

Airborne Transmission of Influenza: Implications for Control in Healthcare and Community Settings

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(See the Major Article by Noti et al, on pages 1569–77.)

The relative importance of alternative modes of influenza virus transmission in humans remains controversial, with consequent confusion over the most appropriate measures for infection control [1–4]. Influenza virus may spread through direct and indirect contact between individuals, and hand hygiene is thought to have some effect in reducing influenza transmission [5–7]. Influenza virus may also spread through larger droplet spray and smaller aerosol particles [1–4].

A number of steps are necessary for airborne transmission from one individual to another to occur. Infectious virus must escape the respiratory tract of the infector, survive the journey between the infector and the infectee either directly or via fomites, and then enter the respiratory tract of the infectee and invade host cells to initiate infection. Although larger droplets only travel short distances before settling [8, 9], smaller aerosolized particles with aerodynamic diameters of $\leq 5 \mu\text{m}$ rapidly evaporate to form droplet nuclei

and then can remain airborne for long periods [2, 3]. Some authors also define as aerosols particles with aerodynamic diameters from 5 to 10 or 20 μm [3, 4]. The study by Noti and colleagues provides important evidence regarding the survival of viable aerosolized virus between an infector and an infectee [1].

Regarding the infector, published data on the amount and characteristics of aerosolized virus shed by infected individuals remain limited [3]. Some studies have reported that influenza virus can be detected in both large and small particles from exhaled breaths and coughs [10, 11] and in the air in medical clinics during epidemic periods [12]. The study by Noti and colleagues demonstrates that artificially aerosolized virus can remain viable while traveling across a room. The airflow rate in the room was not reported, although this could have a substantial effect on the amount of virus reaching the infectee [13, 14]. Noting that the aerosolized virus was generated over an 8-minute period, whereas the samplers collected particles for 60 minutes, it is possible that ventilation rates in the simulation chamber were quite low during the experiments. In addition, the thermal plume generated around humans can affect airflow, and the use of thermal mannequins might be considered in further experiments [15]. In the real world, coughs and sneezes of an infector could aerosolize

influenza virus, but further research is required to confirm whether the characteristics would be similar to the artificially aerosolized virus used in these experiments [1]. The observation that viable aerosolized virus could travel at least 6 feet, and potentially further, might have implications for guidelines on bed spacing.

Volunteer challenge studies have demonstrated that aerosolized virus at relatively low infective doses could cause infection and disease but somewhat higher infective doses were required to cause infection via intranasal inoculation [16]. Many such studies excluded volunteers with antibody profiles suggestive of immunity; some studies found that higher infective doses were required to cause infection in individuals with higher antibody titers [16]. The results of the study by Noti and colleagues could be interpreted to suggest that exposure to infectious doses of influenza should be quite common. Yet at the start of the 2009 influenza pandemic, 1 infected case patient tended to infect on average just 1.5 others [17], and explosive outbreaks with high reproductive numbers were rarely reported. If influenza is indeed highly contagious via small particle aerosols in natural settings, low observed transmissibility could be explained by substantial immunity in the population, preventing most exposures from leading to clinical infection. In natural settings, it is difficult

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to ascertain the degree of exposure faced by individuals because a single exposure may be sufficient to lead to an infection that confers immunity for the remainder of the influenza season [18, 19]. Two detailed community-based studies have followed up the contacts of individuals with confirmed influenza and observed antibody titer rises in some contacts in the absence of any clinical or virological evidence of acute upper respiratory tract infection [20, 21]. These antibody titer increases may have been indicative of exposures that led to abortive, asymptomatic infections. It is unclear whether such infections have the potential for transmission to other individuals [22].

Noti and colleagues reported that approximately two-thirds of infectious virus particles were blocked from entering the mouth by surgical masks or N95 respirators that were not properly fitted and >99% of infectious virus particles were blocked by a properly fitting N95 respirator [1]. These findings are particularly useful when considering exposures in healthcare settings. Annual influenza vaccination is the most effective preventive measure available to protect individuals, including healthcare workers, against infection, but currently available vaccines cannot provide complete protection against infection [23], and vaccination uptake among healthcare workers is low in many countries. Therefore appropriate use of barrier precautions is essential for healthcare workers at risk of influenza infection or transmission. The results reported by Noti and colleagues suggest that a surgical mask could provide some degree of protection against exposures with low infectious doses, but a properly fitted N95-type respirator would provide improved protection [1]. If not tested for fit, N95 respirators may offer no more protection than surgical masks. If transocular infection were an important route of transmission, appropriate eye protection would also be essential [24].

Two studies have explored the use of surgical masks and N95 respirators in

healthcare workers [25, 26]. One study found that N95 respirators conferred no more than a 10% absolute risk reduction (no more than approximately a 50% relative risk reduction) in the risk of influenza infection compared with surgical masks, where the absolute risk of infection for healthcare workers donning surgical masks was estimated as 20% [25]. Both studies were underpowered to determine moderate superior efficacy of N95 respirators, but neither explored in detail potential exposures outside the healthcare setting. In general, healthcare workers are not thought to face a substantially higher risk of influenza infection than other adults in seasonal or pandemic influenza, although the risk of infection for individual staff is likely to vary depending on their responsibilities and setting [27, 28]. One volunteer challenge study using aerosolized live attenuated virus found that N95 respirators conferred greater protection against infection than surgical masks [24]. Further volunteer challenge studies could confirm these findings for nonattenuated viruses [29]. However, large controlled studies in real-life settings are likely to be necessary to confirm superior efficacy of N95 respirators over surgical masks in healthcare settings [26].

In other settings, including the general community, proper fit testing of N95 respirators is usually not feasible. The experimental results reported by Noti and colleagues suggest that surgical masks could provide some protection against influenza infection [1]. Controlled trials of face masks in community settings have not provided conclusive evidence of efficacy [7, 30–38]. If exposure at higher infectious doses is common in these settings, surgical masks might not be able to prevent infection among susceptible contacts [36].

In conclusion, Noti and colleagues should be congratulated for an important study that improves our understanding of influenza transmission and control. Natural extensions to this work could

include consideration of heterogeneity in viral excretion (infectiousness) from the source [3]; the use of masks and respirators for source control [39]; improved realism of the experimental setting, such as the use of a moving (eg, animatronic) mannequin face to explore mask and respirator performance when talking; determination of the role of ventilation and airflow in reducing exposures; and exploration of the protection conferred by other types of face masks, including antimicrobial masks.

Notes

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