

Outbreaks of gastroenteritis due to infections with *Norovirus* in Switzerland, 2001–2003

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SUMMARY

Viral infections, especially those with noroviruses are the most common cause of acute gastroenteritis in Europe. To obtain information about the epidemic situation of noroviruses in Switzerland, an initial study was launched in the German-speaking part of the country to systematically compile *Norovirus* outbreak information between 2001 and 2003. In total, 73 outbreaks were registered. Most affected were closed settings, e.g. nursing homes (34%) and hospitals (25%). Transmission pathways were identified in 74% of *Norovirus* outbreaks. In 81% of these cases person-to-person transmission was the primary route of infection and on seven occasions (13%), a foodborne transmission was the possible cause. Furthermore, *Norovirus* outbreak characteristics of epidemiological importance are highlighted with a discussion of four selected events.

INTRODUCTION

Recent international studies have shown that viral infections, especially those with noroviruses (formerly known as Norwalk-like viruses), are the most frequent cause of gastroenteritis in the community with regard to the endemic and epidemic situation [1–6]. These viruses account for an estimated 6% and 11% of all infectious intestinal diseases in England and The Netherlands respectively [3, 5] and for an estimated 23 million cases in the United States annually [7]. Noroviruses are also the most common cause of outbreaks of infectious intestinal diseases in Western Europe and North America [3, 7]. The illness is characterized by acute onset of vomiting and diarrhoea, after an

average incubation period of 12–48 h. The faecal–oral route is described as the most common route of transmission. Noroviruses are transmitted either by contaminated fomites (such as food and water) and the environment, or directly by person-to-person contact [8]. Noroviruses are often responsible for foodborne outbreaks due to contaminated water, ready-to-eat dishes, seafood, fruits and vegetables. Furthermore, various outbreaks have been associated with the ingestion of contaminated drinking or recreational surface water [9]. During the past 10 years, *Norovirus* outbreaks have been increasingly identified in Switzerland. However, solid epidemiological data were missing because noroviruses are not routinely searched for in diagnostic laboratories and there is no obligation to report known cases except for outbreaks registered by the cantonal (regional) health authorities. For this reason, the Swiss Federal Office

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of Public Health (SFOPH) launched a series of studies to learn more about the national epidemiology of noroviruses [6]. In the context of this programme, systematic investigations of outbreaks between 2001 and 2003 were conducted. They are presented and discussed in summary with a closer look at four outbreaks of epidemiological importance.

METHODS

Between 2001 and 2003 *Norovirus* outbreak information was systematically compiled. For the purpose of this study, a temporary network consisting of the cantonal (regional) food and health authorities (cantonal laboratories and cantonal surgeons) from the German-speaking part of Switzerland and the SFOPH was established. Outbreaks of gastrointestinal disease and clusters that were suspected of being caused by viral agents were reported by members of this network to the Cantonal Laboratory Basel-Landschaft. This institution was in charge of registering *Norovirus* outbreak information from the whole country and conducting separate investigations of outbreaks in close cooperation with the health authorities in the German-speaking part of the country. Switzerland is comprised of 7.4 million inhabitants and the German-speaking part accounts for approximately 64% of the country [10].

Classification of *Norovirus* outbreaks was performed by descriptive and analytical epidemiological investigations, by epidemiological profiling and by laboratory diagnosis. The profiling was based upon the *Norovirus* infection syndrome plus the following additional epidemiological characteristics [6, 11, 12]:

- (i) an incubation period varying between 1–2 days (range 12–48 h);
- (ii) major symptoms of vomiting (frequently explosive) and mainly diarrhoea (sometimes profuse), partially accompanied by nausea, abdominal pain and cramps, muscle pain, headache and sporadic low-grade fever;
- (iii) pathogenic bacterial and parasitic agents of gastroenteritis typically not detected in analysed patient stool samples;
- (iv) secondary cases typical within *Norovirus* outbreaks;
- (v) more than 50% of patients suffering from vomiting;
- (vi) more patients suffer from vomiting than fever, and adolescent patients suffer predominately

from vomiting whereas adult patients suffer predominately from diarrhoea.

