

## Do Public Health and Infection Control Measures Prevent the Spread of Flu?

ERIC TONER

**Not much is known about influenza transmission or ways to prevent it.** An effective response to an influenza pandemic will hinge on the availability of vaccine and antivirals. If they are in limited supply, as is anticipated, then disease control will depend on public health and infection control measures. Unfortunately, not much is known about the efficacy of such interventions for preventing the transmission of flu. In fact, very little is known about influenza transmission. A review of the literature found no English-language experimental studies of person-to-person spread of flu and no studies of the use of masks or hand-washing as means of preventing transmission of flu. Despite the absence of scientific data, some reasonable inferences and extrapolations can be drawn based on what is known, which is discussed below.

**Asymptomatic carriers play an important role.** As many as half of all infections with normal seasonal flu may be asymptomatic, which in part may be due to pre-existing partial immunity.<sup>1</sup> Asymptomatic patients shed virus and can transmit the disease but not at the same rate as symptomatic individuals, thus creating an invisible “reservoir” for the virus. The implication of this is that public health disease containment measures and infection control measures alone may slow but cannot stop a flu epidemic.

**Isolation of the sick may slow the spread of flu.** The degree of viral shedding in flu is directly proportional to the severity of symptoms and level of fever.<sup>1</sup> Therefore, virus is shed to a greater degree by symptomatic individuals as compared with those who are asymptomatic. As a result, isolating the sick can be expected to reduce transmission and therefore slow the spread of disease.

**Flu may not be as transmissible as imagined.** The incubation period for seasonal flu averages 2 days, with a range of 1 to 4 days, and viral shedding may begin as

much 24 hours before symptoms appear.<sup>1</sup> The *generation time*, which is the time between when the first person becomes infectious and when a person in the next “generation” becomes infectious, is estimated to be approximately 2 days as well. The speed with which a contagious disease spreads is a function of the number of additional people infected by each victim ( $R_0$ ) and the generation time.

Influenza, which has a very short generation time, will spread very quickly even if each infected individual does not spread it to many others. The  $R_0$  for the 1918 pandemic is estimated to be only 1.8.<sup>2</sup> Other recent estimates of  $R_0$  for seasonal and pandemic flu typically range from 1.5 to 3.<sup>3,4</sup> In contrast, SARS had an  $R_0$  of 3 (excluding super-spreaders), and measles has an  $R_0$  of 10 to 15,<sup>5</sup> which suggests that flu is not as highly transmissible in a community setting as has been assumed. Flu spreads rapidly because it has a very short generation time rather than a high  $R_0$ . This has two important implications:

1. There is too little time between exposure and disease to perform contact tracing or institute quarantine; and
2. Generally applied efforts to reduce viral transmission, even if only partially effective, may reduce the  $R_0$  enough to slow the progression of the epidemic.

**Contact transmission may not be so important.** The influenza virus can survive on surfaces for hours to days, depending on the surface, but it survives on hands for less than 5 minutes.<sup>1</sup> Hand-washing has been shown to reduce transmission of respiratory illness, in general, in the specific setting of military trainees,<sup>6</sup> but there is no specific scientific evidence related to flu. While it is reasonable to recommend that those who are in contact with the sick wash their hands, there is no evidence to support the notion that frequent routine hand-washing during an

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Eric Toner, MD, is a Senior Associate, Center for Biosecurity of the University of Pittsburgh Medical Center, Baltimore, Maryland. A version of this article first appeared on October 31, 2005 on the *Clinicians' Biosecurity Network* at <http://www.upmc-cbn.org>

epidemic will provide additional protection against transmission of the virus.

**Droplet spread is the primary route of transmission.** Influenza can be transmitted by large droplets, which generally travel 3 to 6 feet, and by small droplet nuclei and aerosols, which can remain suspended in the air for prolonged periods and travel significant distances.<sup>1</sup> Studies have suggested that small particles appear to be more infectious. Both the degree of infectivity and the severity of illness are directly related to particle size.<sup>5</sup> Aerosols smaller than 10 microns have been shown to cause more severe disease and require a smaller inoculum than large intranasal droplets.<sup>1</sup> In experiments with mice, it has been demonstrated that flu can be transmitted by aerosols over long distances.<sup>1</sup> One study of a flu outbreak in a tuberculosis hospital in 1957 showed some clear evidence of airborne transmission consistent with droplet nuclei or aerosols.<sup>1,7</sup> There is also convincing evidence of airborne (droplet nuclei) transmission in an airplane.<sup>8</sup>

On the other hand, analysis of a 1957 nosocomial influenza outbreak among a completely susceptible population showed that transmission was primarily due to contact and droplet spread.<sup>9</sup> And recent hospital studies from the University of Virginia and the University of Rochester implicate large droplets as the primary routes of nosocomial transmission.<sup>1</sup> Thus, the evidence supports the notion that large droplet spread is the principal mode of transmission, but small particle spread of flu may occur as well. Therefore, measures that reduce only large droplet transmission can be expected to slow but not stop the spread of the disease.

