Clinical Infectious Diseases

EDITORIAL COMMENTARY

Symptoms and Viral Shedding in Naturally Acquired Influenza Infections

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(See the Major Article by Ip et al on pages 431–7.)

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Understanding the dynamics of the clinical course and viral shedding (ie, infectiousness) of influenza infections is important for informing control strategies at both the individual and population levels. A sizeable body of literature exists involving experimental volunteer challenge studies of healthy adults, summarized in a systematic review and meta-analysis by Carrat and colleagues [1]. More recently, a number of studies have examined these parameters for natural infections due to the influenza A(H1N1) 2009 pandemic strain [2, 3]. However, fewer studies have examined viral shedding following naturally acquired seasonal influenza infections [3–6].

In this issue of *Clinical Infectious Diseases*, Ip and colleagues [7] used an established platform to prospectively study household transmission of natural pandemic and seasonal influenza infections in Hong Kong over a 7-year period, 2008–2014. With viral shedding results from 224 secondary cases of natural influenza infection, including 127 cases fulfilling a clinical definition of acute respiratory illness, this is one of the larger such studies to date, although 70% of the data have been reported previously [3, 4].

Index cases of influenza infection confirmed through rapid testing were recruited in outpatient clinics, and their households were followed up via a series of 3 home visits by study staff over the course of the following week, on days 0, 3, and 6. Nose and throat swabs were collected by study staff from all household members at each visit, and daily symptom diaries were completed by household members, permitting the identification of influenza transmission within the household as well as the evaluation of the dynamic relationship between symptoms and viral shedding. Strengths of the study design include the use of both reverse transcription polymerase chain reaction (RT-PCR) testing and viral culture to evaluate viral shedding, the collection of samples from all household members irrespective of the presence of symptoms, and the standardized measurement of a fairly comprehensive set of symptoms, all of which contributed to facilitating the identification of both symptomatic and asymptomatic secondary infections. The results of this study build on and confirm previous work by the same group and others, with the larger sample size permitting more detailed analyses [3–6].

The main finding highlighted by the authors is that clinical symptoms and viral shedding are less well correlated for influenza B than for influenza A, with shedding occurring both earlier than symptom peak as well as following symptom resolution. Although this finding of more prolonged shedding for influenza B has been demonstrated in volunteer challenge studies [1], and in this group's earlier study reporting data on a subset of participants for naturally acquired infections [4], explanations for this finding remain elusive and the implications for current practice are uncertain.

One question that remains unanswered is whether influenza-infected individuals who are asymptomatic or paucisymptomatic (ie, having <2 symptoms) can transmit influenza, or whether transmission occurs during the presymptomatic phase. Because index cases in this study had to be sufficiently ill to seek medical attention in order to be included, it is uncertain whether these findings can be generalized to index cases with milder infections, and distinguishing secondary infections resulting from presymptomatic index cases is not possible. Another limitation of the design is that the spacing of the home visits may have led to missing very brief infections that may have occurred between the home visits.

To address both of these issues, establishing a cohort of participants and their household members who would be willing to self-collect nasal swabs on a daily basis for longer periods of time might be the next logical step to move the science forward. With the increased feasibility (ie, increasing availability and decreasing costs) of laboratory testing for influenza, coupled with the fact that self-collection or parental collection of flocked nasal

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(midturbinate) swabs is comparable to the reference standard of nasopharyngeal swabs [8–12] and likely more acceptable than nasopharyngeal or nose and throat swabs, future studies should consider more frequent testing with less invasive methods to achieve greater resolution of viral shedding patterns and allow for the determination of the risk of transmission by asymptomatic and presymptomatic individuals. This would also minimize the chance of missing brief infections through less frequent testing. Such a cohort would allow for the characterization of other respiratory viruses as well. Finally, paired serology should also be included to measure serological responses to various infections.

The clinical and public health implications of this study are that, in addition to the cornerstone of annual influenza immunization, preventing influenza transmission within households may be achieved by implementing nonpharmacologic measures (eg, face masks, hand hygiene) as soon as symptoms arise and maintaining them until symptoms resolve, or at least for 2–3 days [13, 14]. However, if the viral shedding pattern observed for influenza B in this study is real, then transmission of influenza B infections may still occur after symptom resolution. Therefore, having the capacity to rapidly diagnose influenza infection and distinguish the subtype (A vs B) would be ideal. The latest generation of commercially available rapid test kits for influenza compares favorably to RT-PCR [15, 16]. Although such tests are not yet broadly available, in this age of video phone calls, 3D printing, and self-parking motor vehicles, one can envision a future when rapid diagnostic testing for multiple respiratory viruses could become widely available for members of the public to use when they experience respiratory infections. If that time arrives, we will be able to more fully benefit from the findings of this study, as individuals with acute respiratory symptoms will be able to self-diagnose influenza A and B infection and implement the necessary infection prevention and control precautions for the appropriate length of time.

Notes

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