Consequently, a *Norovirus* outbreak was classified as confirmed by exhibiting the typical *Norovirus* profile and by laboratory diagnosis of the pathogen in at least one patient stool sample. In a probable *Norovirus* outbreak, the typical epidemiological profile was present but either no patient samples were obtained or the samples were not analysed for the presence of noroviruses. In a possible *Norovirus* outbreak, either the clinical picture of the persons involved was incomplete, or the epidemiological links in terms of place, person and time were not established or could not be proven due to lack of information. The transmission routes (person-to-person, contaminated water, food or environment) were categorized in analogy to the outbreak classification scheme used.

The *Norovirus* reverse transcription–polymerase chain reaction (RT–PCR) diagnosis was performed at the Cantonal Laboratory Basel-Landschaft. The method used consisted of a genogroup-specific RT–PCR system for the detection of *Norovirus* GGII based on degenerate primers located in highly conserved regions of the RNA polymerase and of a second generic RT–PCR system also based on degenerate primers [13]. Furthermore, this combined system is part of the detection method for noroviruses in water samples recommended by the SFOPH in Switzerland [14].

RESULTS

Overall characteristics of 73 *Norovirus* outbreaks

Between January 2001 and December 2003, 73 *Norovirus* outbreaks were analysed. Ninety per cent (66/73) of the outbreaks were registered in the German-speaking part of Switzerland and a complete epidemiological outbreak investigation was carried out for 20 outbreaks (27%). Key information, e.g. primary transmission mode and number of cases, was collected from the remaining 53 outbreaks. Six out of 73 outbreaks (8%) were classified as *Norovirus* outbreaks by epidemiological profiling only, without laboratory confirmation. In the remaining incidents (92%), noroviruses were detected in patient specimens.

Twenty-five outbreaks (34%) occurred in nursing homes and accommodation for the disabled, 18 (25%) in hospitals and health resorts, nine (12%) in schools and boy-scout camps, six (8%) at social gatherings,

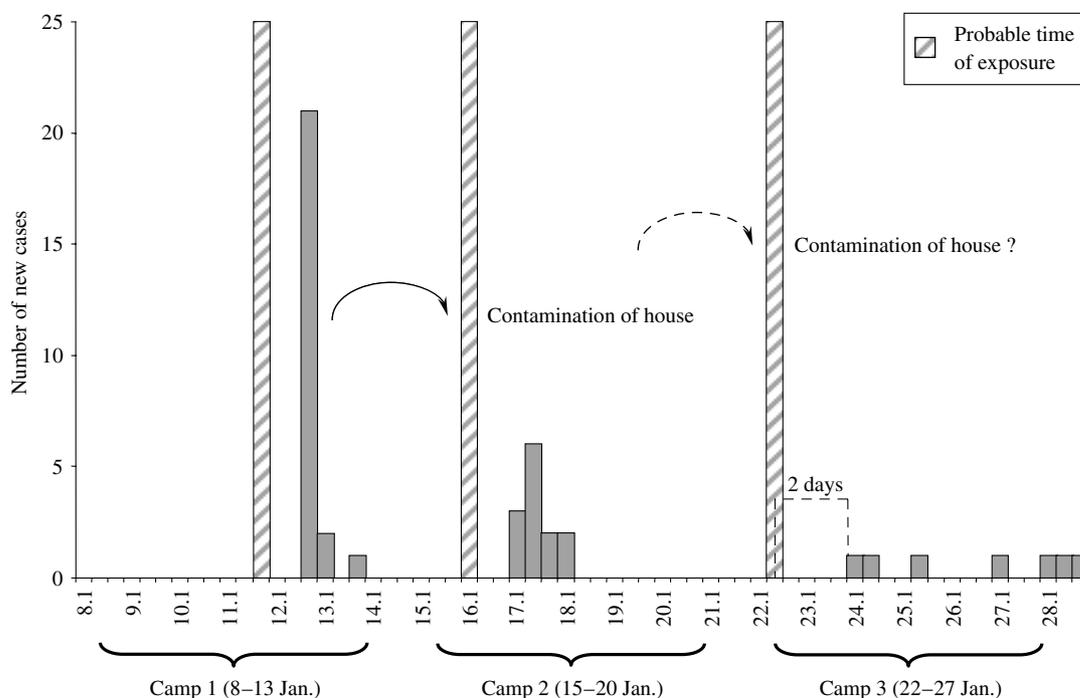


Fig. 1. Epidemic curve of three consecutive *Norovirus* outbreaks in ski camps in January 2001, located at the same accommodation. Each division on the *x*-axis describes a time interval of 8 h. The position of the date illustrates the first time interval from 0 to 8 h. The probable time of exposure in the first and second camp was computed by subtracting the maximal incubation period of the noroviruses of 2 days from the last case and subtracting the minimal incubation period of 1 day from the first case. The overlapping time period corresponds to the probable time of exposure.

five (7%) in hotels, four (5%) in the community, three (4%) in military settings, one (1%) at a pilgrimage and two (3%) in other settings.

