

NORWALK-LIKE VIRUSES

IN A FAMOUS scene from Hitchcock's 1963 film, *The Birds*, Melanie Daniels (Tippi Hedren) sits outside an old schoolhouse, oblivious to the birds massing behind her. From inside, we hear the children singing the old nursery rhyme "Rissoldy Rossoldy."

Only 5 years later, at another old schoolhouse, this one in Ohio (see figure), another horror "emerged" to afflict schoolchildren, teachers, their families, and—over time—people the world over. Thirty-five years later, this virus—or more properly this family of viruses—is the most commonly recognized cause of disease outbreaks in Oregon and the rest of these United States, and quite possibly the overall leading cause of gastroenteritis.

Until recently almost unknown to the public, today—while a Google™ search for "cruise ship disasters" still leads with the *Titanic*—Norwalk-like viruses also make the first page of web hits. Today's article offers busy clinicians an opportunity to get up to speed on this long-since-emerged pathogen.

"Norovirus" has been recently adopted as the generic name for this group of caliciviruses, although sounding a bit ersatz to this ear. Genetic characterization of hundreds of viral isolates has led to sub-categorization of these diverse viruses,¹ which originally were named rather haphazardly, mostly for the place of first identification (e.g., Norwalk, Snow Mountain, Hawaii, Ditchling, ...). For aesthetic and historical reasons, however, we shall continue to refer to them as "Norwalk-like" viruses (NLVs),

Bronson-Norwalk School



although how long we can insist remains to be seen. Not included in this discussion are other, more distantly related, pathogenic caliciviruses, including sapoviruses (the Sapporo agent and its ilk).

It was October 1968 at the Bronson-Norwalk School in Norwalk, Ohio² when epidemiologists collected stool samples that were eventually to yield by electron microscopy the first evidence of these ~27 nm-diameter viruses.³ The prototype Norwalk outbreak was characterized by gastroenteritis with a sudden onset, a high proportion of vomiting among those afflicted, and a high secondary attack rate. Illness was generally short-lived and self-limiting—a little the worse for wear, but no long-term sequelae.

The original outbreak was quite typical, although it is now better appreciated that moderate to severe dehydration can occur in some individuals, and can be fatal in elderly or debilitated patients. Otherwise, Norwalk (*sensu lato*) is generally short-lived and of little lasting consequence.

DISEASE

Most people guess that the source of their foodborne illness was the last thing they ate that someone else prepared. Most people are wrong. The incubation period of Norwalk infections generally falls in the 24–48 hour range. Group averages for Norwalk outbreaks (i.e., median incubation) are usually in the 30–38 hour range. Point-source outbreaks (e.g., from food served at a meal) typically yield a log-normally distributed epidemic curve. Person-to-person outbreaks often have no clear onset peak.

Single NLV infections are impossible to distinguish in clinical groups from other enteric pathogens. Given a group of people afflicted, though, a characteristic picture emerges: vomiting and diarrhea, usually with a higher proportion of the former than the latter. Fever is generally absent or at most low-grade. Headache

and myalgias are common—much more so than reported for most other agents of gastroenteritis. Symptoms rarely persist more than 24–48 hours, although some patients may feel "wrung out" for another day or two. Patients who seek medical attention are probably sicker than average.

Supportive care (i.e., rehydration) is generally about the most that is called for, and that only in a small minority of victims. Antibiotics are obviously a waste. We would reiterate that empiric antibiotic therapy for acute onset gastroenteritis is rarely appropriate in the United States. Studies on the etiology of traveler's diarrhea among visitors to Mexico (for example) are not directly relevant to most outpatient populations in this country. When in doubt, grow it out.

