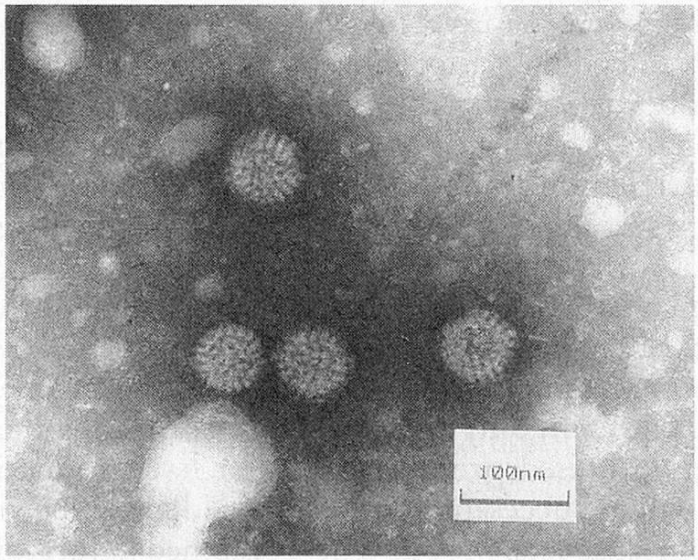

Fig. 6. Rotaviruses (Kindly submitted by Dr. E.O. Caul, Public Health Laboratory Bristol, UK)

Endemic disease

Symptomatic and asymptomatic rotavirus infections together with high prevalence of serum antibodies after three years of age are frequently described in all age groups and in different countries. It implies that sequential rotavirus infections occur throughout life.

Clinical syndrome

The incubation period in young children is between 24–48 hours. In adults the incubation period may be longer than three days. The onset of the disease is sudden and presents with watery diarrhoea and a greater degree of fever and dehydration than other enteric pathogens. It is not possible to distinguish clinically between rotaviral infections and infections with other viral agents.

Virus is usually shed in the faeces for five to seven days. In severe cases rapid dehydration can lead to renal shutdown and death. In adults infections caused by group A rotaviruses are generally milder than those due to non-group A rotaviruses (74).

Outbreak characteristic

Rotavirus is not commonly associated with common source outbreaks of gastroenteritis (73). Rotaviruses survive in the environment i.e. on contaminated hands, surfaces, in tap water, and in sewage. Additionally they are resistant to many disinfectants (71). They are frequently found in paediatric wards with children less than three years old and nosocomial outbreaks are well known in this setting. The highly infectious nature of rotaviruses ensures that, once introduced into a family,

rotaviruses spread to most members (71). In temperate climates, rotavirus disease is a consistent seasonal pandemic of amazingly repeatable onset and duration. The reasons for this seasonality is unknown (73). Rotaviruses are believed to have spread in a number of waterborne outbreaks due to drinking water contaminated with either group A, or in China group B rotavirus. Reports have been published from developed as well as from developing countries (74).

Management of foodborne/waterborne outbreaks

Basically all viral gastroenteritis may be managed similarly to prevent further spread. The description given for Norwalk virus may be used also for rotaviruses. However, rotaviruses in drinking water are less resistant to inactivation with chlorine than Norwalk viruses (20). Exposure to 3.75 mg/l for 30 minutes active chlorine is sufficient to inactivate the agent.

Mode of transmission

The mode of transmission of rotavirus infections is assumed to be faecal-oral and describes a complex interrelationship of vehicles like fingers, flies, food, fomites, fluids (water), classically described as the F-diagram (75).

Food mentioned as vehicles are products like raw vegetables, shellfish, and others with the potential to be contaminated with faeces (74). There is generally a lack of information on the role of food as a vehicle for rotaviruses. It has been suggested that the lack of data is due more to the insufficient investigation of foodborne outbreaks of gastroenteritis than to an inability of rotaviruses to spread via food (76).

The infectious dose is – following results from volunteer studies – believed to be as low as one plaque forming unit, the amount necessary to produce cytopathic effects in selected cell cultures (73, 74).

Diagnosis

The most commonly used detection methods for rotaviruses in clinical specimens at the present time are enzyme immune assays (EIA) and latex agglutination (LA) tests. Several kits are commercially available. Antigen is detected using specific antibodies directed against the virus under investigation. However, electron microscopy remains the gold standard for rotavirus detection (48).

