

Norovirus outbreak in Australian Army personnel visiting Brisbane, Queensland, February 2007

1) Dr Dale L. Thomas, MBBS, MPH, FRACGP, MRACMA, Lieutenant Commander, RANR. 2) Dr Alison E. Thomas, MBBS, DipAvMed, FRACGP Lieutenant Commander, RANR.

Abstract

In February 2007, there was an outbreak of gastroenteritis in a group of Townsville-based Australian Regular Army personnel visiting Gallipoli Barracks in Brisbane, Queensland. Of the 23 patients hospitalised, the majority presented with fevers, vomiting, abdominal cramps and diarrhoea. One patient's presentation mimicked acute appendicitis and he underwent appendicectomy. Stool specimens were negative for parasitic and bacterial pathogens; however, two of the later cases were confirmed as having Norovirus infection. The characteristics of the remaining cases were consistent with Norovirus infection. To our knowledge this is the first reported Norovirus outbreak in Australian Defence Force (ADF) personnel.

Background

Noroviruses are an important cause of epidemic gastroenteritis in both children and adults, particularly in settings such as refugee camps and natural disasters that are characterised by overcrowding and poor sanitation¹. Outbreaks have been reported in passenger cruise ships, nursing homes and youth summer camps in the United States of America (US). Norovirus infection is thought to have been a major cause of morbidity amongst the 240,000 people evacuated from Louisiana to Texas following Hurricane Katrina in September 2005². It is thought that around 90% of all epidemics of non-bacterial gastroenteritis in the US are caused by Noroviruses³.

Amongst military populations, Norovirus outbreaks have been described in forces from the US, Israel, the Netherlands and the United Kingdom in both maritime and land theatres of operations, as well as in military training establishments⁴⁻¹⁰. Attack rates of up to 25% were reported in one study⁵. Although the clinical manifestations are usually self-limited within 48 hours for affected individuals, a Norovirus outbreak can impact significantly on the operational effectiveness of military forces.

We were unable to identify any previous reports in the medical literature of Norovirus outbreaks amongst ADF personnel. There was a later Norovirus outbreak reported in the news media in March 2007 at a Royal Australian Air Force (RAAF) base in Adelaide, South Australia¹¹.

Case Report

Chronology. In early February 2007 members of an Australian Regular Army infantry company travelled by commercial airline flight from Townsville to Brisbane to conduct training at Gallipoli Barracks. During the flight, a soldier was noted to be unwell with vomiting. That evening a 25-year-old male presented to Gallipoli Barracks Health Centre and, following assessment by a general medical practitioner, he was admitted to the ward for observation and rehydration.

On the following day, nine members of the same unit presented with various combinations of vomiting, diarrhoea, abdominal discomfort and fever. Anecdotally it was reported that most of these cases had been seated near the index case on the aircraft. Seating on the aircraft had been allocated in alphabetical order, and the surnames of eight of these nine early cases were clustered between the letters H and O. Although suggestive, it is unclear whether this seating pattern contributed to the early transmission of the illness.

Further cases were admitted over the next week, with the final admission of a member of this group presenting with vomiting 14 days after admission of the index case. The chronology of case presentations appeared to suggest an infectious cause with a relatively short incubation period (see Figure 1). In total, 23 members of the group were admitted with presumed infectious gastroenteritis. Anecdotal reports from patients admitted to the ward suggested that, within the visiting group, there were additional cases

who chose to self-manage their symptoms within the barracks accommodation and did not seek medical attention.

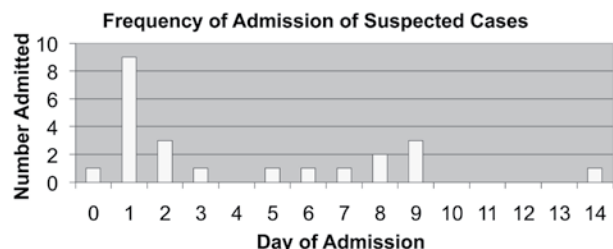


Figure 1. Frequency of admission of suspected Norovirus cases.

Clinical Features. All cases in the group were male. The average age of patients was 25 years, with a range from 19 to 43 years of age. Most of the 23 cases were characterised by vomiting, fever and/or non-bloody diarrhoea. One case had prominent arthralgia and another had cervical lymphadenopathy. These features are summarised in Table 1.

	n (%)
Vomiting	19 (83)
Fever	17 (74)
Diarrhoea	16 (70)
Severe abdominal pain	1 (4)
Lymphadenopathy	1 (4)
Arthralgia	1 (4)

Table 1. Clinical Features.

One soldier from the visiting group, a 19-year-old male, presented with severe abdominal pain associated with moderate neutrophilia (total white cell count [WCC] 14.9; neutrophil count $13.4 \times 10^9/L$). He was referred for surgical assessment and later underwent appendicectomy. Histology showed a non-inflamed appendix with no evidence of malignancy. This case was later included in the group of presumed cases of infectious gastroenteritis.

