Continuing Education

One Flu Over the Cuckoo's Nest:

Is Concern for Avian Flu Warranted in a Busy Clinic?

Julie Watson Brown

ABSTRACT

At present H5N1 is mainly a disease of birds. However, with ongoing mutation, the virus may develop the ability to bind to human upper airway receptors and be easily passed between human beings by coughing and sneezing. Care providers must be prepared to recognize isolated cases, clusters of cases, or possibly sudden, overwhelming numbers of cases. Most importantly, guidelines for recognition and testing suspected cases should be available for reference in each clinic. This article provides background in the biology, epidemiology, and natural history of H5N1 infection, along with guidelines for prevention, diagnosis, and advice for treatment.

Keywords: Avian influenza, bird flu, H5N1, influenza A viruses, pandemic influenza

CE credit is available for $10 per credit hour by mail or online without charge at *www.npjournal.com*.

want. The following summarizes some future forms of male contraception.

Intra Vas Device

The intra vas device (IVD) is a tiny silicone plug surgically inserted into the vas deferens. This device does appear to be reversible. Reversible inhibition of sperm under guidance (RISUG) is composed of styrene maleic anhydride complex with the solvent dimethylsulfoxide. RISUG has two contraceptive effects: partial blockage of the vas deferens and disruption of the sperm that pass through the vas deferens.

Heat Methods

Heat is associated with a decrease in sperm production. Extended periods in hot water and tight-fitting undergarments also are associated with decreased sperm production. Heat is being considered as a potential future contraceptive measure.

Hormonal Methods

A variety of hormonal methods are being considered. Testosterone alone has resulted in the suppression of spermatogenesis. Testosterone injections were associated with weight gain and acne. In addition, testosterone and progestogen combinations were reported to suppress spermatogenesis. However, this combination was associated with a decrease in libido and progestogen-related side effects. Subcutaneous estrogen and testosterone combined implants are reported to increase spermatogenic suppression.

However, estrogenic side effects have occurred in men, especially the occurrence of gynecomastia. The combination of testosterone and gonadotropin-releasing hormone (GnRH) agonist and GnRH antagonist was associated with alterations in spermatogenesis. These contraception methods remain in phases of laboratory and clinical investigations.

Gene Methods

Catsper genes are a set of genes that encode a series of calcium ion exchange channels that are exclusive to the male reproductive tract. Calcium ion exchange is an essential mechanism for cellular motion and sperm motility. Septin 4 gene is critical to normal sperm production by encoding proteins that facilitate the formation of the spermatic tail. Interruption of Septin 4 genes may alter sperm motility from an inadequate sperm tail.

Other Potential Male Contraceptives

- Neem extracts (*Azadirachta indica*) are derived from a tree in India. The compound can be injected into the vas deferens and appears to alter the rate of spermatogenesis.
- Papaya seed extracts (*Carica papaya*) administered orally may be capable of decreasing sperm production.
- Oleanolic acid extracted from flowers of the myrtle family tree appears to alter sperm passage through the epididymis when administered orally. JNP

Demetrius J. Porche, DNS, RN, APRN, is a professor, director of the doctor of nursing science program, and dean of the School of Nursing at Louisiana State University in New Orleans. He can be reached at dporch@lsuhsc.edu.

1555-4155/07/$ see front matter

doi:10.1016/j.nurpra.2007.08.001

Since 1959, human infection with avian influenza has been documented on only 10 occasions. Of the hundreds of strains of avian influenza A viruses, only four are known to have caused human infections. Human infection has resulted in mild symptoms and little severe illness, with one notable exception: the highly pathogenic H5N1 virus.[1]

The exact process of this virus's abrupt increase in pathogenicity remains a mystery, but it probably is the result of mutation and its spread a consequence of bird migration. Today, at least some species of migratory birds are thought to be carrying the H5N1 virus in its highly pathogenic form and introducing it to new areas along their flight routes.[1]

The subsequent spread of avian flu from Southeast Asia to India, Africa, and Europe and its high mortality rate (up to 80%) has raised concern among health officials about an impending pandemic. Much of the literature is devoted to outbreak preparedness and speculation over the possibility of a pandemic. However, is the avian flu (H5N1) something to worry about day in and day out in clinical practice?

