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# VitalLongevity™

Logo: Life's blood flows through the hourglass; the stopcock represents the alteration of aging and disease as biomedical research progresses.

September 2007

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## Avian Flu

Like the color-coded terror alert, avian/bird flu is rarely in our news these days, but the threat persists and research continues. Near OFAS, on the east bank of the Hudson River, is Constitution Marsh Audubon Center and Sanctuary, where its staff has just completed year two of monitoring for avian influenza (AI) in the migratory birds that spend the summer in the Marsh.

The program is part of the Monitoring Avian Productivity and Survivorship program started in 1989 by the Institute for Bird Populations in Point Reyes, CA, which collects specimens and analyzes data from ~500 sites in North America. The program looks specifically for H5N1, a very deadly AI virus that has killed 192 of 319 infected persons as of 7/25/07 and necessitated broad infection-control culling of ~200 million birds, mostly poultry in Asia.

Als are Type A influenzas, as are the annual human influenzas (HI), which likely descended from Als. Most Als are of low pathogenicity (LP), commonly and symptomlessly infecting waterbirds, but some are (or can become) highly pathogenic (HP) like H5N1 did in Asia—that is, deadly and readily transmissible in poultry flocks. The awesome dread is that avian HP-H5N1 could become readily communicable to and among humans.

## Transmission of Flu Viruses

Two glycoproteins (sugar-protein molecules) are key components of AI viruses. One is hemagglutinin, the antigenic component; it comes in 16 forms (H1, H2, etc.). The other component, neuraminidase, has 9 forms (N1, N2, etc.). The N segment allows the virus to move from infected to healthy cells, and anti-virals like Tamiflu® work by interfering with this process. Although all 144 possible combinations of H and N vital strains have been isolated from birds, some are more common and/or more infectious than others, and there are many strains, each with a unique genetic 'fingerprint'.

Influenza viruses infect only epithelial cells by binding their H glycoprotein to cell-surface receptors. Als preferentially bind to receptor type  $\alpha 2,6$  and human flu viruses to type  $\alpha 2,3$ . In humans, type  $\alpha 2,3$  is present on respiratory tract epithelial cells from the nose to the bronchioles, and this is why human flus are so easily spread by sneezing and coughing. The  $\alpha 2,6$  receptor (preferred by Als) is also present on human cells but only at the alveoli, deep within

the lungs where blood is oxygenated; it is this relative inaccessibility that makes it very difficult for humans to get or spread an AI. If avian HP-H5N1 becomes able to bind to the  $\alpha 2,3$  receptors in the human upper respiratory tract, then it would be as highly transmissible as annual flu. [Sadly informative, clusters of infection with avian HP-H5N1 have been noted in blood (but not non-blood) relatives living together, and it is speculated that those infected have a genetic anomaly cursing them with  $\alpha 2,6$  receptors in the upper lung.]

### Influenza Pandemics

Strain	Years	Deaths US (Global)
H1N1* (Spanish)	1918-9	450,000 (>50 million)
H2N2 (Asian)	1957-8	470,000
H3N2† (Hong Kong)	1968-9	435,000
H5N1* (Avian/Bird)		est: 1.7 million (180-360 million)‡

\*Cause of Acute Respiratory Distress Syndrome (see Fig. 1)  
†Still the most major and troublesome in humans  
‡Current population is ~3 times that of 1918

Table 1.

markedly less frequent (and the death rate also lower) in those age 40+ compared to children and young adults, implying widespread immunity. Similarly, in 1918, those age 45-65 were relatively spared.

## Monitoring for H5N1 in North America

LP-H5N1 has been known in North America since 1975 and is not a human health concern. Although Als can be spread by migratory birds, there has been very low movement of Als from Eurasia to North America. As of April 2, 2007, 115,548 North American samples had been tested and reported through the Highly Pathogenic Avian Influenza Early Detection Data System. Expectedly, LP-H5N1 showed up, but no HP-H5N1 was found. Since 2006, the World Organization for Animal Health has required reporting of all LP H5 and H7 viruses because they can mutate into HPs. The USDA also tracks these viruses in wild birds, backyard and community flocks, and wild bird markets because they can pass from wild to domestic birds; the group-housed (e.g., chickens) are especially vulnerable. Historically, three strains have been found (confined to poultry flocks and wild bird markets) and eradicated in the US: an H7 strain (1924), H5N2 (1983, PA), and again H5N2 (2004, TX).

In the wild, ducks, geese, swans, gulls, and shorebirds are especially vulnerable to AI infection. The virus is shed fecally and contracted by feeding at fecally-contaminated shallow water sites where such birds densely congregate

during migration and where the virus can persist for days at 35°C and a month at 4°C. Infection is usually symptomless and rarely fatal, but predators, *e.g.*, hawks, captive carnivores, and carrion feeders, can become infected and might play a role in local transmission.