Treatment of the other 22 cases was symptomatic, with antipyretic and antiemetic medications as well as oral and, in some cases, intravenous rehydration fluids. The mean length of hospital stay was 1.3 nights. The most consistent clinical feature was the prompt resolution of symptoms within 48 hours of admission.

Laboratory Findings. Stool examination for ova, cysts and parasites with culture for bacterial pathogens was negative in four of four specimens. Later specimens were also tested for enteric viruses; none was positive for Rotavirus or Adenovirus. Both of two stool specimens collected from cases presenting later in the outbreak (the 18th and 22nd of 23 cases admitted) tested positive by PCR for Norovirus. Serological testing for Norovirus was not available.

Haematology results are summarised in Table 2. Mild lymphopenia was seen in eight of nine patients who had haematology testing performed, with lymphocyte counts ranging between 0.5 and 1.2 (normal range [NR] 1.5 to $4.0 \times 10^9/L$). Two of these eight patients had mild to moderate neutrophilia of 8.5 and 13.4, while one had a mild eosinophilia. Total WCC was elevated only in the patient who underwent appendicectomy. One patient was noted to have a mild anaemia, with a haemoglobin level of 128 at presentation, which had normalised five days later to a level of 150 g/L. Other haematological parameters were within normal limits, and there were no significant biochemical abnormalities.

Public Health Considerations. On the second day of the outbreak, technicians from the local Army environmental health platoon conducted an investigation aiming to identify the cause of the outbreak. It was considered likely that the responsible pathogen had been spread onboard the commercial aircraft prior to arrival in Brisbane. It was assessed as unlikely that a food-borne pathogen was responsible. There were no secondary cases of gastroenteritis identified among hospital visitors and staff.

	Observed values	Normal range	Units	n (%) observed outside NR
White cell count	5.9 – 14.9	4.0 – 11.0	$\times 10^9/l$	1 (11)
Neutrophils	2.8 – 13.4	2.0 – 7.5	$\times 10^9/l$	2 (22)
Lymphocytes	0.5 – 2.2	1.5 – 4.0	$\times 10^9/l$	8 (89)
Eosinophils	0.0 – 0.5	0.0 – 0.4	$\times 10^9/l$	1 (11)
Haemoglobin	128 – 152	130 – 180	g/l	1 (11)

n=9

Table 2. Laboratory Findings.

Following receipt of positive Norovirus results two weeks later, the Brisbane North regional public health unit was notified. No cases of Norovirus infection had been reported in the local civilian population at that time. It should be noted that Norovirus infection is not a notifiable condition in Australia, so infection of civilian occupants of the aircraft cannot be excluded.

Pathophysiology of Norovirus Infection

Noroviruses – also known as Norwalk-like viruses (NLV) – were first described in 1972¹², and are classified as caliciviruses¹³. At a diameter of 27–32 nm, they are among the smallest of all viruses. Although not enveloped, they exhibit icosahedral symmetry on immune electron microscopy (see Figure 2). Norovirus particles consist of multiple copies of a single structural protein as well as a single-stranded RNA genome. The viral genome was characterised in 1990, allowing the development of better diagnostic tools such as reverse transcriptase polymerase chain reaction (PCR)⁴.

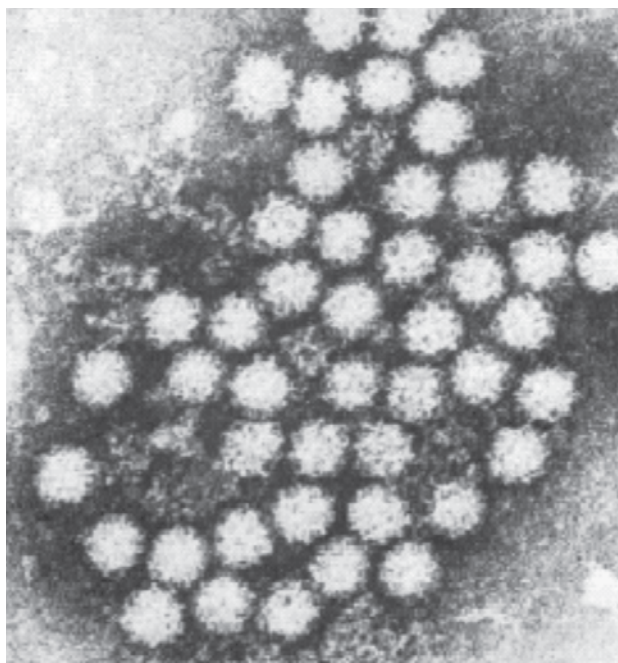


Figure 2. Immune electron micrograph – obtained from *Journal of Virology*¹².