TRANSMISSION

Like most enteric pathogens, Norwalk-like viruses are primarily spread by what we call the fecal-oral route, which needs little explanation to our regular readers. As these are human-only viruses, or at least mostly so, "food-handlers" with poor hygiene are the usual suspects, and justifiably so. But there are some twists that make Norwalk transmission not quite that straightforward. First, vomitus is likely to be infectious also. It is the possibility of an airborne route of spread, however, that has enveloped Norwalk in a cloud of mystery since early in its history.⁴ That and the role of fomites in transmission continue to interest epidemiologists and bedevil infection control practitioners in hospitals, nursing homes, and cruise ships alike. The specifics are poorly understood, but it would appear that an aerosol of particles generated while vomiting (and with diarrhea??) can either infect people directly or settle onto surfaces that then are touched with hands that sooner or later end up in the mouth. Thus, environmental cleaning may be an



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important adjunct to patient isolation as a means of stopping transmission. Our inability to culture Norwalk-like viruses makes it difficult to evaluate the efficacy of various cleaning solutions. Dilute bleach is almost certainly effective, although of limited practicality on some surfaces.

Foodborne and waterborne transmission is common. Typical food vehicles include salads, sliced fruits, sliced meats, wedding cake frosting—anything that gets human handling without subsequent reheating. Raw oysters are another popular choice. In contrast to many bacteria, NLVs don't multiply in foods, so time/temperature abuse (e.g., leaving the chicken out) is not relevant. NLVs are also fairly resistant to chlorine, and outbreaks linked to contaminated drinking water and recreational water outbreaks are well documented also.

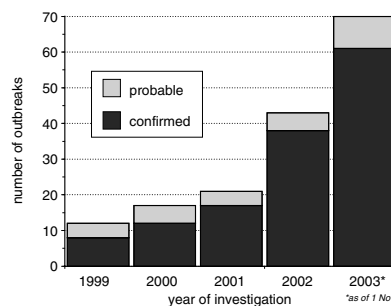
Outbreaks in nursing homes and other institutions are a serious problem. Not only are these venues full of especially vulnerable persons, but crowding and communal living spaces enhance opportunities for person-to-person spread that can involve staff, including food service workers, with potential to amplify the problem. Control recommendations need to be tailored to the specific facility, and often include cohorting of ill patients and enhanced environmental cleaning.

Laboratory confirmation of Norwalk infection depends on PCR. These tests are rarely available in (or desired by) the private sector, but have become very popular among outbreak investigators around the country over the past 5 years. Available primers recognize the many

variants in the Norovirus group. The number of lab-confirmed NLV outbreaks in Oregon has increased steadily since 1999 (see figure), more than anything reflecting the increased zeal of local health department nurses in successfully soliciting stool samples from hapless victims. During that period, at least 158 (50%) of 316 gastroenteritis outbreaks investigated in Oregon were caused by Norwalk-like viruses. (And many of the 63 "unknowns" may have been Norwalk as well.)

NLV shedding persists after symptoms end, with implications for both transmission and diagnosis. Persons can shed virus for at least several days after recovery from symptoms, as many restaurant patrons have learned.⁵ Although the concentration in stool drops quickly,⁶ using newer molecular probes, viral particles (albeit of uncertain infectivity) may be detectable for 10 days or longer. Oregon data indicate that the probability of PCR confirmation (i.e., positive:tested ratio) is essentially constant throughout the first week after onset. While antibodies indicating past exposure are very common, long-term protective immunity rarely develops.

Norovirus Outbreak Investigations in Oregon, 1999–2003



While most of this information derives from outbreak investigations, noroviruses are among the most common causes of "sporadic" community-acquired gastroenteritis. When people talk about "stomach flu," this is often what they mean. Probably. (What *does* that mean?) In a Dutch study, NLVs were found in 5% of patients with gastroenteritis seen in general practice clinics, compared with 1% in controls.⁷ NLVs are major causes of missed school and work, not to mention being frequent uninvited wedding guests.

Hand washing and sick-leave policies are our principal defenses; where they are weak, we are vulnerable. Clinicians are reminded to report promptly rumors of possible common-source outbreaks, including Norwalk-like clusters, to their local health department.

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