## HP-H5N1—The Asian Variety

This nasty virus came from wild-type LP-H5N1 introduced and adapted into poultry, especially chickens. First detected in November 1996 in southeast China, it spreads fast within poultry flocks and has moved throughout Asia, then to Africa and Europe. Until 2005, it was not found in wild birds living distant from domestic poultry, but though now found, the infection rate is ~0.1% in wild geese/ducks vs ~1.8% in domestics. Other species with documented, isolated infection (likely from eating diseased poultry) are pig, civet, marten, mink, ferret, housecat, tiger, and leopard. In humans, its well over 50% fatality rate makes HP-H5N1 a huge concern. Fortunately so far, most documented cases have been persons in close contact with diseased household flocks.

## From Asia by Air or Land

Although infected birds surely can spread HP-H5N1 short distances, there is no conclusive evidence for spread by long-distance, seasonal migration; also, infection is usually fatal, and dead birds don't fly. Infection combined with the rare phenomenon of birds being blown off-course is an unlikely risk. However, whereas legally imported birds have a 30-day quarantine (adequate time to show symptoms/die), importation of HP-H5N1 by illegal bird trafficking (*e.g.*, fighting cocks, exotics) is documented and a serious route that has been ameliorated by the Wild Bird Conservation Act and the EU ban on wild bird imports.

There are two strong modes—not mutually exclusive—for the westward spread. One is by air. In 2005 an outbreak of HP-H5N1 occurred in Qinghai Lake in remote western China. Careful analysis of the virus's genetic lineages have tracked the virus to outbreaks in eastern Europe, Africa,

and the Middle-East, presumably spread by waterfowl using overlapping flyways. The other is over land, its trajectory following roads and rails used in commercial poultry farming activities, *i.e.*, shipping and marketing of live birds and bird products (such as bird droppings for fish farming) and associated contaminated equipment. In this regard, national borders with good inspection regulations and procedures are effective countermeasures; for example, veterinary surveillance and rigorous control of trade has eliminated this source of HP-H5N1 in Japan, Taiwan, and South Korea.

## First Alert: Key Sentinel Species

Recent research using experimentally inoculated, naturally susceptible bird species revealed that the Laughing Gull and Wood Duck are excellent sentinel birds, promptly succumbing to infection, a finding remarkably consistent with the high mortality rate of semi-captive Wood Ducks in a Hong Kong waterfowl park in 2002 where 18 of 26 died,

and 16 of the 18 were positive for HP-H5N1. Other recent research has shown that HP-H5N1 sub-strains do not persist in water as long as LP H5 or H7 strains, thereby possibly shortening the time of exposure risk for congregating waterfowl. Undoubtedly, monitoring sites will be keeping a close eye on their Wood Ducks, which are conveniently present at our local Constitution Marsh in all seasons but winter.

**Note well:** There is no avian HP-H5N1 in North America, and the probability of its appearing seems low. Comfortingly, the CDC monitors suspected cases of H5N1 infection in persons having severe/acute respiratory illness who had recently traveled to an

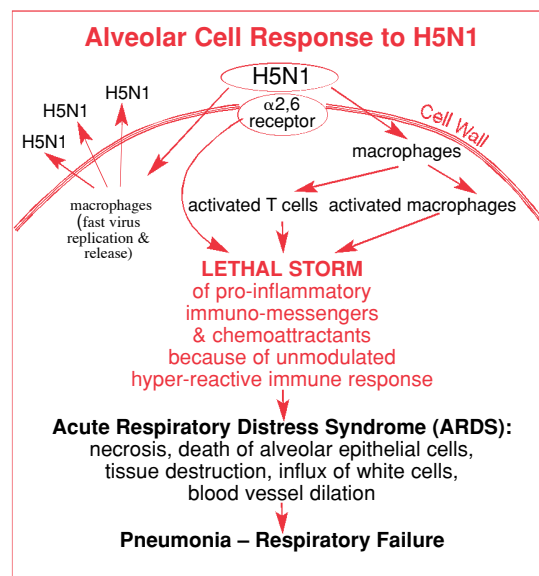


Figure 1.

affected area or who had contact with an infected vector; between February 2003 and May 2006, no H5N1 infections were found in 59 suspected cases. Note also: cooking poultry to an internal temperature of 165°F kills viruses and other pathogens like salmonella.

A PDF of this newsletter, as well as citations for information referred to in this text, authoritative sources for further information, and pandemic preparedness guidance, are available at <[www.orentreich.org](http://www.orentreich.org)>.

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