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Community Mitigation of Pandemic Influenza

In this issue...

Recent events related to the unprecedented outbreak of H5N1 avian influenza in Eurasia and Africa as well as new information about the 1918 pandemic have prompted a great deal of apprehension that the next influenza pandemic may be imminent. Because a strain-specific vaccine is expected to be unavailable and antivirals are expected to be in limited supply in the first wave of a new pandemic, much attention has been focused on public health interventions that may arrest, slow or at least diminish the magnitude of any such outbreak. In this issue, we review the current literature related to what is known about influenza transmission and which public health disease containment measures are likely to work.

THIS ISSUE

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Guest Faculty Disclosure

Eric S. Toner, M.D., has disclosed that he has no relationship with commercial supporters.

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At the conclusion of this activity, participants should be able to:

- Describe both the known and unknown factors about the transmission of influenza;
- Identify the primary community mitigation strategies under current consideration;
- Discuss the strengths and weaknesses inherent in using modeling to create public health policy.

COMMENTARY

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NEWSLETTER ARCHIVE

The Department of Health and Human Services' planning assumptions for an unmitigated and severe (1918-like) pandemic include 9.9 million hospitalizations in the US with 1.5 million patients requiring intensive care, figures which are several times the available capacity of the healthcare system[1]. In fact, the US healthcare system would be seriously challenged by even a mild pandemic[2]. For this reason, public health interventions which might reduce this disease burden have attracted much interest.

The use of such interventions, collectively, has been referred to by a variety of names, including community mitigation, disease mitigation, and community containment. Some authors include in these terms the use of limited amounts of vaccine and antivirals; others include only non-pharmaceutical interventions (NPIs). Among the NPIs being considered are use of masks, hand washing, isolation of the sick and quarantine of the exposed, travel restrictions, and various means of social distancing. Included in the category of social distancing are cancellation of large gatherings, closing public places, and closing schools[3].

The fundamental question is whether such interventions will work, at what cost and who will pay. Since the world has not experienced a severe pandemic in 90 years, there is little direct experience to draw upon. And, surprisingly, as is clearly demonstrated in the paper by Brankston et al, very little experimental research has been done on influenza transmission, and none of the proposed interventions have been tested in a controlled fashion. As such, the purported benefits of most of the community mitigation strategies under discussion are derived from computer modeling, the results of which depend on unproven assumptions about flu transmission and the efficacy of the various interventions[4,5].

The CDC has recently issued its Interim Pre-Pandemic Planning Guidance: Community Strategy for Pandemic Influenza Mitigation in the United States – Early, Targeted, Layered Use of Nonpharmaceutical Interventions[6]. The strategy calls for a flexible response depending on the severity of the pandemic. While the interventions suggested include isolation of the sick, voluntary quarantine of contacts, and adult social distancing, the heaviest reliance is on early and prolonged school closure in the setting of a severe pandemic.

Given the potentially dire consequences of a pandemic, it is reasonable to attempt to reduce the impact of the outbreak by whatever means are available if those means have a reasonable chance of being effective, and if the collateral consequences of their use is well understood and acceptable. At this time, as is shown in the papers by Germann, Haber and Ferguson, there is little empirical evidence to support most of the NPIs being recommended. Further, the modeling studies give inconsistent results (depending upon the assumptions used), and the societal and economic consequences of their use have not been studied.

While the urge to "do something" in the face of an impending pandemic is understandable, caution is advised and we would do well to remember the first dictum of medicine — *primum non nocere* (first, do no harm). One such action that would clearly have only beneficial consequences would be to better prepare our woefully unprepared hospitals[7].

References

1. HHS Pandemic Influenza Plan. November 3, 2005.
2. Toner E, Waldhorn R, Maldin B, et al. Hospital preparedness for pandemic influenza. Biosecurity and Bioterrorism 2006; 4(2).
3. Inglesby T, Nuzzo J, O'Toole T, Henderson D. Disease mitigation in the control of pandemic influenza. Biosecurity and Bioterrorism 2006;4 (4): 366-375.
4. Institute of Medicine. Modeling community containment for pandemic influenza. 2006. National Academies Press.
5. WHO writing group. Nonpharmaceutical interventions for pandemic influenza, national and community measures. Emerg Inf Dis 2006;12:88-94.
6. CDC. Interim Pre-pandemic Planning Guidance: Community Strategy for Pandemic Influenza Mitigation in the United States—Early, Targeted, Layered Use of Non-Pharmaceutical Interventions.
7. Toner E, Waldhorn R. What hospitals should do to prepare for an influenza pandemic. Biosecurity and Bioterrorism 2006;4 (4).