Transmission pathways were identified in 54 of the 73 outbreaks (74%). In 44 of these 54 outbreaks (81%), person-to-person transmission was the primary route of infection. On seven occasions (13%), a foodborne transmission was a possible cause. One outbreak occurred due to an epidemiologically classified probable waterborne incident (discussed below) and another due to a classified possible waterborne episode caused by contamination of the drinking water system by sewage leakage. Within the possible foodborne outbreaks, the attack rates were high (>70%) and a common meal took place during one incubation period (1–2 days) before the onset of illness. Epidemiological investigations identified either no contaminated foodstuff or insufficient information was available. One large outbreak affected different nursing homes and similar institutions during and after a pilgrimage [15]. Generally, it could be observed that outbreaks in hospitals, nursing homes and other similar settings frequently reflected the current *Norovirus* situation in the community. Consequently, community-acquired and imported *Norovirus*

infections into various settings often acted as triggers of outbreaks. In almost all outbreaks with clear person-to-person transmission, the *Norovirus* agent was introduced into the setting by initially ill persons. The mean number of cases was found to be 60 (median 35, range 3–650) within all registered outbreaks and attack rates ranged between 30% and 90%.

Four selected *Norovirus* outbreaks will be presented in more detail below, because of their inherent characteristics such as transmission mode and setting.

Three consecutive outbreaks in ski camps

In January 2001, three consecutive *Norovirus* outbreaks occurred among ski camps, all located in the same accommodation (chalet) in the Swiss mountains. *Norovirus* infection was confirmed by epidemiological profiling and by RT-PCR diagnosis. Only one patient stool sample could be collected. The isolated *Norovirus* strain showed a sequence identity of 88% with the strain OS120458/01 (GenBank accession no. AB071035). Twenty-nine out of 34 persons (85%) were affected in the first ski camp, 21 out of 26 (81%) in the second and 13 out of 30 (43%) in the third. The epidemic curve in Figure 1 shows

that in the first camp, a point-source infection occurred. A foodborne infection seems likely because of the high attack rate (85%) and also because the probable time of exposure could be fixed between late afternoon and midnight the day preceding onset of symptoms. One common meal (dinner) took place during this time period. Within 1·5 days (the average incubation period of noroviruses) after moving into the accommodation, the first symptoms occurred in persons from the second camp. In all probability the infections were caused by a heavy *Norovirus* contamination of the accommodation. The illness in the first camp started the night before and on the day of departure. Therefore, it appears that the toilets and residential rooms were not properly cleaned, as 85% of the persons became ill and suffered from heavy vomiting and diarrhoea. The contamination was confirmed by persons of the second camp who reported the smell of vomitus and contaminated pillow covers. The computed time of exposure occurred on the first night after arriving at the accommodation. The *Norovirus* cases in the third camp showed a completely different pattern and a point-source of infection could be excluded. Nevertheless, the first patients of the third camp may have been infected by the environment of the accommodation during the day of arrival. The persons of the third camp were informed about the gastroenteritis illness in the two previous camps. Disinfectant was used and the toilets and kitchen were cleaned. This may explain the different dynamic of the outbreak that is typical for person-to-person transmission. After the guests' departure from the third camp the establishment was shut down and cleaned professionally before re-opening. Since the re-opening no further cases have occurred.

