Avian Influenza: Critical Considerations for the Primary Care Physician
Robin B. McFee, DO, MPH, FACPM, Larry M. Bush, MD, FACP, and Kevin M. Boehm, DO, MSc

ABSTRACT

PURPOSE: To provide an overview of avian influenza H5N1 and present current management guidelines.

EPIDEMIOLOGY: In 1997, several individuals became infected with an emerging strain of avian influenza H5N1 associated with diseased chickens, resulting in the destruction of Hong Kong poultry flocks. Since 2003, avian influenza A H5N1 has moved from Southeast Asia into Europe, killing more than 150 million birds and more than 50% of the more than 200 persons infected.

REVIEW SUMMARY: Seasonal influenza results in 36,000 deaths in the United States annually. An influenza pandemic occurs when a new influenza virus emerges for which people have little or no immunity, the virus spreads readily from person to person, and no vaccine is available. Experts consider H5N1 a potential pandemic virus. Vaccine based upon Vietnamese H5N1 is not widely available. Two classes of antiviral medications treat seasonal influenza; H5N1 developed resistance to M blockers, and resistance may be increasing against neuraminidase inhibitors, which remain the only widely available countermeasures.

TYPE OF AVAILABLE EVIDENCE: National and international guidelines, expert reviews, and retrospective studies. Some prospective animal studies.

GRADE OF AVAILABLE EVIDENCE: Fair

CONCLUSION: Avian influenza H5N1 is a highly virulent strain of influenza; if it mutates into a virus capable of person-to-person transmission, a pandemic will likely ensue. Containment depends upon early diagnosis and treatment, with rapid implementation of infection control.


In 1997, several individuals became infected with an emerging strain of avian influenza, H5N1, which was associated with diseased chickens, resulting in the almost total destruction of Hong Kong poultry flocks.1-2 Intentional culling allowed the attenuation of the infection.1-3 Since 2003, highly pathogenic avian influenza (HPAI) A H5N1 has re-emerged, starting in Southeast Asia, spreading through Eurasia and into Europe,4-6,9-17 leaving more than 140 million dead birds and killing more than 50% of the more than 244 persons infected as of September 2006 (Table 1).6,14,15 Scientists believe the influenza virus causing the pandemic of 1918 began as an avian influenza strain.18-20 Unlike usual patterns of fatality associated with seasonal influenza—specifically, occurring among the very young and elderly—the 1918 pandemic and the current situation with H5N1 both involve all age groups.

INFLUENZA VIRUSES

“Influenza” describes an acute viral disease of the respiratory tract often caused by viruses...
belonging to the orthomyxovirus family, which includes the genera of influenza virus A, B, and C as defined by the antigenicity of the nucleocapsid and matrix proteins. Generally, A viruses are associated with more severe human illness, epidemics, and pandemics. Influenza A virus is a negative sense, single-stranded RNA virus with an 8-segment genome that encodes for 10 proteins, and is further subtyped by 2 surface proteins: hemagglutinin (H), which attaches the viral particle to the host cell for cell entry, and neuraminidase (N), which facilitates the spread of progeny virus. It is the latter that is a target for the class of antiviral therapy referred to as neuraminidase inhibitors. There are 16 H and 9 N subtypes making up all the subtypes of influenza A by various combinations. It appears to be stable in the environment for up to 6 days. Antigenic drift refers to the various mutations and changes in surface antigenicity of these surface proteins as a response to host immunity. Antigenic shift is an event that can lead to the creation of a novel virus against which humans have little or no immunity. Because influenza has a segmented genome, shuffling of gene segments can occur if 2 different subtypes of influenza A virus co-infect the same cell. Conditions favorable for the emergence of antigenic shift have long been thought to involve humans living in proximity to farm animals—namely poultry and pigs. Pigs are susceptible to infection with avian and mammalian virus. If a human influenza virus, such as H3N2, and an avian H5N1 virus co-infect a human or pig, a new virus H5N2 could emerge—a hybrid that could combine the high virulence of H5N1 with the efficiency of human-to-human transmission found in the “parent” human virus.

Studies suggest this reassortment of genetic material is what happened in the 1957 and 1968 pandemics. This reassortment could also be accomplished in a laboratory for bioterrorism.

