

Editorial: Norwalk-like virus — issues for surveillance

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Recent closures of hospital wards in Australia and Scotland due to Norwalk-like virus (NLV) infections have increasingly focussed attention on these agents as the cause of outbreaks of viral gastroenteritis.^{1,2,3} NLV has been identified as the leading cause of community-acquired gastroenteritis in a number of countries, including the Netherlands.⁴ Since the disease is mild, and specific surveillance for NLV has not been carried out, the actual incidence in the United Kingdom is considered to be more than 1,000 times greater than reported.⁵ Although associated with 'winter vomiting' in temperate climates,^{6,7} there is evidence for the virus causing gastroenteritis year-round. It has been suggested that there are differences in incidence year by year depending on the circulating strain.⁸ Data from Australia suggest that there is both a seasonal peak in NLV activity between late winter and early summer and a variation year by year, with peaks of activity noted in 1995 and 1996.⁹ Foodborne outbreaks of NLV are reported frequently through OzFoodNet.¹⁰ Large outbreaks of NLV gastroenteritis associated with eating oysters and with contaminated orange juice have been reported in Australia.^{11,12}

Australian hospitalisation data for 1998–99 and 1999–00 show 13,026 and 14,110 admissions for viral intestinal infections respectively.¹³ Although only 34 and 36 hospitalisations were identified as due to NLV, 5,526 and 9,133 were for unidentified viral agents in 1998–99 and 1999–00 respectively. Due to difficulties of diagnosis, many of the admissions for gastroenteritis with an unidentified cause could be due to NLV.

It has been hypothesised that NLV strains circulating in humans may represent a spill-over of those in animal reservoirs such as cattle,⁸ although there is evidence that these strains may be distinct.¹⁴ While foodborne transmission of NLV has been frequently documented,^{15,16}

transmission by water,¹⁷ environmental contamination,¹⁸ and aerosol¹⁹ have also been documented. While around 40 per cent of NLV disease in the United States of America (USA) is estimated to be foodborne,²⁰ more recent focus has been placed on person to person transmission.^{1,21}

Transmission from person to person, particularly in the setting of an aged care facility, has important implications for infection control procedures which are discussed in the article in this issue of *Communicable Diseases Intelligence*.¹ There is uncertainty about the duration of excretion of the virus in faeces after infection and whether the virus is shed by asymptomatic people. Following oral administration of NLV to healthy volunteers, 82 per cent were infected, two thirds of these were symptomatic and stool specimens remained positive for the virus for up to 7 days.²² Several reports have since appeared of high levels of NLV excreted up to 10 days after resolution of illness.²³ Another recent study of 99 subjects infected with NLV found 26 per cent were excreting the virus up to 3 weeks after the onset of illness.²⁴ The relatively long term excretion of NLV calls into question infection control guidelines which allow the return of staff to aged care facilities 24 to 48 hours after the cessation of symptoms.

While high rates of NLV infection are found in children early in life,²⁵ NLV is now also recognised as an important cause of gastroenteritis in the elderly.²⁶ Thus, much of the recent prominence of NLV may be due to increasing institutionalisation of the elderly. Among the elderly, immunocompromising conditions may also be important risk factors for NLV infection. Recent genetic work¹⁴ has opened the possibility that some NLV strains may be associated with particular settings such as aged care facilities.²⁶

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Until recently, diagnosis of NLV has been dependent on the identification of the virus particles by electron microscopy. Utilising published genomic sequences a number of investigators have developed reverse transcription (RT)-PCR methods for the detection and differentiation of NLV genogroups.^{27,28} These methods can detect fewer than 100 virus particles in 5µl faecal extract and are six times more sensitive than electron microscopy.²⁸ As these assays become standardised and more widely available, a more accurate assessment of the epidemiology of NLV can be expected.

Although NLV still can not be cultured in cell lines, vaccines based on Norwalk virus-like particles are being developed. The rationale behind such vaccine development is that since the NLV group is restricted to humans, vaccination would be effective in decreasing the disease burden. Although disease is mild and self-limiting in most cases, vaccines could be cost effective by reducing hospitalisations, medical consultations and time lost from work. Vaccines may be particularly useful in preventing disease in aged care facilities. However, the diversity within the genogroups of NLV is large enough to require the inclusion of multiple strains; the correlates of protective immunity are not known, nor is it known why natural infection fails to result in long lasting immunity.²⁵ There is no animal model of NLV disease in which candidate vaccines can be investigated. These factors represent considerable hurdles to vaccine development.

In the context of a high prevalence of gastroenteritis caused by NLV, which is increasingly accurately diagnosed and recognised as the cause of outbreaks, should this disease be included in communicable disease surveillance? What kinds of surveillance would be appropriate? A passive surveillance system would collect data on only a small fraction of cases, since the majority do not seek medical attention. An active surveillance system would be quickly overwhelmed by the sheer number of cases. A sentinel laboratory-based surveillance system, such as the Laboratory Virology and Serology Surveillance Scheme, would be well placed to provide data on the most significant cases, since the scheme includes many of the major hospital laboratories in the country. If there is evidence of NLV genotypes associated with different settings and temporal and geographic variation, genetic analysis of circulating strains would be useful.

Surveillance would also further our understanding of the epidemiology of NLV in Australia and identify viral strains which should be included in a future vaccine.

Acute gastroenteritis is a very common disease with estimates from recent surveys in Australia suggesting that the incidence is approximately one episode per person per year.¹⁰ For many years, acute gastroenteritis cases have been a 'diagnostic void' with a pathogen identified in less than 10 per cent of hospitalised acute gastroenteritis cases in the USA before 1970.²⁹ Improvements in diagnostic technology have identified various viral agents associated with acute gastroenteritis and it now appears that NLV infections represent a substantial proportion of acute gastroenteritis cases.⁴ The low infective dose of NLV (10 to 100 particles),⁷ and the multiple modes of transmission pose great challenges to disease control. We can expect to see further outbreaks of NLV gastroenteritis reported as diagnostic methods improve and are applied more widely. Improved understanding of the NLV virus and epidemiology will bring about new and effective tools of infection control and disease prevention.

Note: Norwalk-like viruses have recently been officially renamed the genus 'Norovirus'.³⁰

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