BIOLOGY, PHYSIOLOGY, PATHOPHYSIOLOGY, AND TRANSMISSION

All birds are thought to be susceptible to infection with avian influenza viruses, and many wild bird species carry these viruses with no apparent signs of harm.[1] These common infections in migrating birds serve to provide a reservoir of influenza viruses that is perpetually circulating around the world. Although most infections in birds are mild and self-limiting, infection with subtype H5N1 virus causes a distinctly different, more severe infection, known as highly pathogenic avian influenza. Highly pathogenic avian influenza is associated with a mortality rate that can approach 100% within 48 hours. In this form of the disease, the virus not only affects the bird's respiratory tract but also invades multiple organs and tissues.[1]

Apart from being highly contagious among poultry, avian influenza viruses are readily transmitted from farm to farm by the movement of birds, people (by shoes and contaminated clothing), and other contaminated fomites (vehicles, equipment, feed, and cages). These viruses can survive for long periods in the environment, especially when temperatures are low. The highly pathogenic H5N1 virus can survive in bird feces for at least 35 days at low temperature (4°C). At a higher temperature (37°C), H5N1 viruses have been shown to survive for 6 days.[1] This supports the observation that seasonal outbreaks of H5N1 mimic those of human influenza, which occur during the winter months.[2]

CURRENT EPIDEMIOLOGY

Direct human infection by an avian influenza A (H5N1) virus was first recognized during the 1997 outbreak in Hong Kong, China.[3] Among birds and between birds and human beings, avian influenza was shown to spread most commonly by the fecal-oral route[4] (although evidence exists that airborne spread can occur between birds in birdhouses).[5]

To date, the following nine Asian countries have reported outbreaks[3] (listed in chronologic order): the Republic of Korea, Vietnam, Japan, Thailand, Cambodia, the Lao People's Democratic Republic, Indonesia, China, and Malaysia. Of those countries, Japan, the Republic of Korea, and Malaysia have controlled their outbreaks and are now considered free of the disease, but elsewhere in Asia the virus has become endemic.[3] Outbreaks of H5N1 avian influenza that began in Southeast Asia in mid-2003 have now spread westward to parts of Europe and Africa (Figure 1). Further spread of the virus along the migratory routes of water birds is anticipated.