Environment

Rotaviruses may be found in different environmental areas and are known to be resistant. Levels of chlorine used in the terminal disinfection of sewage effluents or drinking water are not sufficient to inactivate these viruses. In surface water

rotaviruses remain infectious for several days, depending on the water temperature. Also hands, fomites etc. can harbour infectious particles for serveral hours. In air and on non porous inanimate surfaces, the survival of rotaviruses is favoured by a relative humidity below 50%, maintaining infectivity for several days. Additionally rotaviruses are relatively resistant to commonly used disinfectants and hygienic hand-wash detergents (74). Some authors suggest that public water supplies act as reservoir for the viruses between the seasonal epidemics (77).

Immunity

In reported outbreaks, mothers of infected infants were rarely infected, suggesting that young people retain immunity from earlier exposure, although outbreaks with elderly people involved suggest that this immunity may wanes with age (20).

Conclusion

Rotavirus plays an important role in infant gastroenteritis. Several outbreaks associated with drinking water have been reported. The possibility of transmission via food seems plausible but is not yet confirmed. However, the frequency of outbreaks of gastroenteritis due to non-group A rotaviruses is rising, but the reasons are not yet clear (74). At present rotaviruses do not play a major role in foodborne or waterborne outbreaks, but must be kept in mind during investigations.

Agents of viral gastroenteritis under discussion

During recent decades several agents have been found during investigations of viral gastroenteritis whose etiological role is far from clear and is under discussion. The following agents have been named to be a cause or possible cause of viral gastroenteritis: enteroviruses, adenoviruses, SRV, coronaviruses, toroviruses, picobirnaviruses and pestiviruses (9, 20). Foodborne and waterborne viral gastroenteritis of other than the previous discussed agents have – as far as the author is aware – not been published. Table 2 gives an overview of all agents associated with viral gastroenteritis. Where there are agents under discussion they are marked with a (?).

Adenoviruses

Of the 47 serotypes (fig. 7) at present known, subgenus F, serotype 40 (HAdV-40) and serotype 41 (HAdV-41) are established as a cause of viral gastroenteritis (78). It is estimated that these two serotypes contribute to 5–20% of hospitalisations for childhood diarrhoea in developed countries (20). Occasionally HAdV-31 may also contribute to diarrhoea (79). The clinical syndrome contains diarrhoea more

Table 2. Viral Gastroenteritis. Overview of agents. Outbreaks (OB) relates to foodborne/waterborne outbreaks.

Agent	Abbr.	Synonymes	Family	Genus	Sub-Classification	Etiology established?	role in OB established?
Rotavirus	ROTAV-A,-B,-C		Reoviridae	Rotavirus	A,B,C	yes	yes
Adenovirus	HAdV-40, -41	Enteric Adenoviruses	Adenoviridae	Mastadeno-virus	F (Ad 40, Ad 41)	yes	no
Enteroviruses	–	–	Picornaviridae	Enterovirus	–	no	no
Wollan agent		SRV, candidate parvovirus	Parvoviridae (?)	–	–	no (?)	no
Ditchling agent		SRV, candidate parvovirus	Parvoviridae (?)	–		no (?)	no
Cockle agent		SRV, candidate parvovirus	Parvoviridae (?)		–	no (?)	no
Paramatta		SRV, candidate parvovirus	Parvoviridae (?)	–		no (?)	no
Astrovirus	HastV		Astroviridae	Astrovirus	Serotype 1–7	yes	yes
Calicivirus	HuCV	Human Calicivirus	Caliciviridae	Calicivirus	HuCV: UK1–UK4	yes	yes
Norwalk	NV	SRSV	Caliciviridae	Calicivirus	genogroup II, serotype 1	yes	yes
Hawaii		SRSV, NV-like virus	Caliciviridae	Calicivirus	genogroup I, serotype 2	yes	yes
Snow mountain		SRSV, NV-like virus	Caliciviridae	Calicivirus	genogroup I, serotype 3	yes	yes
Taunton		SRSV, NV-like virus	Caliciviridae	Calicivirus	serotype 4	yes	yes
Southampton		SRSV, NV-like virus	Caliciviridae	Calicivirus	genogroup II	yes	yes
Montgomery county		SRSV, NV-like virus	Caliciviridae	Calicivirus	serotype 1	yes	yes
Bristol		SRSV, NV-like virus	Caliciviridae	Calicivirus	genogroup I	yes	yes
Mexico		SRSV, NV-like virus	Caliciviridae	Calicivirus	genogroup I	yes	yes
mini-reovirus		SRSV, NV-like virus	Caliciviridae	Calicivirus		yes	yes
Otofuke		SRSV, NV-like virus	Caliciviridae	Calicivirus		yes	yes