The cellular site of Norovirus replication has not yet been identified³. Histological changes are seen in the proximal small intestine, with villus shortening, crypt hyperplasia and infiltration of the lamina propria with polymorphonuclear and mononuclear cells. No changes have been described in the stomach or colon.

Norovirus infection is characterised by sudden onset of abdominal cramps, nausea, vomiting and non-bloody diarrhoea^{3,13}. Fever is present in about half of cases. Headache, myalgia and abdominal pain are

common. The incubation period is 18–72 hours and the illness is usually mild and self-limiting, lasting between one and two days³. Asymptomatic viral shedding may persist in faeces for one to two weeks thereafter¹³.

Laboratory tests are of limited value. The white blood cell count is usually normal; rarely there is leukocytosis with relative lymphopenia³. Faecal microscopy shows few if any red and white blood cells. Norovirus has never been successfully cultured in vitro or in non-primate animal models⁵. Norovirus antibodies are found in over 80% of adults in both developed and developing countries, although these antibodies do not appear to confer long-term protection against illness following further viral challenge³. The diagnosis may be confirmed using PCR detection of Norovirus in faeces.

Discussion

To our knowledge this is the first reported Norovirus outbreak in ADF personnel. Although Norovirus infection was confirmed in only two cases from this group, the chronology, clinical features and laboratory findings were considered consistent with Norovirus infection being the causative agent in the remaining cases. The size of the visiting group is unknown, which precludes calculation of an attack rate for this outbreak. We were unable to identify any previous reports of Norovirus infection mimicking acute appendicitis.

The two positive Norovirus results described in this case report only became available two weeks after the patients had recovered from their illness. Thus the test was useful in making a diagnosis in retrospect, rather than being a clinically useful diagnostic tool. US forces have deployed Norovirus PCR testing into the field environment, in order to provide rapid diagnostic testing that can be more clinically useful⁶. PCR can also be used to identify Noroviruses by genotype and strain, which may be useful for epidemiological purposes and for monitoring the spread of outbreaks.

ADF health facilities have a low threshold for admitting unwell military personnel who are living in barracks accommodation. This is partly to ensure that there is a level of supervision and care for the affected individuals, and partly to reduce the spread of infectious disease among personnel living in close quarters. This group of visiting personnel was living in basic transit accommodation, with up to eight soldiers sharing a room. These living conditions may have contributed to the spread of Norovirus, particularly to those cases that presented after the first few days of the outbreak.

It can often be challenging to identify the aetiological agent in outbreaks of epidemic gastroenteritis. Analyses of a large series of cases have typically identified a pathogen in only half of these cases, with the majority of the remainder being attributed to unidentified viral pathogens and toxins^{6,14}. Although laboratory examination of stool specimens for parasitic and bacterial infection is readily available, access to PCR detection of enteric viral pathogens is more limited, and results are often only of public health importance. At the time of the outbreak, the state reference laboratory operated by Queensland Health was the only provider of Norovirus PCR testing in Queensland. Because of the difficulty in confirming the diagnosis, it is likely that Norovirus infection is a common but greatly under-reported cause of epidemic gastroenteritis⁸.

Even with the implementation of standard precautions against bodily fluid exposure, hospital staff are at significant risk of becoming casualties in a Norovirus outbreak. Noroviruses are highly contagious because of their low infectious dose (less than 100 virus particles), prolonged asymptomatic shedding (up to two weeks after clinical recovery), stability with freezing and with heating to 60 degrees Celsius, and ability to resist chlorination (10 ppm chlorine), acid (pH level of 2.7), ether, ethanol and detergent-based cleaners^{8,15}. Nosocomial transmission has been reported in both military and civilian hospitals, resulting in some cases in the temporary closure of health facilities^{8,16}.

The US Centers for Disease Control and Prevention (CDC) advise the use of standard precautions with careful attention to hand hygiene practices when caring for patients with suspected Norovirus infection¹⁷. Hard non-porous environmental surfaces should be disinfected with chlorine bleach at a minimum concentration of 1,000 ppm, and for heavily soiled surfaces up to 5,000 ppm. Phenolic-based disinfectants at usual concentrations have only limited activity against Noroviruses. Because Norovirus particles

are not enveloped, most quaternary ammonium compounds have no significant disinfectant activity against them¹⁷.

In 2007 a group of researchers announced plans for a phase 1 clinical trial in humans of an investigational Norovirus vaccine, which is delivered intra-nasally in powdered form¹⁸. If found to be efficacious and safe, vaccination may offer some protection for groups identified as being at high risk of Norovirus infection, such as healthcare workers and military personnel.

Conclusion

This case series adds to the literature of Norovirus outbreaks amongst military personnel. Most of the 23 cases described exhibited clinical manifestations typical of Norovirus infection, with the exception of the case that mimicked acute appendicitis.

