

PRACTICE ALERT

Public health issues influencing your practice

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The growing threat of avian influenza

In the first half of 2004, an estimated 200 million poultry birds across Asia died or were destroyed in an effort to control a widespread outbreak of avian influenza.¹ Though such outbreaks have occurred before, this one, primarily in China and Southeast Asia, demonstrated increased pathogenicity in poultry, increased resistance to environmental controls, and an expanded range of mammalian hosts.

Lest anyone conclude this is a problem affecting only the birds and the people who raise them, clinical and laboratory evidence since 1997 point to a series of human cases of avian flu (**TABLE 1**), most of which were associated with outbreaks of the disease in poultry.² The change in characteristics of the current outbreak in birds in Asia combined with increased knowledge of the characteristics of human influenza have many scientists and public health officials increasingly concerned that we may be watching the unfolding of the next great flu pandemic. In this article, I describe how this might happen and what we can attempt to prevent it.

Human influenza pandemics

A flu pandemic is a global outbreak of disease among people after the emergence of a new influenza A virus. Three great pandemics occurred in the 20th century, all spreading worldwide within 1 year.

- *Spanish flu (1918–1919)*: 20 to 50 million people died, more than 500,000 in the US. Nearly half of those dying were young, healthy adults.

- *Asian flu (1957–1958)*: Caused about 70,000 deaths in the US.

- *Hong Kong flu (1968–1969)*: Caused about 34,000 deaths in the US.

Both the Asian and Hong Kong flu resulted from a mixing of a human and avian influenza virus; the Spanish flu may have resulted from a mutation in a purely avian virus.³

How avian influenza viruses spread

Avian influenza A viruses vary greatly, owing to the myriad combinations of their 15 hemagglutinins and 9 neuraminidases. The viruses are widespread in migratory birds and waterfowl and are usually of low pathogenicity. Water birds, in particular, act as hosts for influenza viruses, carrying them in their intestines and then shedding them.

Wild bird hosts do not usually get sick, but they can spread influenza to other birds. For instance, there have been 16 outbreaks of H5 and H7 influenza in US poultry since 1997. Usually, such events are from low-pathogenic avian viruses that cause little illness in affected chickens. When highly pathogenic viruses cause outbreaks, 90% to 100% of affected poultry can die. This has been happening in the current Asian outbreaks.

In the past, isolating poultry, culling (destroying) infected flocks, and vaccinating poultry eventually quelled the outbreaks. Such measures have not worked this time, and scientists think it likely that H5N1 infection among birds has become endemic to the region—ie, Cambodia,

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China, Indonesia, Malaysia, Thailand, and Vietnam.⁴

Rethinking how humans become infected

Since humans have distinct receptors for human viruses, as do birds for avian viruses, it was thought that an intermediate host—the pig, with both receptors—was necessary to allow the mixing of the viruses and subsequent human infection with avian influenza. However, recent outbreaks in poultry with proven spread of highly pathogenic virus from chickens directly to humans have challenged this theory (TABLE 1). While the mortality rate so far has been very high, this rate may turn out to be overstated as milder, nonfatal cases of human avian flu are discovered.

New research has raised additional concerns: ducks infected with H5N1 are now shedding virus for longer times while remaining asymptomatic; pigs in China and tigers in Thailand have been infected with H5 virus; and experiments with house cats in the Netherlands have demonstrated they could be infected with H5. These findings are troubling because the reassortment of avian viruses is more likely to occur when they are able to infect multiple species. Moreover, the infection in humans from Vietnam has shown resistance to the older antiviral drugs, amantadine and rimantadine, leaving oseltamivir and zanamivir as the antivirals likely effective against avian influenza A H5N1.⁴

■ Fear of human-to-human transmission

Direct spread of avian influenza from poultry to humans resulting in a high fatality rate is of course a major concern. What worries scientists and public health officials more, however, is the increasing risk of person-to-person transmission as a result of a change in the viral genome. Genomic variation could occur if avian virus genetic material mixes with that of a human virus in an intermediate host such as the pig or in a patient infected simultaneously with both avian and human