Agent	Abbr.	Synonymes	Family	Genus	Sub-Classification	Etiology established?	role in OB established?
Human Coronavirus	HCV	Enteric Coronavirus	Coronaviridae	Coronavirus	Human enteric Coronavirus	(?)	(?)
Corona virus-like particles	CVLP		(Coronaviridae?)	(?)		(?)	(?)
Torovirus		Torovirus like virus	Coronaviridae	Torovirus	animals: Breda /Berne	(?)	(?)
Picobirnavirus	PBV		(?)			no (?)	(?)
Pestivirus			Flaviviridae			(?)	(?)

(?) symbolises under discussion. References are mentioned in the text.
Abbr. = Abbreviations

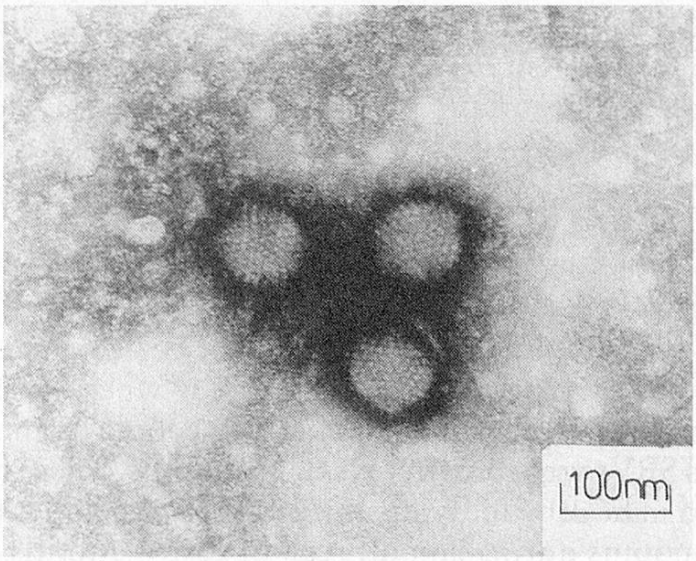

Fig. 7. Adenoviruses (Kindly submitted by Dr. E.O. Caul, Public Health Laboratory Bristol, UK)

predominantly than vomiting after an incubation period of three to ten days (20). The median duration of diarrhoea in children with HAdV-40 is 8.6 days, and for HAdV-41 12.2 days (78). Other symptoms (fever, vomiting) are mild and last for two days approximately.

The mode of transmission is reported to be person-to-person and is presumably the principle mechanism. Food and water have not been reported as vehicles (20).

Outbreaks occur mainly in settings with susceptible children (wards, day care centres) and lead probably to long-term immunity (20). Disease may also occur in immunocompromised hosts (79).

Enteroviruses

Enteroviruses are responsible for a wide spectrum of diseases. However, diarrhoea appears not to be a major symptom. Several enteroviruses (e.g. polio, coxsackie, echo) use the gut as the port of entry to the body and may cause incidental mild diarrheal symptoms. Therefore outbreaks or cases of gastroenteritis should not be attributed to an enterovirus because it was isolated in the stool of affected people (20).

Small round viruses (SRV)

Small round featureless viruses are believed to belong to the family of Parvoviridae and are also referred to as candidate parvoviruses. Conclusive evidence that these human enteric candidate parvoviruses cause gastroenteritis is lacking, they do not fulfil all criteria for establishing them as pathogens (80). More confusion was even established when these agents, containing DNA were grouped together on the basis of particle size, buoyant density, and similarity of clinical syndrome with the

RNA containing SRSV. Already in 1982 *Caul* and *Appelton* (35) realised the differences between these agents in respect to their different morphology under the electron microscope. These authors proposed therefore an interim's classification scheme which is still in use. This scheme helped to define «what virus» in epidemiological studies was mentioned, even when molecular and biochemical information were lacking. Figure 3 shows the classification scheme. The expressions «SRSV» and «SRV» refer specifically to this scheme and are also mentioned by other authors (e.g. 28, 60).

