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AVIAN INFLUENZA: KNOW WHEN THE SKY IS FALLING

MEDIA AND scientific engrossment over flu in Phylum *Chordata,* Class *Aves* represents yet another diversion by this wily virus to distract the public from the havoc even now being wrought by more conventional strains. Each year in the U.S. alone, "routine" influenza kills an estimated 36,000 persons. Over the past two years, fewer than 200 humans worldwide are known to have become ill from a bird strain of influenza known as H5N1; how much should the other 6 billion of us on the planet worry about that strain? Will more cases occur? Will these human infections lead to the next pandemic? We won't tempt fate by guessing the answers; but we do know that Oregon clinicians have already encountered situations where they, or their patients, suspected illness from avian influenza (AI). Our recommendations for human H5 influenza testing follow a brief review and update.

INFLUENZA VIRUS: THE AVIAN CONNECTION

Inside its lipid membrane envelope, influenza A carries 8 separate RNA segments coding for at least 10 different proteins. Two immunogenic surface proteins, hemagglutinin (H) and neuraminidase (N), which function in viral attachment and release, respectively, are the basis of influenza A nomenclature (think H3N2, H1N1). Continuous mutation in both proteins prompts the yearly need and race to develop and distribute a new vaccine.

We know of 16 major subtypes of the H protein and 9 of the N; all are found in wild waterfowl, the natural reservoir for the virus. Genetic archeology now supports an avian source for the rare introduction of new H and N proteins into human influenza (corresponding to the 3 pandemics of the 20th century).[1] However, only 3 of the H types and 2 of the N types have been routinely found in viruses isolated from humans, suggesting that there is a "species barrier," an hypothesis strongly supported by *in-vitro* data.

AVIAN INFLUENZA (AI), A NEW PROBLEM?

Strains of avian influenza (AI) can be classed as "high-pathogenicity" (HP) and "low-pathogenicity." Domestic poultry producers recognize outbreaks of low-pathogenicity AI when hens lay fewer eggs and broilers fail to fatten. These relatively common epizootics are rarely publicized. On the other hand, high-pathogenicity AI strains can kill entire flocks overnight: H5N1 briefly devastated poultry in Hong Kong in 1997 before the strain re-emerged in December 2003 in Asia. Poultry and wild birds in 19 countries have been afflicted in the current outbreak,[2] and over 100 million birds have died from disease or culling.[3] Less publicized are at least 3 other major HPAI outbreaks in Europe and North America since 2003,[3] which have not been associated with widespread serious human illness.

HUMAN INFECTION WITH H5N1 INFLUENZA

Documented human H5N1 infection first occurred in association with the 1997 Hong Kong outbreak (18 cases, 6 deaths).[4] Similarly, coincident with the new poultry outbreak, astute clinicians in Vietnam recognized human H5N1 infection in late 2003 and have diagnosed the majority of cases since (Table)[5]; fewer cases have been recognized elsewhere, but under-diagnosis is suspected. Nearly all cases investigated had close contact with ill or dead poultry or poultry products; in a few instances human-to-human transmission may have occurred.[6] The median period from exposure to onset (when known) was 3 days. WHO reports a case fatality rate of over 50%,[5] mostly from complications of ARDS.[7-9]

Confirmed Human H5N1, 2003-2005

Country	Cases	Deaths
Cambodia	4	4
China	5	2
Indonesia	13	8
Thailand	22	14
Vietnam	93	42
Total	137	70

TESTING HUMANS FOR H5N1 INFLUENZA

Although we think the chances of H5N1 influenza showing up in Oregon at this point are small, we do want to spot it if it comes. We ask that you test persons with acute respiratory illness (as defined in Box, *verso*) if within the 10 days before illness onset they had been in H5N1-affected areas.[2] If you suspect H5N1 infection, institute infection control measures, and then contact the patient's local health department to facilitate specimen handling. At a minimum, control measures should include[10]

- Mask for the patient if possible;
- Mask and eye protection for caregivers;
- Private room, negative pressure if available;
- Hand hygiene before and after patient contact;
- Gown and gloves if contact with secretions is likely.

Should a patient call and volunteer concern about H5N1, attempt to interview by phone, assess the risk, and direct to the best facility for evaluation.

WHO PERFORMS THE TEST?

The Oregon State Public Health Lab performs a rapid, highly sensitive reverse transcriptase polymerase chain reaction (RT-PCR) test for H5 influenza. Local and state health officials are ready

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to discuss cases meeting our suspect definition (and any others that come close). Nasopharyngeal or throat specimens (swabs or aspirates) transported with cold packs are preferred. Since viral culture is slower, less sensitive, and potentially more dangerous for lab workers, we prefer the RT-PCR method; a positive test would prompt additional testing by CDC.

RISK FOR TRAVELERS

So far, H5N1 influenza appears to be transmitted inefficiently from bird to human and even less well from human to human. Of concern, however, are the small number of cases with no bird contact and family clusters in which human-to-human transmission may have occurred.

Nonetheless, the risk for travelers seems very low. For up-to-date travel advice, check the CDC and WHO web sites.[11,12]

Advise potential travelers to update the usual vaccinations—including the annual flu shot; to avoid direct contact with any bird that isn't cooked (and cooked thoroughly); to practice careful handwashing; to eat poultry or poultry products (like eggs) only if they're—you guessed it!—thoroughly cooked; and to seek medical attention if respiratory illness develops overseas or within 10 days of returning home. Patients may request antiviral prophylaxis before departure, but it is expensive and its value for H5N1 prevention is unknown.

THE MANIFEST THREAT IN OREGON

As this issue goes to press, flu activity, nearly all type A, is climbing rapidly in Oregon. Nationally, the circulating strains appear well matched by this year's vaccine. The peak of this influenza season is likely to be several weeks away, so continue to vaccinate your patients as supply allows. See *http://oregon.gov/DHS/ph/acd/flu/influenza.shtml* for information and updates.

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Suspect H5N1 Influenza Case Definitions

1. Hospitalized patient with pneumonia, acute respiratory distress syndrome (ARDS), or other severe respiratory illness for which an alternative diagnosis has not been established;
   and
   History of travel within 10 days of symptom onset to a country with H5N1 infections in poultry or humans.

2. Patient with a milder respiratory illness with documented temperature of >100.4°F (>38°C) ***plus***: cough, sore throat or shortness of breath;
   and
   History of close contact with poultry (e.g., visited a poultry farm, a household raising poultry, or live bird market) in an H5N1-affected country, or with a known or suspected human cases of H5N1 infection within 10 days before symptom onset.

A list of countries where poultry are currently affected can be obtained from:
http://www.oie.int/downld/AVIAN%20INFLUENZA/A_AI-Asia.htm