

Indications for worldwide increased norovirus activity associated with emergence of a new variant of genotype GII.4, late 2012

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Globally, surveillance systems showed an increase in norovirus activity in late 2012. Molecular data shared through the NoroNet network suggest that this increase is related to the emergence of a new norovirus genotype GII.4 variant, termed Sydney 2012. Healthcare institutions are advised to be prepared for a severe norovirus season.

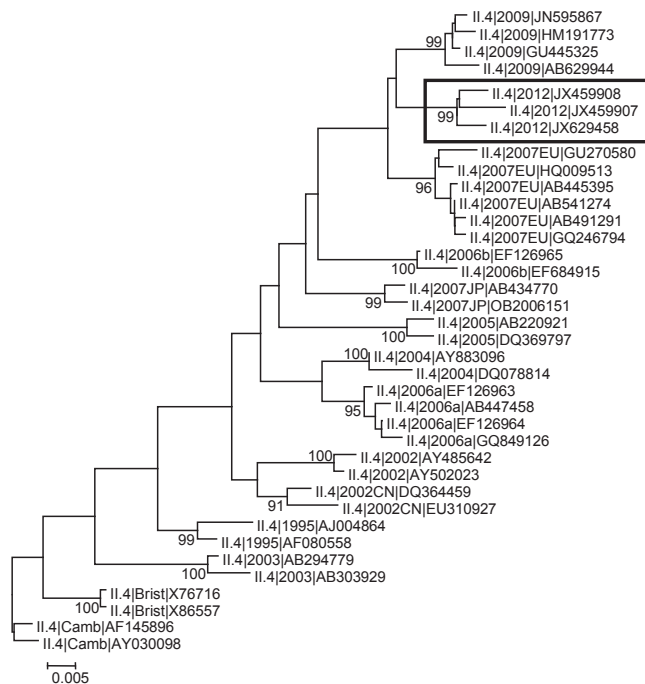
In the United Kingdom (UK), the Netherlands, and Japan, norovirus (NoV) epidemiological and laboratory surveillance systems show increased levels of NoV activity compared to previous seasons, in late 2012 [1-3]. Similarly, increases have been noted in Australia, France and New Zealand (unpublished data). At this stage, and with the limited surveillance of NoV in most countries, it is difficult to conclude if these increases denote early seasonal activity or truly increased incidence, although for the UK the latter has been suggested. On 29 November, and on 4 and 6 December, ProMed (<http://www.promedmail.org/>) messages reported a dramatic rise in NoV hospital outbreaks in England, a 64% higher number of confirmed NoV laboratory reports (hospital- and community-acquired) in England and Wales, and NoV-related deaths in elderly in Japan. The first molecular data uploaded to the international molecular surveillance database NoroNet from Australia, France, New Zealand and Japan indicate that this increase is associated with emergence of a new variant of genotype GII.4 (GII.4). The first report of this variant was from Australia in March 2012 (personal communication P.A. White, September 2012), and the strain sequence was submitted to GenBank (accession number: JX459908.1). In the United States (US), the variant (named Sydney 2012) was detected

in September 2012 in five of 22 (23%) laboratory-confirmed outbreaks, and in November in 37 of 71 (52%) laboratory-confirmed outbreaks (recorded in the US norovirus surveillance network CaliciNet) [4]. In two European countries that have not reported any indications of increased activity, the new variant has been found in outbreaks, two in Belgium (September and December 2012) and one in Denmark (November 2012). Other countries participating in NoroNet have not yet reported the new variant.

NoV is the predominant aetiological viral agent of acute gastroenteritis worldwide and is present throughout the year, but most prevalent in the winter season in temperate climates. In the last decade, strains belonging to NoV GII.4 have been responsible for the majority of outbreaks, as well as community cases of acute gastroenteritis. It has been suggested that hospitalisation and deaths occur more frequently during peak seasons associated with new NoV GII.4 variants [5-7]. Since 1995, new epidemic variants of GII.4 have emerged every two to three years, with population immunity and genetic drift as major evolutionary driving forces [8]. Emergence of new variants has been associated with increased NoV activity early in the season [9-11]. The newly found NoV GII.4 Sydney 2012 variant has evolved from previous NoV GII.4 variants (Figure 1) and will be described in detail elsewhere. Briefly, the NoV GII.4 Sydney 2012 variant has a common ancestor with the dominant NoV GII.4 variants Apeldoorn_2007 and NewOrleans_2009, but is phylogenetically distinct. Amino acid changes are seen in the main epitopes located at the P2 domain, consistent with observations from prior epidemics. This may have led to an escape to

FIGURE

Neighbour-joining tree of norovirus GII.4 capsid amino acid sequences



Representative strains from the variant typing tool were used in this analysis. The taxa are named with genotype|variant name|accession number. Taxa representing the recent NoV GII.4 Sydney 2012 variant are boxed. The bootstrap values in percentage of 500 replicates are shown next to the major branches. The evolutionary distances were computed using the Poisson correction method in the units of the number of amino acid substitutions per site with the exclusion of gaps leaving a total of 536 positions in the final dataset. Phylogenetic analyses were conducted in MEGA4 [12].

existing herd immunity and might explain the observed increased outbreak activity.

The reference set of the Norovirus Typing Tool has been updated to correctly assign GII.4 Sydney 2012 sequences. This web-based tool (<http://www.rivm.nl/mpf/norovirus/typingtool>) is publicly available for genotyping of NoV sequences and was developed to facilitate standardisation of nomenclature [13].

Conclusion

Various countries around the globe have reported a higher incidence of NoV outbreaks or illness late 2012, and the first molecular data available via NoroNet suggests that this increase is related to emergence of a new variant of NoV GII.4. More data is needed to confirm the association between a higher NoV incidence and the new NoV GII.4 2012 variant. For this, we invite new members to join the NoroNet network (<http://www.noronet.nl>). Noronet is a worldwide network for NoV molecular and epidemiological surveillance, through

which countries in Europe, Asia, and Australasia have shared NoV outbreak data, sequences, and other information. The NoroNet database, including analysis tools, is accessible for all NoroNet members.

With the early signs of a severe NoV season, health-care institutions are advised to be prepared for NoV introductions. Outbreak management measures, like stringent hygiene measures and quarantine of infected cases, can help to reduce the size of outbreaks [14,15].

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