HIGH NUMBER OF NOROVIRUS OUTBREAKS ASSOCIATED WITH A GGII.4 VARIANT IN THE NETHERLANDS AND ELSEWHERE: DOES THIS HERALD A WORLDWIDE INCREASE?

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An increasing number of acute gastroenteritis outbreaks have been reported in the Netherlands since October 2004 to the Rijksinstituut voor Volksgezondheid en Milieu (RIVM, the Dutch National Institute of Public Health and the Environment) [TABLE]. The early onset of the 'winter vomiting disease' season and the high number of reports are unusual. Outbreaks have been reported from different settings, most of which are institutional. So far, all of the outbreaks for which the diagnostic evaluation has been completed are caused by norovirus. This situation may be indicative of a wider trend as several countries have reported higher incidences recently through the global electronic reporting system ProMED-mail (http://www.promedmail.org).

TABLE

Number of norovirus outbreaks reported in the Netherlands in the winter seasons from 2000/2001 to 2004/2005

	September	October	November	December	January	February	March
2000/2001	3	1	4	3	13	11	8
2001/2002	2	6	8	14	18	12	8
2002/2003	7	11	33	52	26	12	2
2003/2004	1	1	1	2	9	4	3
2004/2005	9	18	31	13**	-	-	-

**: Number of norovirus outbreaks reported in the first 2 weeks of December. An additional five outbreaks are under investigation.

We would like to share this observation, because we suspect a repeat of the situation in 2002. In that year, the Food-borne viruses in Europe network (FBVE, http://www.eufoodborneviruses.co.uk/) saw a sharp increase in the number of norovirus outbreaks across Europe, and an increase was also reported in the United States. This had a major impact on hospitals and other settings such as nursing homes and cruise ships. The large increase in 2002 was associated with the introduction of a new variant norovirus within the GGII.4 genotype. This virus was first detected early in 2002, and had replaced the resident virus population by mid-summer in all the countries in Europe that were participating in the Food-borne Viruses in Europe network [1,2]. In the United Kingdom, the cost of the 2002 epidemic was calculated to be approximately US$184 million [3].

In the Netherlands outbreaks analysed so far in 2004, another new lineage (GGII.4-2004) within the GGII.4 genotype has been found. This variant is distinct from the 2002 variant strain (GGII.4-2002). Since the beginning of August 2004, 71 norovirus outbreaks have been reported in the Netherlands. Of these, viruses from 44 outbreaks were characterised by sequence analysis, and all 44 belong to the new GGII.4 lineage.

This variant has already been highly active in Australia during the 2004 southern hemisphere winter season (personal communication, Michael Lyon, Public Health Virology Laboratory, Queensland Health Scientific Services, Brisbane, Queensland, Australia, 2004). It caused many outbreaks in different settings and has now almost completely disappeared in the southern hemisphere with the onset of warmer weather.

Since the outbreak season for norovirus in the Netherlands normally starts in December and peaks in January, we believe that a warning that a worldwide increase of outbreaks comparable to 2002 might be on its way is appropriate.

Although data analysis needs to be finalised, we have indications from the FBVE surveillance that GGII.4 is more commonly associated with outbreaks in institutional settings than other norovirus variants; this suggests that the norovirus GGII.4 genotype has properties facilitating transmission, and thereby has the propensity to cause epidemics.

We are continuing to monitor the situation in Europe and are studying the difference in virulence between strains, biological background of the mechanism for its rapid dissemination, and insight into the micro-evolution of noroviruses. Details on the genetic background of these variant noroviruses can be obtained by sending an email to fbve@rivm.nl. We have used the polymerase gene primers for monitoring purposes, and sequence properties are given below. The FBVE network will monitor noroviruses as part of the activities in the EU-funded DIVINE project. We would also be interested to hear from parties outside the participating countries.

Prevention

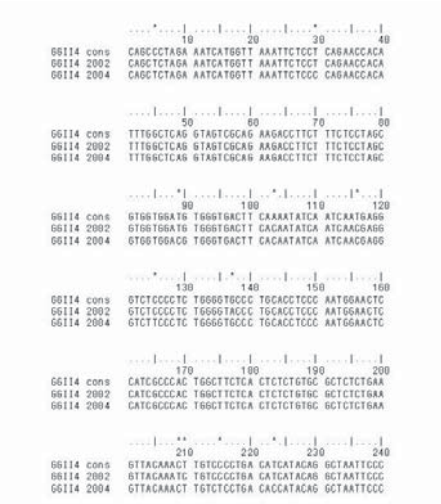
There are some protocols for healthcare settings [4], hotels and cruise ships available in the literature. Guidelines in these protocols are partly evidence-based and partly common sense, and the effectiveness of some of these measures is subject to debate. Therefore, controlled intervention studies are needed in order to apply evidence-based practice during outbreaks in institutional settings, especially nursing homes and homes for the elderly. Until results of such studies are available, their effectiveness in controlling outbreaks is not clear for all settings.