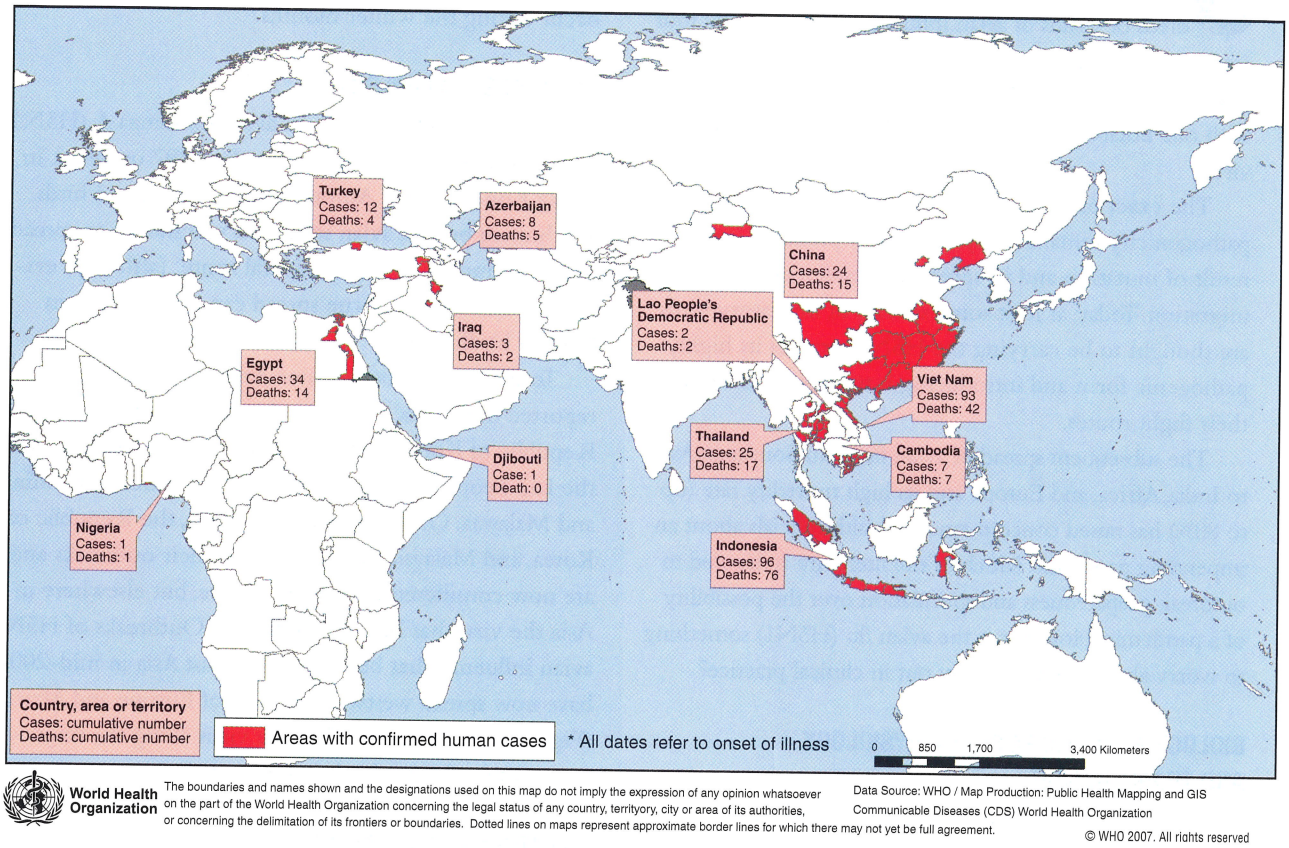
INFECTION AND MUTATION

Historically, all outbreaks of the highly pathogenic form of avian influenza were caused by viruses of the H5 and H7 subtypes. Typically of low pathogenicity, these two subtypes can transform into highly pathogenic strains even after short periods.[1]

However, bridging from birds to human beings requires a significant mutation, which does not seem to have occurred yet. Despite the infection of millions of birds over large geographical areas since mid-2003, fewer than 200 human cases were confirmed.[1] This may be attributed to human genetics; although a few persons posses the requisite receptor sites in the upper airway, current thinking is that most human beings do not.[2,6] However with ongoing mutation, the virus may develop the ability to preferentially bind to human upper airway receptors where it can be easily passed by aerosol with coughing and sneezing.[6]

Theoretically, H5N1 could improve its transmissibility among human beings by two principal mechanisms. The first is *reassortment or antigenic shift*, in which genetic material is exchanged between human and

Figure 1. Areas with confirmed human cases of H5N1 avian influenza since 2003. Status as of 16 May 2007 (latest available update). *Available at: http://gamapserver.who.int/mapLibrary/Files/Maps/Global_H5N1inHumanCUMULATIVE_FIMS_20070516.png.*



avian viruses during coinfection of a human being or animal, such as a pig[7] (infected domestic cats were discovered in Germany in 2006).[8] Reassortment would result in a virus to which human beings would have no immunity.[4] Such reassortment would be heralded by a surge of cases with pandemic spread. The second mechanism would involve a more gradual process of *adaptive mutation* or *antigenic drift*, whereby the capability of the virus to bind to human cells increases during repeated human infection. Adaptive mutation, expressed initially as small clusters of human cases with evidence of human-to-human transmission, would probably give the world some time to take defensive action, if detected sufficiently early.[7] It is unclear whether the increasing use of influenza vaccines would contribute to or detract from the risk from such adaptive mutation.[9]

GUIDELINES FOR ASSESSING, TESTING, AND DIAGNOSIS

Because of these two distinct and different possibilities, care providers must be prepared to recognize isolated cases and clusters of cases, or possibly sudden, overwhelming numbers of cases. Most importantly, guidelines for recognition and testing of suspected cases should be available for reference in every clinic, as ordinarily the index of suspicion of infection with H5N1 is low, and early detection of an outbreak is crucial to delay the spread and morbidity of an impending pandemic.

History and Physical

Because H5N1 is endemic in specific locations, positive screening includes a history of travel to those areas, potential exposure to contaminated birds, or both. A positive history also includes influenza-like illness, especially with fever greater than 38°C (100.4°F) and symptoms in the lower respiratory tract early in the illness (particularly difficulty in breathing around day five of infection). Respiratory distress, a hoarse voice, and inspiratory rales are common. Sputum production is variable and sometimes bloody. Vomiting, abdominal pain, chest pain, and bleeding from the nose and gums

have been reported as early symptoms, and watery diarrhea without blood appears to be more common in H5N1 than in seasonal influenza. Important to remember, the spectrum of clinical symptoms may be broader, and not all confirmed patients have presented with respiratory symptoms.[10]

Course

Although acquired through the upper airway, H5N1 is an infection of the *lower* airway, where nearly all human beings carry the appropriate receptors.[6] Once the infection reaches the lower airway, the virus can replicate and cause serious illness that progresses rapidly.