Outbreak within two communities

Within two weeks in January 2001, two communities were affected by a large outbreak with more than 650 cases. *Norovirus* illness was confirmed by epidemiological profiling and by *Norovirus* RT-PCR on patient stool samples. The two communities were mainly supplied with drinking water from a waterworks that distributes purified and processed water from a nearby lake. During 8 days within the 2-week outbreak, the water treatment plant in the waterworks exhibited major deficiencies regarding the application of chlorine and/or ozone. Two samples were drawn on the last day and following treatment

failure. The samples neither exceeded the official bacteriological criteria for drinking water, nor were noroviruses detected by RT-PCR. However, there is evidence that Swiss surface waters are generally contaminated with noroviruses [6]. For an estimation of the number of cases, a selection of general practitioners, nursing homes and schools within the two communities were questioned and the extracted numbers of patients were then extrapolated to the whole population of the two communities. Parallel investigations of the local pharmacies supported the estimation. Eight patient stool samples were found to be *Norovirus*-positive by RT-PCR and seven RT-PCR products were sequenced. Three samples showed a sequence identity of 89·7% with the Norwalk virus (GenBank accession no. NC_001959·1), three samples showed a sequence identity of 88·0% with the Camberwell virus strain (NC_002614·1) and the last sample exhibited an identity of 98·0% to the White-rose virus strain (HCA277610). This high variety within the discovered *Norovirus* isolates clearly supports the hypothesis of drinking water as the source of the outbreak.

Outbreak following a banquet

In a small outbreak, at a family gathering, 21 out of 25 persons (84%) were found to be suffering from gastroenteritis approximately 1·5 days (the average incubation period of noroviruses) following a banquet. *Norovirus* was confirmed by epidemiological profiling and by *Norovirus* RT-PCR on two patient stool samples. One *Norovirus* isolate was sequenced and showed a sequence identity of 94% with Chiba virus (GenBank accession no. NC_002613). A cohort study on the consumed food items could not define any foodstuff as a risk factor. Because of the low statistical power of the analysis due to the high attack rate and small size of the cohort, the foodborne route of infection cannot be excluded. However, the food was delivered to the banquet by a catering service. Investigations with the catering company showed that no further cases could be found within their clientele. Further investigations revealed that the *Norovirus* agent was most probably introduced into the setting by a young girl from family A (probable time of exposure III). The further transmission pathway from the girl to the other guests at the banquet, e.g. by personal contact or by contamination of some food items, remained unclear. Looking back at the chain of infection, it could be seen that the brother of the

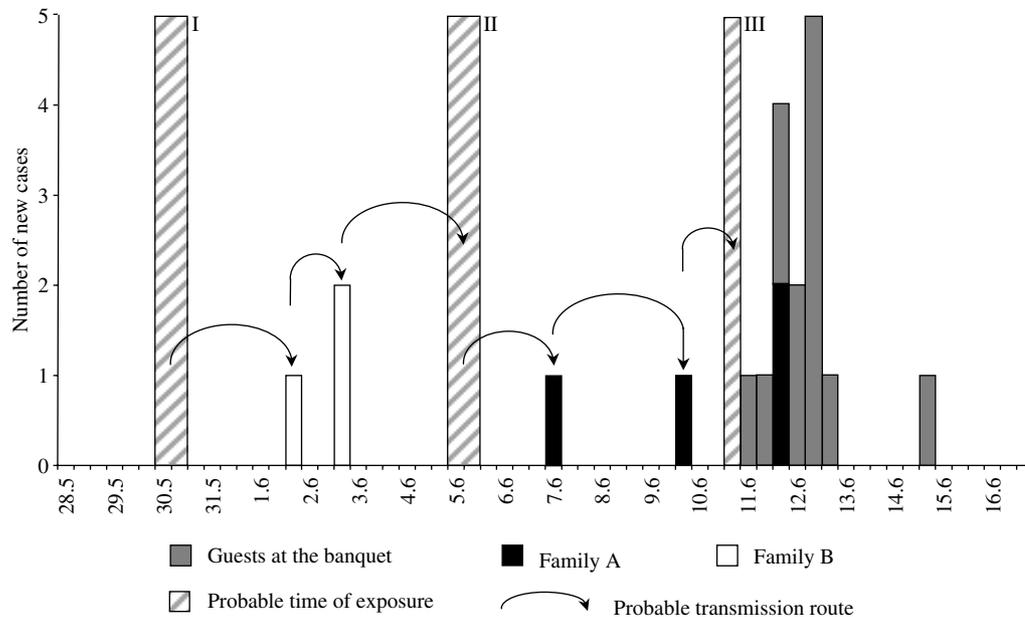


Fig. 2. Epidemic curve of an outbreak following a banquet in June 2001. Each division on the x-axis describes a time interval of 8 h. The position of the date illustrates the first time interval from 0 to 8 h. The three different probable times of exposure (I–III) are indicated by hatched bars. See text for further explanation of the introduction and transmission of noroviruses.

young girl was suffering from *Norovirus* illness 3 days previously. Two days before, two ill children of family B had been looked after by the parents of the boy and girl (probable time of exposure II). The mother of family B had been incapacitated with gastroenteritis 24 h earlier. Finally, this mother was herself visiting a third family with an ill boy (probable time of exposure I). All cases were classified as probable *Norovirus* by epidemiological investigation (see Fig. 2).

