

BRANCH OUT

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By: Andrea Woodland, Health Sciences Center

It was my pleasure to attend PPC in Toronto this January with the help of the Apotex/CSHP NL Branch Travel Grant. My gratitude goes to Apotex, our Branch and the individual who finally drew my name out of the hat! PPC is defined as "the largest pharmacy conference in Canada" and of course it is. This is arguably an understatement in that PPC is much more than large in size. The conference offers four complete days of top-notch educational programming for hospital pharmacists. The topics and speakers this year were current and relevant; it was difficult to make choices between concurrent sessions. It was a great opportunity and I encourage anyone who has the resources to attend in the future, and of course to put your name in for the prize next year!

I attended sessions covering various topics including cardiology (MI, atrial fibrillation, cardiac diagnostic testing), interpreting liver and kidney function, medication reconciliation and infectious diseases. The session I chose to focus on for this article was about pandemic influenza. It was presented by Dr. Susan Poutanen who is a microbiologist and infectious diseases physician at University Health Network and Mount Sinai. Dr. Poutanen provided an overview of pandemic influenza, specifically focused on the next pandemic and the need to plan for its potential arrival.

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Pandemic Influenza: Plan or Pandemonium?

By: Andrea Woodland, Health Sciences Center



You've undoubtedly heard about it on CNN or CBC as you've watched the flocks of poultry being culled, and more recently the reports of human to human transmission. But what does it all mean on a global scale or is it just a problem in currently affected countries? After the session with Dr. Poutanen and some subsequent research on the topic, I hope to provide some explanation.

First to review the basics of the influenza virus: There are three types: A, B and C.

- ◆ **Influenza A** is found in humans, swine, equine, avian, and marine mammals, it occurs seasonally, undergoes antigenic shift and drift, and may cause large pandemics with significant mortality.
- ◆ **Influenza B** is found only in humans, causes disease seasonally most often in the elderly or high risk, it undergoes antigenic drift only and does not cause pandemics.
- ◆ **Influenza C** is found in swine and humans, it undergoes antigenic drift only and causes mild disease without seasonality.

(Antigenic drift refers to relatively minor antigenic changes with viral surface antigens and this normally occurs every few years. Antigenic shift is a dramatic antigenic change resulting in a new virus to which the population has no immunity.)

As influenza A is the type which can cause pandemics, it will be the focus of the remainder of this discussion. Influenza A is subtyped based on the surface antigens – H and N. Many different combinations of H and N are possible, each representing a different subtype.

Hemagglutinin (H):

- 16 subtypes
- responsible for cell attachment
- epidemiologically more important than N as governs attachment, entry and subsequent multiplication of virus to date only H1, H2 and H3 found in humans, H1-H15 have all been in birds

Neuraminidase (N):

- 9 subtypes
- responsible for virus release from cells

“Avian influenza” is influenza A that normally only infects birds and sometimes swine. On rare occasions, these have crossed the species barrier and infected humans. There are two forms of avian influenza seen in poultry.

The “low pathogenic” form causes mild symptoms and may not even be noticed. The “highly pathogenic” form is caused only by H5 and H7 subtypes. This form spreads rapidly through flocks and has a very high mortality rate (up to 100%). Therefore, anytime H5 or H7 virus is found in poultry it is a cause for concern. It is noteworthy that not all H5 and H7 viruses are highly pathogenic, and that they may start out in a low pathogenic form and mutate into a highly pathogenic form.



Current outbreaks of highly pathogenic H5N1 avian influenza began in South East Asia in 2003 and are the most severe and largest on record. The virus is now considered endemic in many regions in Asia despite an estimated 150 million birds dying or being destroyed. *(cont on page 3)*



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Wild waterfowl are the natural reservoir of all influenza A viruses; it is believed that they introduce low pathogenic H5 and H7 viruses to poultry flocks where the viruses mutate to become highly pathogenic. In the past it was believed that wild waterfowl did not directly spread pathogenic avian influenza viruses from one region to another. Recent events indicate that migratory birds are spreading H5N1 in its highly pathogenic form as evidenced by the number of geographic regions where it is appearing compared to avian influenza in the past.

There are two main risks for human health from H5N1. The first is direct infection from poultry to humans which results in very severe disease. The second risk is that the virus could change into a form that is highly infectious and spreads easily from human to human, thus facilitating a pandemic.

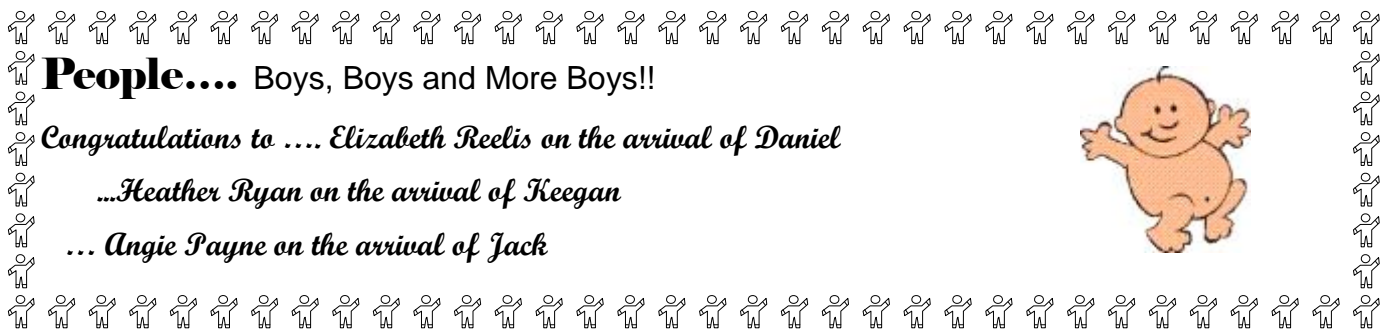



Three conditions must be met for a pandemic to occur:

- 1. Susceptible population.** Humans are currently susceptible to H5N1 as there has been very limited exposure in humans therefore immunity has not developed.
- 2. Virulence.** A pandemic virus must be pathogenic, causing serious illness in humans. H5N1 has demonstrated its virulence as over half of the infected humans to date have died from it. It follows an aggressive course with rapid deterioration. Primary viral pneumonia and multi-organ failure often occur. Most cases are in previously healthy young adults and children.
- 3. Transmissibility.** The virus must spread easily and sustainably among humans. So far, efficient and sustained human to human transmission of H5N1 has not taken place. This is the final of the three prerequisites which must be met for a pandemic to begin.

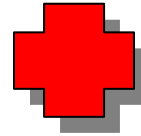
Transmissibility can be improved by two mechanisms. The first is reassortment whereby a host cell becomes infected with two different influenza viruses which recombine and form an entirely new virus which can then be passed on to other human hosts. This could result in a fully transmissible pandemic virus with a sudden surge of cases and fast spread. The second mechanism is via adaptive mutation where a change mutation occurs in the virus which is followed by natural selection. This would happen slower, with small clusters of human cases and potentially some time to take defensive action. Each human case of H5N1 gives the virus an opportunity to improve its transmissibility and develop into a pandemic strain.

There have been rare cases of human to human transmission of H5N1. These have occurred among very close contacts of an ill individual and have not continued beyond one person. It is difficult to determine if human to human transmission has in fact occurred as the people are often exposed to the same animal sources. The New England Journal of Medicine (NEJM) published a case report of probable person to person transmission of H5N1 in Thailand (NEJM 2005;352:330-340). A child contracted H5N1 from interaction with birds; the child's caregiver subsequently acquired H5N1 but had no exposure to the birds. (Cont on page 5)


People.... Boys, Boys and More Boys!!
Congratulations to ... Elizabeth Reelis on the arrival of Daniel
...Heather Ryan on the arrival of Keegan
... Angie Payne on the arrival of Jack




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How can pandemic influenza be treated or prevented?

The first important point to note is that a vaccine against pandemic H5N1 is not available. It is under development in several countries, but will not be widely available until several months after the start of a pandemic. The vaccine must closely match the pandemic virus and therefore cannot be produced until after the pandemic is declared and the virus is identified. Also, global vaccine production capacity falls short of the expected pandemic demand.

The older antiviral class of M2 inhibitors, including amantadine and rimantadine, could potentially be useful, however resistance develops rapidly and some currently circulating H5N1 strains are fully resistant to these agents. In the event of an entirely new virus emerging via reassortment these agents may be efficacious.



Neuraminidase inhibitors, oseltamivir and zanamivir, can reduce the severity and duration of illness caused by seasonal influenza. Of course, the efficacy of these agents is dependant on administration within 48 hours of the onset of symptoms. It is believed that these agents may improve the prospects of survival as the H5N1 virus is expected to be susceptible to them but there is little clinical data available. Cost constraints and limited production capacity will likely restrict the usefulness of these agents in a pandemic. It is estimated that stockpiles large enough to supply 20-25% of a given population will be required to sufficiently treat most of the clinical cases and lead to a significant reduction in hospitalization. It is thought that in Canada we now have enough for approximately 12% of the population.

Resistance of H5N1 to oseltamivir is also a growing concern. In December 2005, an article in NEJM reported oseltamivir resistant strains of H5N1 in two Vietnamese patients who both subsequently died. The authors suggest that resistance can emerge during oseltamivir treatment of H5N1 even when initiated early and at recommended doses. (NEJM 2005;353:2667-2672) Physicians have been inundated with requests from patients for personal supplies of oseltamivir as fear of a potential pandemic increases. There are concerns that in the event of a pandemic, such personal stockpiles could lead to misuse of the antiviral agent (inadequate dose or duration) resulting in inadequate treatment and subsequent resistance development in the virus.

The World Health Organization has recommended that all countries prepare a pandemic plan and has provided recommended strategic actions to respond to a pandemic threat. Only around 40 countries have done so. One of the recommendations is for countries that are able to stockpile antiviral drugs. Approximately 30 countries are attempting to do this, but the manufacturer does not currently have the capacity to fill the demand. It is likely that most developing countries will not have any access to vaccines or antivirals throughout the duration of a pandemic. In countries such as Canada with limited supplies, the challenge will be to distribute the drugs in a prioritized and timely manner.

Dr. Poutanen stressed the importance of pandemic planning with the goals of minimizing serious illness, overall deaths, and societal disruption. The World Health Organization recommendations have been adapted by the Public Health Agency of Canada into the Canadian Pandemic Influenza Plan. The intention is then for each province to adapt the plan in more detail to enable ease of implementation. Beyond the provincial level, it is recommended that there should be plans at the hospital level and even for individuals in the community. She advised that pharmacists should be aware of the plan at their own institution and what their specific role will be in the event of a pandemic influenza.

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