Current data for H5N1 infection indicate an incubation period ranging from 2 to 8 days and possibly as long as 17 days.[10] Almost all patients develop pneumonia, and clinical deterioration is rapid.[10] Common laboratory abnormalities include leukopenia, mild-to-moderate thrombocytopenia, elevated alanine transaminase, and possibly disseminated intravascular coagulation.[11]

Testing and Diagnosis

Testing for H5N1 virus infection is recommended, optimally within 3 days of symptom onset. The Centers for Disease Control and Prevention (CDC) recommends testing a patient who has an illness that[11]

1. requires hospitalization or is fatal; *and*
2. has or had a documented temperature of ≥38°C (≥100.4°F); and
3. has radiographically confirmed pneumonia, acute respiratory distress syndrome, or other severe respiratory illness for which an alternate diagnosis has not been established; *and*
4. has at least one of the following potential exposures within 10 days of symptom onset:
   - A. History of travel to a country with influenza H5N1 documented in poultry, wild birds, or human beings *and* had at least one of the following potential exposures during direct contact with (eg, touching) sick or dead domestic poultry:
     - a. direct contact with surfaces contaminated with poultry feces
     - b. consumption of raw or incompletely cooked poultry or poultry products
     - c. direct contact with sick or dead wild birds suspected or confirmed to have influenza H5N1
     - d. close contact (approach within approximately 3 feet) of a person who was hospitalized or died as a result of a severe unexplained respiratory illness
   - B. Close contact (approach within approximately 3 feet) of an ill patient who was confirmed or suspected to have H5N1;
   - C. Worked with live influenza H5N1 virus in a laboratory

Testing can be considered on a case-by-case basis, in consultation with local and state health departments, for a patient with mild or atypical disease (hospitalized or ambulatory) who has one of the exposures listed above (criteria A, B, or C), or a patient with severe or fatal respiratory disease whose epidemiologic information is uncertain, unavailable, or otherwise suspicious (travelers from influenza H5N1–affected countries with unclear or suspicious histories of exposure, those having contact with sick or well-appearing poultry, etc).

A variety of specimens are suitable for laboratory evaluation of infections in the upper respiratory tract. Dacron-tipped oropharyngeal swab specimens are preferred because they appear to collect the highest quantity of virus for H5N1 detection.[11] Nasal or nasopharyngeal swab specimens are acceptable, but they may recover less virus and therefore not be optimal for virus detection. Specimens should be stored at 4°C and transferred using universal precautions to the state public health laboratory or a CDC-designated local public health laboratory where the Influenza A/H5 (Asian Lineage) virus real-time reverse transcription–polymerase chain reaction rapid assay test, approved by the Food and Drug Administration (FDA) just last year, yields results within hours.[12]

In the clinic, rapid testing for influenza type A should be conduced as well. However, results must be interpreted with caution; these tests have relatively low sensitivities, and a negative result would not exclude a diagnosis of H5N1. In addition, a positive result does not distinguish between seasonal and avian influenza A viruses.[11]

Serologic testing for H5N1-specific antibody may also be considered. Paired serum specimens from the same patient are required for H5N1 diagnosis: one sample should be tested within the first week of illness, and a second sample 2 to 4 weeks later. A demonstrated rise in the H5N1-specific antibody level is required for a diagnosis of H5N1 infection. Currently, the microneutralization assay, which requires live virus, is the recommended test for measuring H5N1-specific antibody.[11]

Table 1. WHO Rapid Advice Guidelines for Treatment and Prophylaxis of Human Influenza Type A Infection: Adults

Purpose of Drug	Oseltamivir[a,b]	Zanamivir	Amantadine[b]	Rimantadine[b]
Treatment	Age ≥13 y :75 mg BID × 5 d	10 mg BID × 5 d	Age 10-65 y: 100 mg BID × 5 d Age > 65 y: 100 mg, QD × 5 d	Age ≥ 12 y: 100 mg BID × 5 d
Prophylaxis	Age ≥ 13 y: 75 mg QD × 7–10 d after last known exposure	10 mg BID × 7–10 d after last known exposure	Same as treatment, except duration 7–10 d after last known exposure	Age ≥ 10 y: 100 mg BID for 7 d after last known exposure

[a]*See warnings for adverse effects.*
[b]*Renal adjustments are necessary.*
Adapted from the World Health Organization.[10]

Definitive diagnosis either directly from patient specimens or from viral culture requires additional laboratory testing in biosafe laboratories (level 3) approved by the US Department of Agriculture (USDA) and epidemiologic assessment in consultation with national influenza surveillance experts.[12]

Treatment

Antivirals may be of value in the treatment of avian flu as they have been in the treatment of seasonal influenza. Amantadine (Symmetrel) and rimantadine (Flumadine), both used historically for the prophylaxis and treatment of seasonal influenza A, block penetration of influenza virus into the cell and uncoating of viral DNA for replication. However, drug resistance through a single gene mutation can happen quickly. In fact, most H5N1 viruses that have caused human illness and death in Southeast Asia appear to be resistant to amantadine and rimantadine,[13] presumably because of their widespread use in agricultural settings in those areas.