Consecutive *Norovirus* outbreaks in a hospital with an affiliated nursing home

Between the end of January and the beginning of April 2003, a series of *Norovirus* cases occurred in a Swiss hospital and an affiliated nursing home. In total, 140 persons were affected by gastroenteritis: 34 patients from the hospital, 28 patients from the nursing home and 78 staff members. Twelve patient stool samples tested positive for *Norovirus* by RT-PCR. The epidemic curve with information from 132 patients is plotted in Figure 3. Obviously, the curve is divided into three separate peaks. The *Norovirus* cases within the second and third peak were confirmed by laboratory results, whereas the cases from the first peak were classified as probable *Norovirus* cases by epidemiological profiling only. It is of interest that the incident consisted of three separate outbreaks

rather than a single protracted one. From the 140 patients involved, 132 could be clearly allocated to the hospital, respectively to the nursing home. The 28 *Norovirus* cases (21% out of the 132 patients) allocated from the first peak originated exclusively from the hospital and the second peak consisted of 29 patients (22%) from the hospital and six patients from the nursing home (5%). Finally, the last peak was dominated by 48 patients (36%) from the nursing home and also included 21 patients (16%) from the hospital. The 12 *Norovirus*-positive stool samples all exhibited a sequence identity of 95% with the *Norovirus* strain Miami Beach (GenBank accession no. AF414424). Phylogenetic analyses, conducted with the software packages Clustal W, Phylip 3.6a3 and Emboss matcher 2.0u4, revealed that the *Norovirus* sequences discovered formed two separate clusters as shown in Figure 4. The division of the *Norovirus* sequences into the two clusters corresponded exactly to a local distribution of the patients. All *Norovirus* isolates of cluster I originated from patients from the second peak, whereas all isolates from cluster II came from patients from the third outbreak peak. The sequences within cluster I exhibited an average sequence identity of 100%, whereas the sequences within cluster II showed an average identity of 99.9%. The computed sequence identity between ID01 (cluster I) and ID10 (cluster II) was 97.9%. The predominant

