The Persistence of Influenza Infection

To the Editor: The report by Pinsky et al. (1) is interesting, but it raises some major questions. The finding of influenza virus in stool is not new (2). Of more interest is their statement regarding the prolonged shedding of influenza virus in the stool (for >2 months) and respiratory secretions (for >1.5 years). How frequently were respiratory samples collected and tested to confirm that the same virus was shed for these periods in these samples? Influenza virus, like most other acute respiratory viruses, typically does not cause long-term latent or persistent infections in humans. The authors need to exclude the possibility of frequent reinfection with contemporary circulating seasonal hemagglutinin 1 (H1) influenza viruses. However, they do not provide any data to this effect.

Currently, with the wider availability and more stringent expectations of modern molecular techniques, such strains may be associated with community outbreaks are necessary. However, the primary norovirus genotype identified in the leafy greens samples (GI) is not the norovirus that has primarily caused human illness in recent years (GII).

Ready-to-eat packaged leafy greens are widely eaten. One third of respondents to the 2002 FoodNet Population Survey reported eating prepackaged salad in the week before interview (2). In the absence of evidence linking this contamination to norovirus outbreaks, it is premature for consumers to change how they handle or eat ready-to-eat packaged leafy greens.

The authors provide data on the apparent viral loads they observed and cite data to suggest that washing and disinfecting produce before eating it could reduce viral loads below the level of an infectious dose. However, the Food and Drug Administration does not recommend rewashing prewashed produce and does not recommend washing fresh produce with soap, detergent, or commercial produce washes (3). Because the products sampled in the study by Mattison et al. were prewashed, whether washing them would further reduce viral loads is not clear. In addition, rewashing ready-to-eat produce creates a potential risk for cross-contamination of the produce in consumers’ kitchens. Soap, detergents, or sanitizers could leave potentially harmful residues if rewashed produce is not thoroughly rinsed. These potential risks need to be weighed against the uncertain potential benefits of rewashing ready-to-eat packaged leafy greens. Given the ubiquity of these products, any change in recommended handling practices could have far-reaching consequences.

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In Response: The report by Mat
tison et al. about detection of noroviruses in 6% of ready-to-eat packaged leafy greens sampled in Ontario, Canada, suggests that these products could be vehicles for widespread dissemination of norovirus (1). As they suggest, this finding should lead to studies evaluating the potential risk from such contamination. In particular, prospec
tive attempts to identify whether these

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data might be obtained by collecting and sequencing several genes (ideally full genomes) from contemporary circulating seasonal H1 viruses and comparing them, phylogenetically, with the virus shed, contemporaneously, from the child, at monthly intervals, for example (if the child tolerates this testing). Even with this testing frequency, several influenza infection episodes may go undetected. Although the child’s virus, if it truly persists, may undergo some minor host-induced mutations, new infections with seasonal H1 viruses will likely demonstrate a greater, sudden sequence variability, which enables them to be relatively easily distinguished from the more minor, gradually accumulated mutations that can be seen in a persisting infection (3).

Second, ribavirin is not recommended for treating influenza infection (4,5). Can the authors explain why this child was taking ribavirin for influenza infection, and how often was his condition treated with this drug during the 1.5 years when influenza H1 was shed? Was his treatment regimen eventually changed? Currently, the recommended treatment for influenza is with the neuraminidase inhibitors (oseltamivir, zanamivir), which have a much safer adverse effect profile, and their effectiveness has been shown to be cost-effective (5).

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In Response: We appreciate Dr Tang’s insightful letter (J) regarding our article (2) and are encouraged that this case report may have evoked increased interest in the phylogeny of the influenza sequences obtained during this patient’s longstanding illness. We were acutely aware that we had not provided evidence that it was indeed the same influenza A virus found in these samples. Even though we proposed sequencing studies in the article’s discussion section, in hindsight, we should have further expanded the discussion to include the points Dr Tang raises. At that time, however, we made a conscious decision not to include sequencing data in the manuscript for the following reasons.

First, we believed that finding that influenza A virus could be isolated from stool needed to be rapidly disseminated during the pandemic to reinforce awareness of the potential risk of acquiring influenza A infection through this source. During the summer of 2009, when we wrote this article, only influenza A (H5N1) had been reported to be cultivable from human stool (3). Viral nucleic acids of seasonal influenza A had been demonstrated in stool in several studies (4–6), but of course, identification of viral nucleic acids remains an imperfect correlate to the presence of infectious virus.

Second, we considered the time, personnel, and funding required for a viral sequencing project of the type suggested and determined that we should attempt this as a follow-up study. Samples were obtained from the patient nearly every other week for >2 years, providing valuable data to further investigate this important question.

Dr Tang makes an additional point regarding the use of ribavirin to treat the patient’s condition. As laboratory, we had similar questions and never found satisfactory answers. The patient did eventually receive oseltamivir, but this occurred >4 months after his last positive influenza A test result. The antiviral drug course was given empirically after the patient was admitted to the pediatric intensive care unit with fever and mental status changes, which were ultimately determined to be due to coagulase-negative staphylococcal septicemia.

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etymologia

Baylisascaris
[ba"lis-as'kə-ris]

From the Greek term for intestinal worms, askaris. This genus of nematodes was named after H.A. Baylis, a parasitologist at the British Museum of Natural History, London, who studied these organisms in the 1920s and 1930s. The most common cause of baylisascariasis in humans and animals is infection with the roundworm Baylisascaris procyonis, which takes its name from Procyon, a genus of raccoons. The species was first isolated from raccoons in the New York Zoological Park in 1931.

Source: Gavin PJ, Kazacos KR, Shulman ST. Baylisascariasis. Clin Microbiol Rev. 2005;18:703–18. PMID: 16223954

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