Oseltamivir (Tamiflu) and zanamivir (Relenza) work through inhibition of neuraminidase, which is necessary for viral infectivity. Both neuraminidase inhibitors were developed for the treatment and prophylaxis of seasonal influenza A and B. However, neuraminidase inhibitors should not be considered a panacea for any influenza infection. In a 2005 study, H5N1 virus collected form a Vietnamese girl was resistant to oseltamivir, yet sensitive to zanamivir.[14] Data on the clinical effectiveness of oseltamivir and zanamivir in avian flu is so limited that to date no CDC clinical recommendations exist specifically for H5N1 treatment with neuraminidase inhibitors.

In 2006, the World Health Organization (WHO) published a summary and evaluation of available data on effectiveness of antivirals in treating H5N1 infection in adults and children[4,10] (Table 1 and Table 2). This rapid advice guideline presents suggested dosing; however, because it is based on a dearth of research, most of the evidence available is categorized as low or very low in quality. Evidence on the existence of adverse events was of a slightly higher quality (moderate), so these drugs should be used with caution and close oberservation.[10] For all treated patients, consideration should be given to monitoring changes in viral load, drug susceptibility, and drug levels.

PREVENTION AND CAUTION WITHOUT PARANOIA

Limiting Exposure

Most cases of avian influenza infection in human beings have resulted from contact with infected poultry or surfaces contaminated with the secretions and excretions from infected birds. Exposure to H5N1 this way is unlikely in the United States because of the short lifespan of infected birds, federal surveillance programs, and widespread pasteurization of eggs. However, even if poultry or eggs were to be contaminated with the virus, proper cooking as recommended by the USDA and the FDA would destroy it. So to stay safe, the advice is the same for protecting against any infection from poultry or eggs:

- Wash hands with soap and warm water for at least 20 seconds before and after handling raw poultry and eggs.
- Clean cutting boards and other utensils with soap and hot water to keep raw poultry from contaminating other foods.

Table 2. WHO Rapid Advice Guidelines for Treatment and Prophylaxis of Human Influenza Type A Infection: Children

Purpose of Drug	Oseltamivir	Zanamivir[a]	Amantadine	Rimantadine[b]
Treatment	Age ≥ 1 y: BID × 5 d Weight 0–15 kg: 30mg 15–23 kg: 45mg 23–40 kg: 60mg ≥ 40 kg: 75 mg	Age ≥ 7 y: 10 mg BID × 5 d	Age 1–9 y: 5 mg/kg/d in 2 divided doses, (max = 150 mg) × 5 d Age 10-12 y: 100 mg BID × 5 d	Age ≥ 12 y: same as adult dose
Prophylaxis	Age 1–13 y: QD for 7–10 days after last known exposure Weight 0–15 kg: 30mg 15–23 kg: 45mg 23–40 kg: 60mg ≥ 40 kg: 75 mg	Age ≥ 7 y: 10 mg QD for 7–10 d after last known exposure	Same as for treatment, except duration is 7–10 d after last known exposure	Age < 10 y: 5 mg/kg/d in 2 divided doses (max = 150mg) Age ≥ 10 y: same as adult dose

[a]*Not approved for children younger than 7 years.*
[b]*Not approved for children younger than 12 years.*
Adapted from the World Health Organization.[10]

- Use a food thermometer to make sure you cook poultry to a temperature of at least 165°F. Consumers may wish to cook poultry to a higher temperature for personal preference.
- Cook eggs until whites and yolks are firm.[5,15]

Because no efficient human-to-human transmission of the virus is known to be occurring anywhere, simply traveling to a country with ongoing outbreaks in poultry or sporadic human cases does not place a traveler at enhanced risk of infection, provided the person did not visit live or "wet" poultry markets (where slaughter or butchering occurs), farms, or other environments where exposure to diseased birds may occur.[16]

Vaccination

An inactivated vaccine has been developed from a human strain of H5N1 and is intended for adults at increased risk of exposure to the avian influenza virus. The vaccine, developed by Sanofi Pasteur, was purchased by the federal government as part of the Strategic National Stockpile for distribution by public health officials in an epidemic, but it is not available commercially to date.[17]