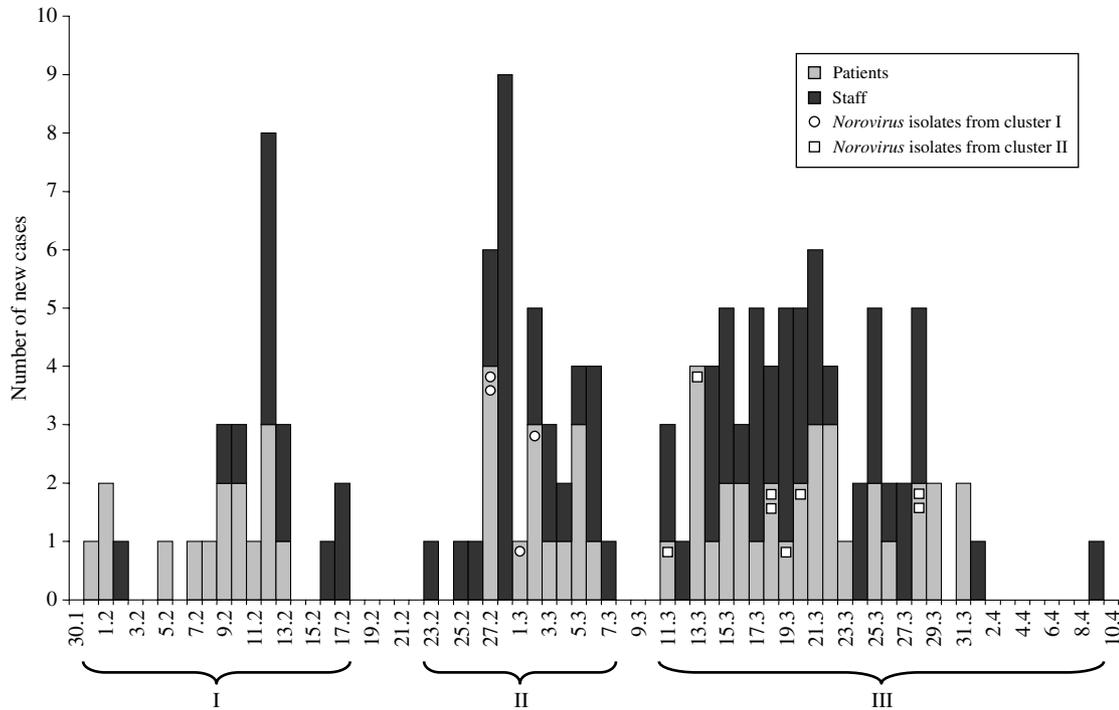


Fig. 3. Epidemic curve of consecutive *Norovirus* outbreaks in a hospital with an affiliated nursing home between the end of January and beginning of April 2003. The three distinct peaks correspond to local distribution of cases and differences between *Norovirus* isolates.

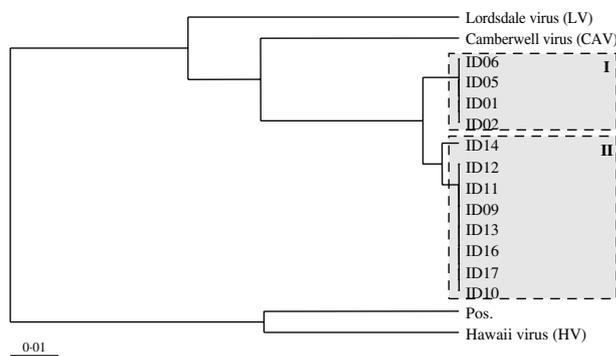


Fig. 4. UPGMA tree (Kimura matrix) showing the phylogenetic relationship between *Norovirus* sequences from patient stool samples (IDs) compared to the following reference strains: Camberwell virus (CAV; AF145896), Hawaii virus (HV; U07611), Lordsdale virus (LV; X86557) and the used positive control (Pos.). The *Norovirus* sequences of clusters I and II are allocated to the second peak (23 February to 7 March), and the third peak (11 March to 10 April) respectively of the epidemic curve as displayed in Figure 3.

transmission mode in all three consecutive outbreaks was the person-to-person route. No information about the entry pathway of the noroviruses could be obtained. At the time of the outbreak, community-acquired *Norovirus* infections were reported and may

have played an important role in transporting the agent into the hospital setting. Sequence information of the noroviruses from each cluster (ID01 and ID10) was submitted to GenBank (GenBank accession nos. AY551087 and AY551088).

DISCUSSION

Between the years 2001 and 2003, 73 *Norovirus* outbreaks were registered by the study network consisting of cantonal food and health authorities and SFOPH. This figure will certainly not account for the real number of outbreaks during this time period in Switzerland, because first, 90% (66/73) of the outbreaks were registered in the German-speaking part of Switzerland due to the study design and second, because of the lack of an established nationwide reporting system for *Norovirus* infections. Germany, for example, has operated such a reporting system since 2001 [16]. Prior to 2001, only very rudimentary *Norovirus* outbreak data from Switzerland were available. Furthermore, within this period foodborne transmission was thought to be the dominant transmission pathway [8]. From the total 156 registered foodborne outbreaks in Switzerland in the six years from 1993 to 1998, only 25 (16%) were confirmed or

possible *Norovirus* infections [17]. In England & Wales, Germany, and The Netherlands, a striking increase in *Norovirus* outbreaks occurred in 2002. This coincided with the detection and emergence of a new predominant *Norovirus* GGII variant [18]. This emergence of a new strain can most probably be used to explain the high number of registered outbreaks presented in this study.

With respect to settings, the registered outbreaks occurred predominantly in nursing homes (34%), hospitals (25%), camps (12%) and hotels (7%). The investigation of 1877 *Norovirus* outbreaks between 1992 and 2000 in England & Wales revealed a similar situation. In total, 40% of the outbreaks occurred in hospitals, 39% in residential-care facilities, 8% in hotels, 4% in schools, 6% were linked to food outlets and the remaining 4% occurred in other settings [3]. These proportions were confirmed in a further study for 2002 in England & Wales [19].