There is potential for larger outbreaks of Norovirus amongst ADF personnel, which may limit their operational effectiveness. There remain significant challenges in the early detection and containment of outbreaks, particularly in deployed environments.

Acknowledgement

A version of this paper was presented at the Australian Military Medicine Association annual scientific meeting in Melbourne on 21 October 2007. The authors wish to acknowledge the contribution of 2nd Health Support Battalion and Gallipoli Barracks Health Centre staff in providing care for the patients described in this case report, and in assisting with data collection for preparation of this paper.

*Authors affiliation: 1. Deputy Director Medical Services, Redcliffe Hospital, Anzac Avenue, QLD 4020, Australia
2. General Practitioner, Telegraph Road Clinic, Telegraph Road, Bracken Ridge, QLD 4017, Australia
Contact author: Dr Dale L. Thomas, MBBS, MPH, FRAGGP, MRACMA Lieutenant Commander, RANR,
Email: nnavmedc@bigpond.net.au*

References

1. Norwalk-like virus-associated gastroenteritis in a large, high-density encampment--Virginia, July 2001. *MMWR* 2002 Aug 2; 661-663.
2. Palacio H, Shah U, Kilborn C, et al. Norovirus outbreak among evacuees from Hurricane Katrina - Houston, Texas, September 2005. *MMWR* 2005 Oct 14; 1016-1018.
3. Greenberg HB. Viral gastroenteritis. Chapter 192 in: Braunwald E, Fauci AS, Kasper DL, et al, editors. *Harrison's Principles of Internal Medicine*. 15th ed. New York: McGraw-Hill, 2001; 1135-1138.
4. Matson DO. Norovirus gastroenteritis in US Marines in Iraq [editorial]. *Clin Infect Dis* 2005 Feb 15; 40(4):526-527.
5. Thornton S. Detection of Norwalk-like virus infection aboard two U.S. Navy ships. *Mil Med* 2002 Oct 1; 167(10): 826-830.
6. Thornton SA, Sherman SS, Farkas T, et al. Gastroenteritis in US Marines during Operation Iraqi Freedom. *Clin Infect Dis* 2005 Feb 15; 40(4): 519-525.
7. Grotto I, Huerta M, Balicer RD, et al. An outbreak of Norovirus gastroenteritis on an Israeli military base. *Infection* 2004 Dec 1; 32(6): 339-343.
8. Brown D, Gray J, MacDonald P, et al. Outbreak of acute gastroenteritis associated with Norwalk-like viruses among British military personnel--Afghanistan, May 2002. *JAMA* 2002 Jun 26; 287(24): 3203-3204.
9. Centers for Disease Control and Prevention. Norwalk-like viral gastroenteritis in US Army trainees--Texas, 1998. *JAMA* 1999 Apr 14; 281(14): 1266.
10. Norwalk-like viral gastroenteritis in U.S. Army trainees--Texas, 1998. *MMWR* 1999 Mar 26; 225-227.
11. Opposition claims 50 affected by air base gastro outbreak. Sydney: ABC Premium News 2007 Mar 28 [accessed 2007 Jul 19]. Available from: <http://proquest.umi.com/pqdweb?did=1245642151>
12. Kapikian AZ, Wyatt RG, Dolin R, et al. Visualization by immune electron microscopy of a 27-nm particle associated with acute infectious nonbacterial gastroenteritis. *J Virol* 1972 Nov; 10(5): 1075-1081.
13. Drew WL. Human enteric caliciviruses: Norwalk and related viruses. Chapter 38 in: Wilson WR, Drew WL, Henry NK, et al, editors. *Current Diagnosis and Treatment in Infectious Diseases*. New York: Lange, 2001; 429-430.
14. Schwaber MJ, Grotto I, Balicer RD, et al. Infectious diarrheal outbreaks in the Israeli military. *Mil Med* 2005 Jul 1; 170(7): 634-637.
15. Dolin R. Noroviruses – challenges to control. *NEJM* 2007 Sep 13; 357(11): 1072.
16. Christiansen M, Wray M. Virus closes hospital wards. Brisbane: The Courier-Mail, 2007 Jul 18 [accessed 2007 Jul 19]. Available from: <http://www.news.com.au/couriermail/0,23739,22093137-3102,00>
17. Centers for Disease Control and Prevention. Norovirus in healthcare facilities fact sheet. Atlanta: CDC, 2006 Dec 21 [accessed 2007 Jul 24]. Available from: http://www.cdc.gov/ncidod/dhqp/id_norovirusFS.html
18. Vaccines; LigoCyte Pharmaceuticals initiates US clinical trial of Norovirus vaccine. *Clinical Trials Week* 2007 Apr 16; 49.