A study of this vaccine was conducted by the National Institute of Allergy and Infectious Diseases (NIAID) and published in 2006.[18] Of 451 healthy adults, 54% of the 99 participants who received 90 μg of the vaccine followed by another 90-μg dose 28 days later showed that neutralizing antibodies rose high enough to confer protection against H5N1 influenza. The vaccine was generally well tolerated; most common side effects included pain and tenderness at the injection site, headache, malaise and myalgia, and nausea and feverishness. The NIAID investigators concluded that the vaccine was appropriate for licensure but cautioned that much more study was needed, particularly with children, older adults, and immunocompromised persons. Currently, studies of both populations are under way at Princess Margaret Hospital for Children in Australia.[19,20]

In phase 1 clinical trials at NIAID, Center for Immunization Research, is a live attenuated vaccine delivered intranasally.[21] A phase 2 Brazilian study is also under way of a combined seasonal flu/H5N1 vaccine conducted by Novartis.[22]

Until the actual emergence of the influenza virus strain responsible for an influenza pandemic, there will be no direct evidence of the effectiveness of vaccine or drug strategies for lowering rates of mortality and morbidity in an influenza pandemic.[23] The WHO stresses

that the world still lacks the manufacturing capacity to meet potential global demand for a pandemic influenza vaccine; current capacity is estimated at less than 400 million doses per year for a world of 6.5 billion people.[4] In response, WHO launched the Global Pandemic Influenza Action Plan to increase vaccine supply,[24] but this program will take years to implement. Until then, education about disease transmission to those at risk and proper cooking of poultry are the best strategies for prevention of infection.

INDIVIDUAL PREPAREDNESS

Practitioners may be asked to write prescriptions for patients so they may maintain an emergency supply of antivirals at home, but this practice is discouraged both by public health officials and the American Medical Association.[25] Based on observed patterns of H5N1 resistance to antiviral medications, and the possibility that symptoms unrelated to H5N1 infection may prompt initiation of the medications and thus a larger shortage of them where and when they are needed, practitioners must avoid this practice. Instead, information about how to otherwise prepare for a pandemic can be provided. The US Department of Health and Human Services recommends that persons keep a supply of up-to-date prescription and nonprescription medicines (antipyretics, pain medication, cough and cold medicine, and antinausea and antidiarrheal medication as well as electrolyte solutions and vitamins) on hand, stock a 2-week supply of food and water, and plan for home care with friends and family who are or may become ill.[26] Practitioners may choose to review strategies that reduce the spread of disease, such as proper handwashing technique. Finally, patients (and practitioners) can volunteer for their local Community Emergency Response Team or Medical Reserve Corps. Information about these volunteer opportunities is available at *www.citizencorps.gov/cert/* and *www.medicalreservecorps.gov/HomePage*, respectively.

CONCLUSION

Although avian influenza is not common in human beings, health care providers must recognize that infection does occur, and rates are increasing each year.[27] Residents of the United States are at low risk of H5N1 infection today, but a higher level of suspicion with recent travelers to and new immigrants from endemic areas is warranted. Strategies for prevention should be provided to travelers at risk. Screening and testing procedures should be made available in every clinic, along with contact information for public health officials. At the same time, reassurance is necessary that human-to-human transmission is not occurring, yet. JNP