SRVs (fig. 8) are often found in ill as well as in healthy individuals. *Davidson* reported a study of elderly people during one year where of 348 stools samples examined 33% contained SRV. Only five out of 40 people did not excrete SRVs. In 89% of the samples SRVs were present in small amounts. These findings show, that SRVs are also found in healthy individuals. *Davidson* concludes that «the detection of SRVs in small amounts during an outbreak of gastroenteritis does not suggest a causal role» (81).

The PHLS working party on Viral Gastroenteritis finally concluded, that «none of these viruses have been shown to cause gastroenteritis». And further on «that the clinical picture, in conjunction with an asute onset and high secondary attack rate, characterises SRSV outbreaks. When such features are detected in an incident it may be predicted with a high degree of probability that SRSVs are the cause» (76).

Coronaviruses

Coronaviruses (fig. 9) are well known intestinal pathogens in new-born animals (20, 82). An etiological role in human gastroenteritis has long been proposed. However, others have failed to establish such a role of human coronaviruses in man.

Enteric coronaviruses or coronavirus-like particles (CVLP) were associated with gastrointestinal disease in neonates as well as in infants under the age of 12

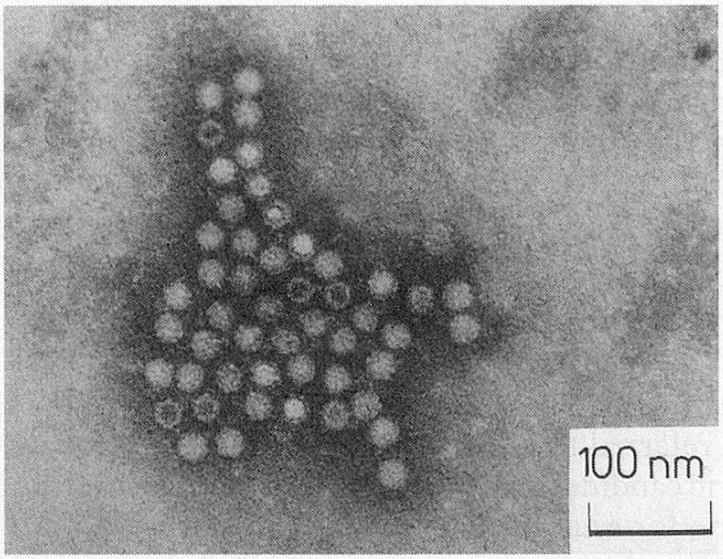

Fig. 8. Parvoviruses (Kindly submitted by Dr. E.O. Caul, Public Health Laboratory Bristol, UK)

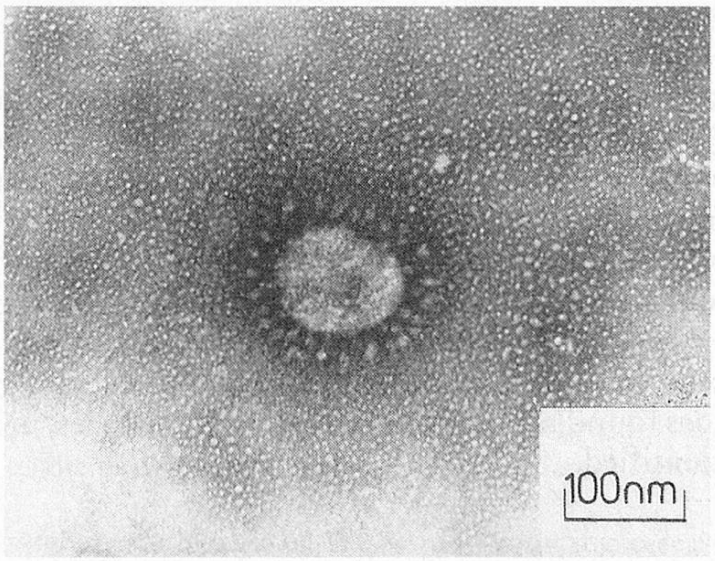

Fig. 9. Coronaviruses (Kindly submitted by Dr. E.O. Caul, Public Health Laboratory Bristol, UK)

