Specimen testing strategy and the challenge in respiratory and enteric outbreak management in long-term care homes – The case of Ontario, Canada

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Acute respiratory infections (ARIs) and gastroenteritis represent a significant burden of illness in long-term care homes, and are a major cause of morbidity [1, 2, 3]. In Ontario, like other parts of Canada, a significant proportion of infections or outbreaks are caused by viral pathogens. Based on data from Public Health Ontario Laboratory (PHOL), the most common viruses causing ARIs are influenza A and B, rhinovirus, coronavirus, respiratory syncytial virus, parainfluenza, and metapneumovirus [4]. These respiratory viruses, though from different genera, can cause similar acute respiratory symptoms such as cough, sore throat, runny nose, nasal congestion, headache, low-grade fever, sneezing, malaise, and myalgia. There exists, however, some variability in terms of the incubation period, or period of communicability. For most of these viruses, the onset of symptoms usually begins one to three days after exposure, and may last for 7–10 days or more. When outbreaks are suspected, the case definition is usually two or more cases of ARIs within 48 hours on one unit [1]. Nasopharyngeal swabs are typically collected from the initial symptomatic patients to determine the causative organism.

On the other hand, the most common viruses causing gastroenteritis are rotavirus, norovirus, sapovirus, astrovirus, enterovirus and adenovirus [5]. Referred to as enteric viruses, they are part of a wide spectrum of viruses which invade and replicate in the mucosa of the intestinal tract. Symptoms typically include nausea, vomiting, diarrhea, malaise, abdominal pain, and cramping [3, 5]. Symptoms usually last for one to five days, and it is difficult to distinguish between etiological agents without full multiplex PCR testing. Transmission of these viruses is often linked to direct contact with an infected person, indirect contact via fomites, or by ingestion of contaminated food or water [6]. Gastroenteritis outbreaks frequently occur in settings such as long-term care homes, hospitals, schools, and cruise ships [7, 8]. In long-term care homes in Ontario, the suspicion of gastroenteritis is based on any one of the following criteria: two or more episodes of diarrhea (watery stool) within a 24-hour period, **or** two or more episodes of vomiting within a 24-hour period, **or** one episode of diarrhea and one episode of vomiting within a 24-hour period, **or** laboratory confirmation of a known gastrointestinal pathogen and at least one symptom compatible with gastrointestinal infection [2].

Both respiratory and enteric viruses can be detected by multiplex PCR assays in public health laboratories [9, 10]. However, according to the Ontario Ministry of Health and Long-Term Care's guidance document titled "Control of Respiratory Infection Outbreaks in Long-Term Care Homes", only a maximum of four specimens should be taken during any initial respiratory outbreak investigation for full multiplex PCR testing [1]. The guidance document further states that if additional testing is desired, the home must contact PHOL's customer service centre for further consideration. Considerations for additional testing may be determined at the discretion of the laboratory on the basis of changes in disease severity, new cases in a prophylaxed population during a confirmed influenza outbreak, suspicion of a non-viral agent, new cases in other parts of a facility, ongoing cases after a substantial period of time, or for other reasons [1]. On the other hand, the PHOL uses multiplex gastroenteritis viral real-time PCR (MGVP) assay to detect adenovirus, rotavirus, and norovirus (but not sapovirus and astrovirus), and a maximum of five outbreak specimens are routinely accepted for testing [11].

Significant challenges exist in the application of these guidelines, and some health units or PHOLs have been hesitant to consider more testing once the same viral agent has been identified in the initial two or more specimens. In this editorial, I discuss some of the issues this could create in the overall outbreak response effort, with a focus on two aspects that are relevant in disease transmission considering the fact that effective diagnosis is critical in evidence-based outbreak management [12].

Conflicts of Interest: None to disclose.

Acknowledgements: Sincere thanks to Anna George, Regional IPAC Specialist at Southbridge Care Homes and Dr. Devon Metcalf, Associate Editor of the Canadian Journal of Infection Control for their review and useful suggestions.

First, the testing of enteric viruses in Ontario is limited to adenovirus, rotavirus, and norovirus (both genogroup I, or GI, and genogroup II, or GII). Astrovirus and sapovirus are not tested routinely. It should be noted that co-infection or the detection of multiple viral pathogens in respiratory or stool samples of both sick and healthy (asymptomatic) individuals has been reported globally [5, 9]. Typically, during common-source gastroenteritis outbreaks, such as those which occur from contaminated water, co-infection with multiple unrelated viruses can be common. For example, during a paediatric gastroenteritis outbreak in Finland, in which contaminated drinking water was the source, a combination of rotavirus, norovirus and sapovirus co-infection was detected [5]. Therefore, it may be plausible that the mere identification of a pathogen in a sample, or in all initial four specimens, does not mean that this is the only agent which may be circulating in all symptomatic or even asymptomatic contacts. The less samples tested among probable cases, the less chances of understanding if multiple pathogens may be circulating at the same time [13]. In a recent respiratory outbreak in a long-term care home in London, Ontario, respiratory syncytial virus was detected in nine residents. Additional testing revealed the circulation of metapneumovirus and coronavirus (OC43/229E/NL63/HKU1) in residents and staff at the same time. Although the identification of single or multiple etiologic agents is unlikely to significantly alter the transmission-based precautions or the overall outbreak response strategy, it is necessary to assess the scope, prognosis, and discern a true period of communicability in order to have an accurate determination of how the outbreak may evolve, or when it may be over.

Next, the issue of asymptomatic infection or transmission is often not fully considered. Although respiratory or enteric viral agents may be detected in individuals with symptoms, the causality between the detected virus and symptoms is often difficult to prove. There are several reports in literature of respiratory and enteric virus infection among healthy persons [14, 15, 16, 17]. For example, the human gut virome studies that specifically test for viral pathogens have shown that some individuals with detectable enteric virus loads in the stool may be free of clinical symptoms or disease pathology [18, 19]. In an earlier study, we showed that about 35% of adults in a cohort were infected with enteric viruses, but remained asymptomatic, and were a source of infection to susceptible or other vulnerable persons [13]. Also, virus detection in asymptomatic persons has been observed considerably during the COVID-19 pandemic, and it has been shown that asymptomatic individuals also contribute to transmission [20].

Together, the identification of the full aetiology of disease outbreak allows for a better understanding of the prognosis, and this can help to accurately identify persons (both symptomatic or asymptomatic) who may be carrying the pathogen or multiple pathogens as they constitute risk of transmission to others. Also, knowing both symptomatic and asymptomatic infected individuals would give a more accurate idea of the scope of the outbreak, and transmission could be more profound if there is a likelihood of asymptomatic carriage, or persons with mild symptoms which are not reported. Testing just the initial four or five symptomatic residents neglects the fact that there may be asymptomatic infected persons who are part of the transmission network, and this can significantly impact epidemiological tracking, case isolation, and cohorting.

In conclusion, breaking the chain of transmission during an outbreak requires a full understanding of the epidemiological picture. Besides the PHOL criteria for additional testing, it is important to also consider exposure and risk assessment, regardless of symptoms.

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