References

1. World Health Organization. Avian influenza ("bird flu") fact sheet. *Available at: www.who.int/mediacentre/factsheets/avian_influenza/en/index.html.* Accessed May 17, 2007.
2. Webster R, Govorkova E. H5N1 influenza-continuing evolution and spread. *N Engl J Med.* 2006;355(21):2174-2177.
3. Areas with confirmed cases of H5N1 avian influenza since 2003. Status as of 16 May, 2007. *Available at: http://gamapserver.who.int/mapLibrary/Files/Maps/Global_H5N1inHumanCUMULATIVE_FIMS_20070516.png.* Accessed May 22, 2007.
4. Thomas J, Noppenberger J. Avian influenza: a review. *Am J Health Syst Pharm.* 2007;64(2):140-165.
5. US Food and Drug Administration, Center for Food Safety and Applied Nutrition. What consumers need to know about avian influenza. *Available at: www.cfsan.fda.gov/~dms/avfluqa.html.* Accessed June 11, 2007.
6. Shinya K, Ebina M, Shinya Y, Ono M, Kasai N, Kawaoka Y. Influenza virus receptors in the human airway. *Nature.* 2006;440(7083):435-436.
7. Centers for Disease Control and Prevention. Transmission of influenza a viruses between animals and people. *Available at: www.cdc.gov/flu/avian/gen-info/transmission.htm.* Accessed May 22, 2007.
8. World Health Organization. H5N1 avian influenza in domestic cats. *Available at: www.who.int/csr/don/2006_02_28a/en/index.html.* Accessed June 4, 2007.
9. Tauberger KJ, Morens D, Fauci A. The next influenza pandemic: can it be predicted? *JAMA.* 2007;297:2025-2027.
10. World Health Organization. WHO rapid advice guidelines on pharmacological management of humans infected with avian influenza A (H5N1) virus. *Available at: www.who.int/medicines/publications/WHO_PSM_PAR_2006.6.pdf.* Accessed May 22, 2007.
11. Centers for Disease Control and Prevention. Updated interim guidelines for laboratory testing of persons with suspected infection with avian influenza A (H5N1) virus in the United States. *Available at: http://www2a.cdc.gov/han/ArchiveSys/ViewMsgV.asp?AlertNum=00246.* Accessed June 7, 2007.
12. Centers for Disease Control and Prevention. New laboratory assay for diagnostic testing of avian influenza A/H5 (Asian lineage). *Available at: www.cdc.gov/mmwr/preview/mmwrhtml/mm55e203a1.htm.* Accessed May 17, 2007.
13. World Health Organization. Updated interim guidelines for laboratory testing of persons with suspected infection with avian influenza A (H5N1) virus in the United States. Annex 3. *Available at: www.who.int/medicines/publications/WHO_PSM_PAR_2006.6.pdf.* Accessed May 22, 2007.
14. Le QM, Kiso M, Someya KT, et al. Isolation of a drug resistant H5N1 virus. *Nature.* 2005;437(7062):1108.
15. Questions and answers about avian influenza (bird flu) and avian influenza a (H5N1) virus. *Available at: http://www.cdc.gov/flu/avian/gen-info/qa.htm.* Accessed June 4, 2007.
16. World Health Organization. WHO recommends relating to travelers coming from and going to countries experiencing outbreaks of highly pathogenic H5N1 avian influenza. *Available at: www.who.int/csr/disease/avian_influenza/travel2005_11_3/en/index.html.* Accessed May 22, 2007.
17. Food and Drug Administration. First 'bird flu' vaccine for humans approved. *Available at: www.fda.gov/consumer/updates/birdflu043007.html.* Accessed June 4, 2007.
18. Treanor J, Campbell J, Zangwill K, et al. Safety and immunogenicity of an inactivated subviron influenza A (H5N1) vaccine. *N Engl J Med.* 2006;354(13):1343-1351.
19. Study of a pandemic influenza vaccine in children. *Available at: http://clinicaltrials.gov./ct/show/NCT00370864?order=12.* Accessed June 8, 2007.
20. Study of a pandemic influenza vaccine in elderly participants. *Available at: http://clinicaltrials.gov./ct/show/NCT00376402?order=13.* Accessed June 8, 2007.
21. Safety of and immune response to a bird flu virus vaccine (H5N1) in healthy adults. *Available at: http://clinicaltrials.gov./ct/show/NCT00347672?order=4.* Accessed June 8, 2007.
22. Immunogenicity, safety and tolerability of prepandemic influenza and seasonal influenza vaccine in adult subjects. *Available at: http://clinicaltrials.gov./ct/show/NCT00478816?order=2.* Accessed June 8, 2007.
23. Goodman C, Mukherjoo D, Faulkner E. How effective would antiviral vaccinations and antiviral drug prevention and treatment strategies be for reducing the impact of the next influenza pandemic? *Available at: www.euro.who.int/Document/E88034.pdf.* Accessed June 4, 2007.
24. WHO reports on avian-influenza vaccines-- some promising results. *J Environ Health.* 2007;69:84.

25. American Medical Association. AMA on pandemic flu-new national strategy and individual stockpiling. *Available at: www.ama-assn.org/ama/pub/category/15701.html.* Accessed: June 14, 2007.
26. Pandemic flu planning checklist for individuals and groups. *Available at: www.pandemicflu.gov/plan/individual/checklist.html.* Accessed June 14, 2007.
27. Hunter A, Deniman-Vitale S, Gerzon L, Alfen PJ, Schumann L. Global infections: recognition, management and prevention. *Nurse Pract.* 2007;32(2):34-41.