**Surgical masks can help, but they may not be enough.** Surgical masks, when worn by infected patients, reduce the dispersal of large respiratory droplets; however, there have been no studies of the use of masks for preventing transmission of flu. Surgical masks were clearly associated with protecting healthcare workers from SARS.<sup>10</sup> N95 masks and powered air purifying respirators (PAPR) provided additional protection.<sup>11</sup> Current CDC guidelines for influenza infection control call for the use of droplet precautions, which include the use of surgical masks.<sup>12</sup> This is reasonable in the context of a disease with a low case fatality rate, widespread partial immunity, and widespread community transmission such as is the case in a normal flu season. In the setting of a highly lethal novel virus, however, such as might be the case in an H5N1 pandemic, airborne precautions that include the use of N95 masks or PAPRs would clearly be advisable, at least until the virus becomes ubiquitous. This is consistent with the current CDC guidelines for avian influenza.<sup>13</sup>

**Closing schools may help.** In a typical flu outbreak, children become ill first, which is attributed to several factors: they have less immunity; their contact with other

people tends to be closer; they spend a great deal of time in crowded schools; and they have a longer period of viral shedding.<sup>1</sup> It is also believed that children play an important role in the spread of the disease. While there have been no studies of the impact of closing schools on the community spread of flu in the U.S., when schools were closed in Israel during a flu outbreak in 2000, there was a significant reduction in physician visits for respiratory disease among the students during the period of school closure.<sup>14</sup> Whether this had an impact on the course of the epidemic is not known. Since children and schools are believed to play an important role in the spread of flu, closing schools may well slow the propagation of an epidemic. This is only likely, however, if children are not then regrouped in daycare or other such facilities.

**Quarantine, as commonly conceived, is of unproven utility.** *Quarantine* commonly means the large-scale sequestering of people with the purpose of trying to stop the spread of a contagious disease. It is different from *isolation*, in which symptomatic people with a contagious disease are isolated individually so they do not infect others.

There are no studies of quarantine in the setting of influenza. Experience with the SARS epidemic suggests that large-scale quarantine of a population or geographic location is logistically very difficult.<sup>15</sup> Further, mathematical models of quarantine for flu show that there must be a nearly perfect degree of limitation of travel to be effective.<sup>16</sup>

One method of disease containment that might be appropriate during a flu epidemic would be the isolation of people of a small discreet group, such as people on a contaminated airplane or ship. In such a case, all passengers and all crew members could be confined in isolation for the duration of the incubation period. In this scenario, the isolated individuals would need to be separated from one another to avoid increasing their risk of exposure. Another appropriate use of isolation might involve sequestering healthcare workers who have been exposed to lethal and contagious cases of flu strain (such as a pandemic H5N1 strain); this would no longer make sense once such a disease was circulating widely.

**H5N1 is different from “normal” flu.** The avian flu strain of H5N1 currently circulating behaves very differently in people than “normal” human flu viruses, and it has a very limited ability to be transmitted from person to person. The factors responsible for influenza transmissibility are complex, multifactorial, and not well understood. Should H5N1 become transmissible between humans, it may not act like a typical human flu virus, and any change in transmissibility may not be a simple binary phenomenon. There may be intermediary degrees of transmissibility, which could have a significant effect on the usefulness of disease control measures.

**The existence (or not) of asymptomatic carriers is key.** The experience with the H5N1 virus in humans to date suggests that the virus is very different from a “normal” flu virus, which makes it difficult to predict exactly how it will behave if it gains the ability to transmit efficiently between humans. The systemic symptoms of seasonal flu are caused by cytokine release, which is part of the human immune response. People who lack a vigorous immune response or who have partial immunity may shed virus, even though they have limited symptoms. This may not be true with H5N1. Unlike the previous pandemic viruses (H1N1, H2N2, and H3N2), H5N1 is a *highly pathogenic avian influenza virus* (HPAI), which means that it contains a polybasic amino acid insertion in the hemagglutinin cleavage site,<sup>17</sup> a characteristic that makes the virus *pantropic*, or able to infect multiple organ systems. All human flu viruses, including the 1918 virus, infect only the respiratory tract; however, the limited data from human H5N1 cases indicate that the H5N1 virus may infect other tissues in humans as well.<sup>18</sup> Since the disease may affect the brain, gut, and other organs, there may be many fewer asymptomatic H5N1 patients spreading the disease in the community.

In addition, since the H5N1 virus is completely novel to humans, there is no preexisting immunity that is thought to play some role in asymptomatic carriers. Therefore, H5N1 may spread less like a typical flu and more like SARS. If that is the case, then public health and infection control measures may be much more effective than they would seem to be in controlling the community spread of typical influenza epidemics—perhaps as effective as they were in controlling SARS. Since there has never been an epidemic of a HPAI influenza virus,<sup>17</sup> only time will tell.

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