

## A/H5N1 INFLUENZA IN HONG KONG

*Some say the world will end in fire,  
Some say in ice.*

*From what I've tasted of desire  
I hold with those who favor fire.  
But if it had to perish twice,  
I think I know enough of hate  
To say that for destruction ice  
Is also great  
And would suffice.*

—Robert Frost, *Fire and Ice*<sup>1</sup>

**W**HILE FOR popular fiction writers, it seems that hemorrhagic viruses are the preferred agents of apocalyptic epidemics, many experts believe that the most likely candidates are not Ebola, Lassa fever, or the like, but rather the almost plebeian influenza. Reappearing every winter, influenza viruses sweep through naive populations, causing misery and—for some 20,000 Americans each year—death, either directly or (more commonly) by fostering secondary infections, typically in debilitated patients. There was a time, however, not so long ago and not so far away, when influenza struck the young and healthy, and the blow was often fatal. In 1918–19, pandemic influenza (A/H1N1) killed more than 20,000,000 people world-wide—500,000 in the U.S.—with attack rates highest in young adults.

In recent weeks, a handful of cases in Hong Kong, with several deaths, has renewed speculation about the potential for a pandemic of highly virulent influenza. This issue of the *CD Summary* provides a brief overview of the Hong Kong situation and its significance.

In May 1997, a 3-year-old Hong Kong boy died of ARDS and Reye syndrome subsequent to an upper respiratory illness. Influenza virus was isolated from a tracheal aspirate, but of a type (A/H5N1) never previously found in humans. (Seasonal flu epidemics in recent years have been caused by type A/H3N2, A/H1N1, and occasionally B viruses.) A/H5N1 flu viruses are not new; the subtype was first identified in 1961 and is a known pathogen for waterfowl and poultry. What was

new was the infection of—and pathogenic effect on—a human. It was suspected that the child acquired the virus from a sick chicken kept at his nursery school.

The May case remained an anomaly until November, when four additional cases were identified in Hong Kong; six more have been confirmed to date in December. Among these 11 cases, illness has been severe; all have been hospitalized, and four have died. It is unclear if the increasing number of cases reflects a genuinely increasing incidence or merely stepped-up surveillance.<sup>2</sup>

### WHERE'S THE PORK?

While person-to-person transmission has not been confirmed, the avian-to-human link apparently responsible for most if not all of the current cases is itself of concern. Most experts believe that new strains of influenza typically derive from human and bird strains coinfecting a third species, usually a pig. A/H5N1 seems to have bypassed the pig.

Influenza and other orthomyxoviruses have a segmented RNA genome, and it is the reassembly of these segments during replication that makes recombination particularly likely to occur. If cells are coinfecting with influenza viruses from, say, two different sources, it is possible via recombination to spawn novel viruses. Such antigenic “shifts” can be associated with increased transmission, reflecting the dearth of natural immunity to the novel virus in the population. In contrast, antigenic “drift” occurs constantly in response to evolutionary pressures, and accounts in large measure for the ever-changing formulation of the influenza vaccine cocktail, as well as the partial immunity enjoyed by survivors of previous infections or those with a history of recent vaccination.

While these cases are alarming, it is important to stress that, at present, there is no evidence of person-to-person transmission, which is a prerequisite of pandemic influenza. Epidemiological links have been established between three or four of the cases (children in an extended family), but

they may all have had common exposures to infected birds. Moreover, it will be one thing to establish that person-to-person transmission is possible, and another to establish that it is common enough to sustain an epidemic.

Hong Kong epidemiologists, working with experts from the WHO, CDC, and other agencies,\* are feverishly trying to assess the extent of the current outbreak. Even if transmission is only bird-to-human, it may be extensive, given that there are over 200 chicken farms on Hong Kong alone, and some 70,000 live chickens were being imported daily from adjoining Guangdong province. (Although of uncertain benefit to outbreak control, chicken movements have now been somewhat restricted in the Hong Kong area, and demand for poultry has plummeted. There is no evidence to suggest that influenza is spread by dead chickens, dead pigs, or any other food source, though.) Isolation wards have been established at Hong Kong hospitals to treat potential victims.