TABLE 1

Avian influenza infection in humans

Hong Kong (1997):	18 people hospitalized with 6 deaths
China and Hong Kong (1999):	2 cases in children who recovered
Virginia (2002):	1 person with serologic evidence of avian flu
China and Hong Kong (2003):	2 adults cases with one death
Netherlands (2003):	89 human cases with 1 death; most cases were of conjunctivitis, some with flu symptoms. The antiviral drug oseltamivir was used to help control spread
Canada (2004):	Human infections among poultry workers consisting of eye infections
Asia (since January 2004):	55 cases with 42 deaths in Vietnam, Thailand, and Cambodia

influenza strains; or it could occur with spontaneous mutation of an avian virus. A recent report provided strong evidence of avian influenza that spread from the index patient to her mother and aunt (both the 11-year old girl and her mother died). No further spread occurred, suggesting the infection resulted from a purely avian virus with no human virus involved.⁵

■ How effective will preventive measures be?

The current danger to people from avian influenza has been recognized sooner than the threats that preceded previous influenza pandemics, which burst upon the world with little warning. Lessons from the severe acute respiratory syndrome (SARS) epidemic in 2003, advances in science and public health surveillance, and cooperation among countries and organizations such as the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) have allowed us to observe the emergence of avian influenza in rural Asia and consider its wider implications. CDC's response has focused on enhanced surveillance and laboratory

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TABLE 2

CDC response to avian influenza

1. Recommendations for enhanced domestic surveillance and detailed laboratory testing procedures of avian influenza A H5N1
2. Provided training workshops for state labs on techniques to identify H5N1 viruses
3. Collaborative efforts with the Department of Defense and the VA on antiviral drug stockpiles
4. Collaborative work with WHO to investigate H5N1 infections in Vietnam and laboratory testing of H5N1 viruses from Thailand and Vietnam
5. A \$5.5 million initiative to improve influenza surveillance in Asia.
6. Conducted training sessions to improve local areas' ability to conduct surveillance for human cases of H5 infection
7. Issued a ban with the USDA (US Department of Agriculture) on the import of all birds from affected areas of Southeast Asia

TABLE 3

General precautions for travel to countries with avian influenza outbreaks*

1. Avoid places where live poultry are raised or kept, such as poultry farms and bird markets, and avoid sick or dead poultry
2. Practice frequent handwashing; consider bringing a waterless alcohol-based hand rub on your trip
3. All foods from poultry including eggs should be thoroughly cooked

* As of February 4, 2005 this was directed at travelers to Vietnam only; see reference #6 for complete details.

testing for human and avian influenza in the US and Asia and work on vaccine development with WHO and the National Institutes of Health (TABLE 2). CDC has not recommended avoiding travel to any of the involved countries, but has released guidelines for travel to affected areas (TABLE 3).⁶

In the event of an avian flu outbreak in humans, there will be questions about the best public health response, the use of antiviral agents, and infection control in health care settings. The SARS outbreak

was substantially controlled through the use of the traditional public health measures of isolation (separating ill or infected people from others) and quarantine (separating people exposed to infected people from others in order to prevent the further spread of the infection). Whether such measures would be successful with a highly contagious viral infection like influenza is debatable. Stohr of WHO has outlined a research agenda that includes study of hospital infection control practices, vaccine clinical immunogenicity, early interventions such as use of antivirals or vaccine to slow the spread of an emerging pandemic virus, the role of animal and bird species in influenza virus development, and risk assessment.⁷

Awareness the best defense now

If avian influenza makes the leap to person-to-person transmission, family physicians across the globe will be at the forefront of diagnosis and treatment. Though no immediate actions are necessary, we all must follow developments and support the work of health departments at improving their ability to monitor emerging outbreaks. The interconnectedness of global health is well exemplified in the concern about avian flu and the efforts to prevent an influenza pandemic.

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