months (83). Studies in different parts of the world have demonstrated excretion of coronavirus-like particles in healthy as well as in ill children (e.g. 84), so that the role of CVLP in gastrointestinal disease has been questioned (48). Epidemiological studies, however, also have demonstrated higher prevalences of coronavirus-like particles (CVLP) in low socio-economic groups with poor standards of personal hygiene (20, 82). Particles also have been found in the stools of adults with AIDS (83).

The role of human enteric coronaviruses in infant gastroenteritis is still not known and remains an enigma (82). However, in adults there is no evidence that human enteric coronaviruses are the etiological agent in outbreaks or in sporadic cases (82). A role in foodborne or waterborne gastroenteritis has not been established.

Toroviruses

Toroviruses of the genus torovirus also belong, like the above described coronaviruses, to the family of the Coronaviridae. This genus consists of two strains, Breda virus (BRV) and Berne virus (BEV), which are known to cause diarrhoea in animals (calves, horses) (20, 85). Identification of torovirus-like agents in human specimens have been reported (86, 87).

However, *Woode* concludes that «it is probable that we shall discover in the future that toroviruses, like coronaviruses, are not confined to the alimentary tract for replication or disease» (85). A role of these agents in outbreaks is not known.

Picobirnaviruses

Picobirnavirus (PBV) was first reported from Brazil in animals and also in human cases (20). These viruses contain a bisegmented double-stranded RNA genome. The prevalence of this virus in the population was studied by Gallimore and co-workers in human stools collected between 1982 and 1993 in the UK. The authors report a similar prevalence of 9–13% in patients with and without gastroenteritis and throughout the age range. These findings suggest that PBV are widespread in humans but no disease association could be demonstrated (88). In this study specimens were also examined from outbreaks with gastroenteritis, and although the authors found higher rates of PBV in some cases, in all these outbreaks SRSV were also identified.

Pestiviruses

Pestiviruses recognised as an enteric pathogen in animals were also reported in a study investigating children of an Indian reservation in the US with diarrhoea of unknown origin (89). In this study the authors concluded that pestivirus are a major agent of diarrheal disease in young children in this area. However, the relevance of this findings for other regions remain unclear and it is not known whether these findings were anecdotal or show a possible agent associated with viral gastroenteritis, because no other reports have yet been published.

Summary

This review summarises the agents of food and waterborne viral gastroenteritis. Various agents, their clinical symptoms, their outbreak characteristics as well as their epidemiology are described.

The following agents were mentioned to be a possible cause of viral gastroenteritis: astroviruses, caliciviruses, Norwalk viruses (SRSV), rotaviruses, enteroviruses, adenoviruses, parvoviruses (SRV), coronaviruses, toroviruses, picobirnaviruses, and pestiviruses.

Zusammenfassung

Dieser Übersichtsartikel gibt eine Zusammenstellung viraler Gastroenteritiden. Die verschiedenen Agenzien, ihre klinischen Symptome, ihre Charakteristika bei Epidemien wie auch ihre Epidemiologien werden beschrieben.

Die nachfolgenden Viren wurden mit Gastroenteritiden in Zusammenhang gebracht beziehungsweise werden als Ursachen von diesen diskutiert: Astroviren, Caliciviren, Norwalk-Viren (SRSV), Rotaviren, Enteroviren, Adenoviren, Parvoviren (SRV), Coronaviren, Toroviren, Picobirnaviren und Pestiviren.

Résumé

Cet article résume les gastro-entérites virales. La variété des agents, leurs symptômes cliniques, leurs caractéristiques lors d'épidémies ainsi que leur épidémiologie y sont décrits.

Les virus suivants ont été mis en rapport avec les gastro-entérites, c'est-à-dire sont considérés comme cause possible: astrovirus, calicivirus, Norwalk-virus, rotavirus, enterovirus, adenovirus, parvovirus, coronavirus, torovirus, picobirnavirus et pestivirus.

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