Julie Watson Brown, RN, FNP-C, ND, teaches primary care and epidemiology at the Fay W. Whitney School of Nursing, University of Wyoming, in Laramie, WY. She has experience as a public health nurse and a family nurse practitioner. She is a PhD student in epidemiology at the College of Preventive Medicine at the University of Colorado and Health Sciences Center. She can be reached at Julie@uwyo.edu. *In conjunction with national ethical standards, these authors report no relationships with business or industry that represent a conflict of interest.*

1555-4155/07/$ see front matter

doi:10.1016/j.nurpra.2007.07.018

The Journal for Nurse Practitioners Continuing Education Credit Application

Please Print Clearly

Title: **Concern Over Avian Flu** # Contact Hours: **1.0** CE Code **TJNP1007** Valid until: **October 2009**

Name: _____ Address for mailing certificate: _____

Phone Number: _____ Email: _____

To receive CE Credits, read the article, answer each question, and mail this whole page, along with your processing fee check for $10 made out to Elsevier, PO Box 540, Ellicott City, MD 21041-0540. CE is provided without charge to registrants at *www.npjournal.org* and to ACNP members at *ACNPWeb.net.*

Circle the best answer for each question. Required minimum passing score is 70%.

1. **The H5N1 strain of the influenza A virus is the latest strain of highly pathogenic avian flu. Many strains of influenza A infect wild birds, and H5N1 is also known to infect:**
   a. Mosquito populations around the world
   b. Domestic bird populations in some areas
   c. Domestic cattle in the Western Hemisphere
   d. Humans in North America

2. **Avian influenza is thought to survive on surfaces for long periods (up to 35 days) in certain environmental conditions. These include:**
   a. Spring weather: 21°C (69.8°F)
   b. Summer weather: 37°C (98.6°F)
   c. Fall weather: 10°C (50°F)
   d. Winter weather: about 4°C (39.4°F)

3. **Migrating birds have spread H5N1 from Hong Kong, China, to parts of Africa and across the continent of Eurasia, as far west as:**
   a. The United Kingdom
   b. Thailand
   c. Turkey
   d. France

4. **H5N1 can infect only a small subset of human beings who carry a certain receptor at the site of primary infection. The site of primary infection is:**
   a. Dermis
   b. Epidermis
   c. Lower airway
   d. Upper airway

5. **Screening for infection includes assessment of risk factors for exposure to H5N1. Therefore, a thorough history should include inquiry about:**
   a. Travel to endemic areas
   b. Ingestion of properly cooked poultry
   c. A family or household member with seasonal influenza A
   d. The practice of unprotected sex during travel abroad

6. **Symptoms that distinguish H5N1 from seasonal influenza include:**
   a. Rapidly progressing lower respiratory symptoms early in the illness
   b. Absence of fever
   c. Centripetal petechial rash that fades in 24 hours
   d. Injected conjunctiva

7. **A vaccine against H5N1 is included in the US National Vaccine Stockpile for use in an outbreak but is not available to the public. Why might this the case?**
   a. The vaccine has been tested only in animal studies.
   b. Intolerable side effects exist with proper dosing, even in healthy adults.
   c. The two-dose series confers little to no protection in 90% of subjects tested.
   d. Safety in immunocompromised or elderly patients and children has not been shown.

EVALUATION OF CE ACTIVITY

1. Listed below are the educational activity objectives. Please rate the extent to which you are now able to meet each of the objectives (with 1 as the lowest ranking; 5 as the highest ranking):

		Low				High
a.	Describe circumstances that could lead to an H5N1 outbreak in human beings	1	2	3	4	5
b.	Summarize current recommendations for prevention and testing of H5N1 infection	1	2	3	4	5
c.	Describe appropriate treatment for H5N1	1	2	3	4	5
2.	The objectives clearly relate to the purpose/goals of the activity.	1	2	3	4	5
3.	The teaching method was appropriate and effective for the content presented.	1	2	3	4	5
4.	The information presented was accurate, current, and at an appropriate level.	1	2	3	4	5
5.	This activity met my personal professional expectations.	1	2	3	4	5
6.	This content was relevant to my practice as a nurse.	1	2	3	4	5
7.	Overall, I would rate this activity.	1	2	3	4	5

8. Minutes required to read the article and complete the questions _____

COMMENTS:

This 1.0 contact hour educational activity is provided by Nurse Practitioner Alternatives, Inc.
NPAI is an approved provider of continuing nursing education by the Maryland Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation.
This credit is calculated on a 60-minute hour. For questions, contact *info@npedu.com*.