In our study, in only seven of the 54 outbreaks (13%) with a known infection route for noroviruses could a foodborne transmission have occurred. Outbreaks due to contaminated food and water vary from country to country. Finland reported 24%, The Netherlands 17%, Slovenia 14%, Spain, England & Wales 7% [4]. The predominance of the person-to-person transmission route (81% of all outbreaks with known transmission route) confirms the results of an English study, where a rate of 85% was found [3].

The three consecutive outbreaks in ski camps clearly demonstrated the epidemiological potential of *Norovirus*-contaminated environments. Earlier studies have clearly shown that *Norovirus* particles may keep their infectivity for lengthy periods [20–22]. For example, on carpets they stay infectious for up to 12 days [20]. Therefore, treatment of contaminated environments with an appropriate disinfectant (noroviruses are non-enveloped viruses) is of the utmost importance in halting the chain of infection [6]. Adequate treatment of contaminated clothes and linen, e.g. pillow covers, should also be performed [6]. Outbreaks in camps should generally be reported to the management of the establishments so that disinfection of the rooms can be organized. Waterborne outbreaks with noroviruses were shown to be associated with contaminated septic tanks, industrial water systems and swimming water as well as drinking water worldwide [23]. Two waterborne outbreaks occurred in Switzerland in 1998 and 1999 [6, 24, 25]. The first outbreak with 3500 cases was a result of a pump

failure producing a spill of sewage into the groundwater [24], the second outbreak with 1400 cases occurred due to the use of contaminated and accidentally untreated surface water [6, 25]. In 2001, the probable waterborne outbreak described in the present study was registered. The most recent case occurred in 2002 in a ski region of the Swiss Alps. Here, 100–150 persons suffered from acute gastroenteritis during a period of 2 weeks. Noroviruses were detected in patient stool samples and investigations revealed that the drinking water system was contaminated by faeces from a sewage leakage [Schmid, H. (SFOPH), personal communication]. There is a strong tendency that such outbreaks in Switzerland are most often the result of deficiencies in the infrastructure or in the water treatment process [6, 26].

In the previously reported banquet incident, various facts pointed to a foodborne scenario, however, a cohort study demonstrated that no association existed between consumed foodstuff and illness. The introduction of noroviruses into the setting by the young girl who was ill shortly before the banquet is a scenario often found in outbreaks, particularly in camps and nursing homes. The simplicity of transmission of noroviruses can be explained by the low infectious dose (10–100 particles) [6, 8], the effective transport of the agent by air after projectile vomiting of infected persons [6, 27] and by the prolonged shedding of viruses [6, 8]. Because of the simple and rapid transmission of noroviruses from person-to-person, every patient has a literally inherent potential to initiate outbreaks, at least within his own family. Public health institutions in particular, have to account for this possibility. Due to modern-day travel, noroviruses can easily cross national borders as demonstrated by two recent studies [15, 28]. Furthermore, a US study demonstrated the global circulation of a single *Norovirus* strain [29].

The previously presented example of consecutive outbreaks in a hospital with an affiliated nursing home illustrates how important it is not only to perform tests to detect noroviruses but also to conduct phylogenetic analysis of *Norovirus* RT-PCR products. Together with the results of the epidemiological investigation, it was feasible to determine that the incident was not one protracted outbreak, as initially thought, but consisted of different autonomous outbreaks. This was also meaningful in terms of the quality evaluation of the accomplished outbreak management. A very similar situation was found in another hospital, where from the beginning of

November to the end of December 2002, 130 persons (patients and staff) were affected by *Norovirus* infections. Nine *Norovirus* isolates from patient stool samples were phylogenetically analysed and again exhibited two different clusters. These clusters were allocated to patients that stayed locally and temporally on different floors and departments of the hospital (data not shown). It is also important to note that these hospital outbreaks all reflect the *Norovirus* situation in the community. In each hospital outbreak, a number of patients had acquired their infection outside the hospital, i.e. in the community. Thus far, there exists only one Swiss hospital outbreak which has been previously described; in March 2001 with 63 patients [30].

Epidemiological profiling, also recommended by authors from the United States, is a strong tool to conduct a fast and first assessment of a suspected *Norovirus* outbreak scenario [31]. This is important because of the current lack of routine analysis for noroviruses in Switzerland. Furthermore, the rapid implementation of outbreak control measures, even prior to the confirmation of norovirus infection, is crucial.

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