The current epidemiological investigations undoubtedly include active case finding and special studies (e.g., serosurveys) to assess background exposure and infection rates. Given the severity of the infections identified, it is quite possible that there is a hidden epidemic of mild or even asymptomatic cases.

### HOW CAN WE BE SAVED?

Current vaccines offer little if any protection against A/H5N1 influenza, although rimantadine and amantadine should be effective both prophylactically and as treatment; the Hong Kong isolates are susceptible in vitro. Efforts are underway to identify candidate H5N1 strains that could be used for vaccine production, although this is a precautionary measure only, and no production is underway. New vaccine formulations don't appear overnight, and technical challenges peculiar to the H5N1 virus may complicate production (e.g., the inoculated eggs die

\*although surprisingly not yet including the Health Division—a risky stance, to be sure.

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before they make significant quantities of virus). Once these problems are solved and a commitment is made, a minimum of six months would be needed to produce commercial stocks.

No special recommendations are presently in effect for travelers to Hong Kong or elsewhere. Despite all the deserved attention these H5N1 cases are getting, keep in mind that attack rate is very low. (Hong Kong's population is ~6,500,000.)

### MEANWHILE, BACK IN OREGON

Should you see patients with influenza-like illness following travel to Hong Kong or Southern China, collect throat wash specimens for viral culture. Consider empiric rimantadine or amantadine for these patients, although benefit may be minimal if not initiated within 48 hours of onset.

While the eyes of the epidemiological world are focused on Hong Kong, the outbreak underscores the importance of global surveillance for influenza, including our own efforts here in Oregon. To date, 88 specimens have been submitted to the Public Health Laboratory; none have been positive for influenza. With cases in Washington, California, and many other states, however, it is unlikely that we will be able to hold out much longer. Nationwide, almost all isolates have been A/H3N2. Specimens from patients with influenza-like illness can be submitted for culture at the OSPHL if they can be collected within three days of symptom onset.

Although ineffective against H5N1, let's not lose sight of the fact that the biggest influenza threats to Oregonians today are the plain vanilla types—all

covered by this year's vaccine. Immunizations should still be offered to the following groups<sup>3</sup>:

- persons aged 65 years or greater
- residents of nursing homes and other chronic-care facilities
- adults and children who have chronic disorders of the pulmonary or cardiovascular systems, including children with asthma.
- adults and children who have required regular medical follow-up or hospitalization during the preceding year because of chronic metabolic disease (including diabetes mellitus), renal dysfunction, hemoglobinopathies, or immunosuppression (including that caused by medications)
- Women in the second or third trimester of pregnancy
- Children on chronic salicylate therapy who would be at increased risk for the development of Reye syndrome
- medical personnel and others who are household or occupational contacts of any of the above
- anyone else who wants to reduce their risk of influenza, because it is not fun.

The H5N1 story is changing daily, and this account will surely be somewhat outdated by the time you read it. We will keep you posted of major developments in these pages. Media accounts to date have been generally accurate and informative. A large and ever-changing volume of information about the cases is available on the internet, including official announcements from the Hong Kong Department of health ([www.info.gov.hk/dh](http://www.info.gov.hk/dh)), WHO ([www.who.ch/programmes/emc/flu/flu.htm](http://www.who.ch/programmes/emc/flu/flu.htm)) and CDC ([www.cdc.gov/ncidod/diseases/flu/virus.htm](http://www.cdc.gov/ncidod/diseases/flu/virus.htm)).

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2. CDC. Isolation of avian influenza A (H5N1) viruses from humans—Hong Kong, May–December 1997. *MMWR* 1997 46:1204-1207.
3. CDC. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1997;46(No. RR-9):1-25.

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### Corrigendum: Lead-Ridden Zips

The correct URL for the secret list is: [www.ohd.hr.state.or.us/cdpe/eoi/welcome.htm](http://www.ohd.hr.state.or.us/cdpe/eoi/welcome.htm).

[What better way to end the year?]