With these caveats, the following common prevention measures are recommended:

- isolation of affected persons;
- use of gloves and facial masks while cleaning contaminated areas;
- cleaning of contaminated areas with disinfectants containing 1000 – 5000 ppm of hypochlorite, carpets with steam. Chadwick et al suggest the use of hypochlorite at 1000 ppm for disinfection [4], although recent reports suggest that this concentration may be too low for efficient inactivation of NoV and levels of 3000 to 5000 ppm free chlorine may be more appropriate [5,6];
- washing of contaminated bed linen at least at 70° C using detergents, preferably containing bleach;
- particular attention to door handles, taps, toilet or bath rails;
- frequent handwashing;
- no return to work until 48-72 hours after compete resolution of symptoms for affected staff, and education on virus shedding which may continue for weeks.

FIGURE

Sequence alignment of norovirus GGII.4 lineages



GGII.4 cons is the consensus sequence of strains prevalent before 2002, GGII.4 2002 is the consensus sequence of the strain that was dominant in the 2002/2003 winter season, GGII.4 2004 is the consensus sequence of the strain that has become dominant during 2004. The sequence is from the RNA dependent RNA polymerase gene, the region upstream of the conserved YGDD motif. Eleven informative positions in the alignment have been highlighted with an asterisk above the sequence. In these positions one sequence is different from the other two.

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First vancomycin-resistant *Enterococcus faecium* outbreak reported in Hungary

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The first healthcare-associated vancomycin-resistant *Enterococcus faecium* (VRE) outbreak in Hungary occurred between April and September 2004 at a haematology and stem cell transplantation unit of a hospital. Fourteen cases of infection and seven cases of intestinal colonisation were detected.

During the outbreak, *E. faecium* was identified in blood samples (9 patients), urine (12 patients) and wound secretions (two patients). The vancomycin-resistant isolates had vancomycin minimum inhibitory concentrations (MICs) of 48-128 µg/ml and were teicoplanin susceptible (MICs 1-2 µg/ml) (the so-called *vanB* phenotype). During the epidemiological investigation at the haematology unit in September, *E. faecium* isolates were also identified in three environmental samples (a surgical bowl, a sheet from a ward, and a wash basin from the bedpan-washing room). As part of the investigation, stool samples from forty patients were tested. Eight VRE positive samples were identified (colonisation in seven cases and one symptomatic case).

Two patients with symptomatic illness had undergone stem cell transplantation. Twelve of the 14 infected patients had malignant haematological disease. Five colonised patients also had haematologic malignancies, and one colonised patient had a benign form of disease.

Presence of the *vanB* gene in resistant *E. faecium* strains was confirmed by polymerase chain reaction testing. Twelve isolates analysed by pulse gel field electrophoresis (PFGE) showed similar patterns for resistant isolates that were different to the patterns seen with isolates of vancomycin-susceptible *E. faecium* strains found in the unit and with the set of *vanB E. faecium* isolates identified in the country.

Bacteriological surveillance data in Hungary show that, in 2003, vancomycin-resistant *Enterococcus* species isolates were less than 1% of all *Enterococcus* isolated in Hungary that year (15 933) [1]. The monoclonal origin of the strains suggested that the emergence of the outbreak strain was recent and has not reached an endemic level.

During the outbreak, all patients were screened on admission. Patients were isolated until their screening results were negative. VRE-infected and/or colonised patients were isolated in separate rooms, and were nursed only by certain staff. The importance of hand hygiene and surface disinfection was emphasised. The outbreak ceased after the control measures were implemented. The last VRE-positive patient was identified on 2 September 2004.

This outbreak demonstrated the importance of strengthening infection control measures in the hospital, introduction of surveillance of multi-resistant pathogens, and revision of disinfection technologies and antimicrobial policy [2].

This is the first such outbreak reported in Hungary. The source was not identified cases were only identified by routine microbiological cultures. Three publications connected with the outbreak, on microbiological diagnosis of VRE [3], manifestations and therapy [4], and prevention and infection control [5]) have been Published on the website of the National Center for Epidemiology, in Hungarian only.

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Cases of rabies in Germany following organ transplantation

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On 16 February 2005, the Deutsche Stiftung Organtransplantation (German Foundation for Organ Transplantation, http://www.dso.de/) announced possible rabies cases in three of six patients who received organs from a donor who died in late December 2004 [1].These three patients, who received lung, kidney and kidney/pancreas transplants following the donor's death, are in a critical condition. The remaining three organ recipients (two corneal, one liver) have not shown any signs of rabies.

The organ donor suffered cardiac arrest in a hospital, where she was resuscitated several times. Her circulatory system was stabilised, but prolonged hypoxemia led to brain death. There were no clinical indications that the donor patient was infected with rabies.

The Bernhard-Nocht-Institute for Tropical Medicine in Hamburg (http://www.bni-hamburg.de/) and the Konsiliarlabor for Rabies at the University Clinic in Essen's Institute of Virology confirmed the diagnosis of rabies in the donor and two of the recipients on 16 and 17 February, 2005 [2]. As a precaution, all contacts of the infected donor and the infected patients in Germany have received rabies immunoglobulin and started a course of rabies vaccination. A warning was posted on the European Early Warning and Response System on 18 February.

The risk of rabies infection in Germany is extremely low. The last two deaths due to rabies in Germany occurred in 1996 and 2004