

**An overlooked role for fecal transmission of SARS-CoV-2?**

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On March 19, 2003, a SARS-CoV-1 case visited his brother at the Amoy Gardens housing complex in Kowloon [1]. While there, he had diarrhea and used the toilet. Aerosolization of the resulting fecal matter created an infectious plume that infected over 180 people and helped fuel the ongoing epidemic in Hong Kong. While respiratory transmission remained the main driver of transmission for the rest of the SARS-CoV-1 epidemic, this event proved a clear risk from spread through aerosolized fecal matter, and suggested infection control practices should not focus on respiratory droplets alone.

Strangely, despite this event, there has been little focus on the potential of role fecal matter in the potential transmission of SARS-CoV-2. This is true even though it has been shown that culturable virus is recoverable from stool [2], and stool can test positive by RT-PCR long after the virus is no longer detectable in nasal pharyngeal swabs [3]. The lack of attention to the potential role of fecal matter is likely because there have been few reports of transmission tied this route of spread (in contrast to airborne transmission [4] or close household contact [5]).

Recent papers, including one by Zhicong et al. in this issue of *Clinical Infectious Disease*, may help remedy this situation. In their paper, Zhicong and co-authors present compelling circumstantial evidence that sewage played a role in infecting at least six individuals in Guangzhou, China in April 2020. The conclusion that sewage led to these infections is supported by epidemiologic evidence including an environmental survey, detection of virus in swage samples, pathogen sequencing and strong associations between infection and activities that would increase exposure to sewage.

A role for or fecal matter in transmission is consistent with many aspects of SARS-CoV-2 spread. For instance, such a route could contribute to the much higher risk of transmission from household exposures compared to close contacts in other venues [5,6], though this is also consistent with the important role of respiratory droplets (aerosolized or not) in transmission. Rapid spread in schools and other institutional settings with shared bathrooms [7] and the link between dining at restaurants and infection in the United States [8] are also consistent with some role for fecal spread; though they do not require it. In other words, an epidemiologically significant role for this route of transmission is completely plausible given current evidence, but is not necessary to explain observations so far.

Likewise, while the evidence presented by Zhicong et al. is compelling, it is far from a definitive case for the role of sewage. Some unknown aberration of airflow or a case taking an ill-timed walk while effusively shedding virus could have caused these secondary cases, all of whom live in reasonably close proximity to the index cases. There may have been other, undetected, transmission chains stemming from the market T outbreak, where the index cases were infected, that led to the observed cases. However, these alternatives require a series of unlikely and unfortunate coincidences to have occurred to cause the observed infections, so Occam's Razor demands that we accept exposure to sewage as the likely cause (barring new evidence).

If we accept a potential role for fecal matter in SARS-CoV-2 transmission, it becomes important to understand under the necessary conditions for fecally-mediated transmission to occur. Are aerosolizing processes, such as that implicated in the SARS-CoV-1, required to facilitate transmission? In Zhicong et al.'s study shoe cleaning was associated with infection and provides a possible activity where aerosolization or production of inhaled droplets might have occurred; through there were also ample opportunities for infection through touching the eyes, nose or mouth

with contaminated hands in this process. Another recently published report of potential fecal spread of SARS-CoV-2 also suggests aerosolization as a part of the pathway (this time though the waste disposal system) [9].

If aerosolization of fecal matter is important, it can occur by more pedestrian means than a massive aerosolization event in an apartment complex's waste disposal system or cleaning sewage-soaked footwear. Studies have shown that aerosolization of bacteria and other fecal contaminants occurs when toilets are flushed [10,11], though clear implication of this as a route of spread for any disease remains elusive. The evidence does seem strong enough, however, to consider the role of toilets when developing infection control plans for particularly vulnerable populations (e.g., in long term care facilities) or in frequently trafficked areas.

Regardless of the impact of fecally mediated transmission on the overall SARS-CoV-2 epidemic, the outbreak reported by Zhicong et al. should serve as a reminder to be careful not to assume too much or overgeneralize about SARS-CoV-2 transmission. One hundred years after the 1918 influenza pandemic, we are still refining our understanding of influenza transmission and making new discoveries; and we should not be surprised that we still have things to learn about SARS-CoV-2 spread. It is likely that, as with influenza [12], that the most important mechanisms of SARS-CoV-2 transmission vary across settings, with both the natural and man-made environment playing an important role. As we investigate outbreaks, and implement control measures, we should be careful not to let ourselves be blinded by what we "know" about transmission, lest we miss critical routes of spread that may be helping to maintain the outbreak and placing vulnerable individuals at risk.

#### **CONFLICTS OF INTEREST**

J.L. reports serving as a paid expert witness for Paul, Weiss, Rifkind, Wharton & Garrison LLP on a case where the length and impact of the COVID-19 pandemic is of issue.

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