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NEWSLETTER ARCHIVE

MODELING MITIGATION MEASURES IN A SMALL TOWN

Haber M, Shay D, Davis X et al. **Effectiveness of interventions to reduce contact rates during a simulated influenza pandemic**. Emerg Inf Dis 2007;13 (4).

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The investigators in this study used a computer model to simulate an influenza outbreak in a small US town assuming no vaccine or antivirals were available. The model tested the effect of school closings, confinement of the sick and their household contacts, and reductions in contact rates of long term care facilities. The model used a basic reproductive number (R0) of 2.7. This is the number of people infected by a source patient at the onset of an outbreak to which everyone is susceptible. In other words, each infected individual on average infects 2.7 other people. In various simulations, school closed when 10, 15 or 20% of the children were sick, and remained closed for 7, 14 or 21 days. The model assumed an attack rate of 62% among school age children. The model also assumed that kids not in school had increased contacts with others outside of school. Both the delay in confinement of the sick after the onset of symptoms and the confinement compliance rate could be varied as well.

When school were closed relatively early on (when 10% were sick) and remained closed for 14 days the rate of illness in the community dropped from 32% to 26%. However, when a school closing threshold of 20% was used instead, the rate of illness did not significantly change. If 60% of the sick confined themselves to home 2 days after the onset of symptoms, there was a 33% decrease in illness in the community. This decrease figure rose to 80% if household contacts were also quarantined.

The authors conclude that voluntary isolation (withdrawal to home) of ill persons is a more effective strategy than closing schools in reducing the impact of a pandemic. The disease burden in the community can be further reduced by voluntary home quarantine of household contacts. The relative lack of efficacy of school closing found in this model (compared to some other models) is related to the fact that Hays' model assumes schools will not close until at least 10% of kids are sick, and that students who are out of school will have increased household and community interactions. Other models assume that schools will close earlier in the outbreak and that kids out of school will remain segregated.

WHAT IS KNOWN ABOUT INFLUENZA TRANSMISSION

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NEWSLETTER ARCHIVE

Brankston G, Hirji Z, Lemieux C, Gardam M. **Transmission of Influenza A in human beings**. Lancet Inf Dis 2007; 7(4):257-65.

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Despite 70 years of research on influenza, debate continues about even the most basic facts pertaining to influenza transmission. These include whether the virus is spread primarily by a respiratory or contact route and, if respiratory, whether it is by large droplets that travel a few feet or by small aerosols that can remain suspended for long distances and a prolonged time. Because key decisions about infection control and disease containment depend upon an accurate understanding of the mode of transmission of influenza, Brankston et al set out to assess the actual scientific basis of commonly held assumptions. They undertook a systematic review of the English language experimental and epidemiological literature pertaining to the mode of transmission of influenza in mammals. Of 2012 initial citations found, only 32 articles were ultimately felt to be relevant after review by at least two researchers. These 32 articles were then analyzed in detail and abstracted.

Six experimental studies examined the survival of aerosolized influenza in the environment, demonstrating that various influenza strains remain viable after artificial aerosolization and can infect several cell types. Additionally, studies found that while some influenza virus can be detected in the air for up to 1 to 24 hours after aerosolization (depending upon the relative humidity), the concentration in the air drops fairly quickly. Two studies demonstrated that the virus can survive on non-porous surfaces for several hours. No studies, however, looked at whether humans can be infected by contact with contaminated surfaces.

Thirteen studies showed that clinical influenza can be produced in humans and a variety of other mammals by exposure to an artificial aerosol containing influenza virus. Four studies demonstrated that these aerosol-infected animals can then transmit the infection secondarily to other animals. One study showed that virus can be found in the air around infectious animals. No study has looked at person-to-person transmission after artificial infection. One study showed that influenza can be transmitted between mice separated by 2 cm by double wire mesh, and that the rate of infection was no different than if they were housed in the same cage. Another study showed that influenza can be transmitted between ferrets connected only by a 2.5 m long S-shaped tube.

Nine observational studies were found that examined natural outbreaks of influenza in people. Three of the studies suggested the possibility of airborne (aerosol) transmission and six of the studies were more suggestive of a primarily droplet or contact route of transmission. Four studies suggested the need for close person-to-person contact. All the studies were confounded by multiple factors and none could be considered definitive. Only one study was found that reported on the use of control measures in a hospital outbreak that was not confounded by use of vaccine or antivirals. That outbreak ceased after implementation of isolation of infected patients, cohorting of staff, and droplet and contact(but not airborne [aerosol]) precautions.

In summary, no studies were found that demonstrated clear evidence of contact transmission; although none disproved it either. Several studies showed a relationship between close proximity and transmission which could result from contact, large respiratory droplets or small particle aerosols. Artificial aerosol transmission has been demonstrated in people and in animals, but whether natural aerosols behave in the same manner is not known. Natural aerosol transmission has been documented in ferrets, but since species differ in their relative susceptibility to infection one must be cautious in extrapolating from one species to another.

In the end, all that can be concluded, other than that much more research is needed, is that transmission of flu in humans is probably primarily by a respiratory route, that infection usually results from close proximity, and that droplet precautions seem to be sufficient to prevent infection. It should be noted that studies involving seasonal influenza, to which there is widespread immunity in the population, may not be applicable to a completely novel pandemic virus to which no one has immunity.

MODELING MEASURES TO MITIGATE NATIONAL SPREAD OF INFLUENZA

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NEWSLETTER ARCHIVE

Germann T, Kadau K, Longini I, Maken C. **Mitigation strategies for pandemic influenza in the United States**. PNAS 2006;103(15):5935-5940.

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Ferguson N, Cummings D, Fraser C, et al. **Strategies for mitigating an influenza pandemic**. Nature 2006;442:448-452.

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Germann and colleagues performed a computer modeling study that examined the spread of an influenza pandemic across the entire US, and investigated the impact of several mitigation interventions, including travel restrictions, school closings, and targeted use of limited amounts antivirals and vaccine. The R0 was varied from 1.6 to 2.4.

Similarly, Ferguson and his colleagues created a computer simulation that modeled the spread of influenza across the US and the UK assuming an R0 of 1.7-2.0. They examined the impact of travel restrictions, school closure, case isolation and quarantine, and targeted use of vaccine and antivirals.

The Germann study found that travel restrictions had minimal impact: imposition of a 90% reduction in domestic travel only slowed the spread of the virus by a few days and had no affect on the eventual size of the outbreak. The Ferguson group found similar results.

School closure, in the Germann study, was found to have significant impact only if R0 was set at 1.6 and schools closed within 7 days of the onset of the pandemic. For larger values of R0, school closure and other attempts at social distancing only slowed the spread of the virus modestly and did not affect the total number of sick. Likewise, Ferguson found that although school closure could reduce peak attack rates by 40%, it had little impact on overall attack rates.

Germann's group found that for scenarios involving an R0 value of 1.6, targeted use of antivirals to treat the sick and prophylaxis of household contacts proved an effective strategy. If, however, R0 was set at 1.8 or above, the amount of antivirals needed became probative. Ferguson also found that early treatment with antivirals could have a modest but significant impact, but only if 90% of cases are treated within 1 day of the onset of symptoms. If antiviral treatment was delayed by more than 1 day, there was little reduction in attack rates. Ferguson also found antiviral prophyaxis of household contacts to be a highly effective strategy, but noted that implementation would require stockpiling enough antivirals for half the population.

Both studies found that early, targeted use of limited amounts of vaccine, even if was not very effective, significantly reduced the number of sick. This was especially true if the vaccine was used preferentially in schools. Germann found, however, that this was only the case if the R0 was less than1.9. In both studies it was assumed that vaccination could start very early in the outbreak (within 2 weeks) and proceed at a rapid rate (10-21 million vaccinations per week).

These studies demonstrate two important points. First, they show how difficult it is to reduce the impact of a pandemic using community mitigation measures. Both models show that only very aggressive, and perhaps unrealistic, interventions are likely to be effective in reducing the disease burden in a pandemic – and then only if the virus is not very transmissible. Early isolation and treatment of the sick, and confinement and prophylaxis of contacts, were found to be the most effective strategies. School closure was found to have relatively little impact, and then only if the children were separated while out of school. Targeted vaccination of school children (assuming schools are not closed) also appeared to be effective in some cases, but only if vaccination could be started immediately and proceed very quickly

Secondly these studies show how sensitive models can be to small alterations in the assumptions used. Almost any intervention appears to work if R0 is less than 1.6 and few, if any, work if R0 is set at >2.0. Since estimates of R0 for the previous pandemics vary from 1.6 to 3, and the R0 of a novel pandemic virus that has not yet emerged can only be guessed at, the suggested beneficial effects of the interventions modeled in these studies must be taken with a grain of salt.

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