### Avian Influenza Epidemiology

Avian influenza is primarily an infectious disease of birds occurring worldwide. Although avian influenza has cause more than 100 deaths, seasonal influenza has caused significant illness for centuries, and remains a global public health problem resulting in millions of cases of severe illness, in addition to approximately 500,000 deaths worldwide, 36,000 deaths in the United States, and more than 200,000 hospitalizations in the United States annually.

Despite the efforts of the international health community to contain the avian influenza epidemic that emerged in Southeast Asia in 2003/2004, sporadic
cases of human influenza A H5N1 infection are still reported and carry a high case-fatality rate (Table 1).1,7,8,14,15,55

Currently, H5N1 affects domesticated poultry (e.g., chickens, ducks, and turkeys) and migratory birds (e.g., wild ducks, geese, and swans); it is the latter that do not honor borders, are not readily contained or culled, and that may enhance the global spread. Of note, the more ordinary strains of avian influenza usually infect migratory birds and do not result in disease; the H5N1 is killing these animals, suggesting the virus has adapted and, with that, increased its virulence and capacity to harm or kill. Avian influenza infects birds via the intestinal tract, which is why it is found in feces. The commonness of bird feces on the ground promotes contamination to people, other animals, and poses a risk to water.

Avian influenza infects people via the respiratory tract, which can occur through fomites, inhalation, or hand contact to the mucosa. Fortunately, people cannot contract avian influenza from eating properly cooked poultry. Eating raw eggs, poultry blood, or undercooked bird meat are ways in which persons can become infected and are practices in countries where human avian influenza cases have been recorded.

Three factors must be present for the emergence of a new influenza virus to result in an influenza pandemic: (1) people have little or no immunity for the virus; (2) the virus spreads readily from person to person; and (3) no vaccine is readily available.3,6,14-17 Although data suggest there have been a few cases resulting from human-to-human transmission, the infection stopped at the second person in those cases, usually involving a family member.1,2,15,35-51 If avian influenza mutates into a more humanlike influenza (i.e., capable of efficient human-to-human transmission), it is likely to spread rapidly in a sustained fashion across the globe, and result in thousands, perhaps millions, of deaths, similar to the influenza pandemic of 1918 that resulted in 20 to 50 million deaths worldwide.1,4,16,17,25,26,35

Experts agree the most likely mechanisms that H5N1 influenza can arrive in the United States will be from human travel, migratory birds, the poultry trade, or a combination of these factors. Illegal importation of sick animals is also a consideration; recall the monkeypox patient in 2003 from an illegally imported West African rodent.3,5,6,38-41

Whereas much effort has been focused on hospital, public health, and government responses to an influenza pandemic, the private physician remains somewhat disenfranchised.4,6,29,42-44 Yet, it is likely a community clinician may diagnose the sentinel case of avian influenza in the United States, reminiscent of the diagnosis of the index case of inhalation anthrax in 2001.1,45 Most scenarios describe a significant number of people becoming quite ill over a relatively short period of time. It is important to realize that a sick individual may precede such an outbreak, underscoring the value of early recognition or suspicion of emerging pathogens, given rapid diagnosis can save lives and alert the medical community of a developing threat.26,45-46

Pathogenesis of Avian Influenza

H5N1, like the 1918 pandemic flu strain, has the ability to kill directly. Seasonal influenza destroys the cells that line the upper respiratory tract, facilitating development of bacterial pneumonia, especially in immune-compromised patients. Avian and Spanish flu, on the other hand, attack within the lung and initiate a severe immune response, causing tissue necrosis and hemorrhage. H5N1 induces proinflammatory cytokines, such as interferon γ-inducible protein and tumor necrosis factor α in human macrophage cells, which may lead to a cytokine storm and death without extrapulmonary viral dissemination.3,49-54 The hemagglutinin of H5N1 may also attach to respiratory epithelial cells, causing inhibition of epithelial sodium channels, leading to pulmonary edema, alveolar flooding, and early acute respiratory failure—events that rarely accompany seasonal influenza.3,52-54

Clinical Presentation

The severity of H5N1 is reflected by the early presenting symptoms that are similar to acute community-acquired pneumonia: rapid onset of high, persistent fever; impaired consciousness; respiratory distress; and/or multiorgan dysfunction. The fever spike is 101°F or greater. An almost universal symptom is difficulty breathing.3,4,5,9 Avian influenza illness is not subtle; it will not present like the common cold or the average case of seasonal influenza. Analysis of human H5N1 infections in Hong Kong, Vietnam, Thailand, and Cambodia revealed that fever and cough were the most common initial symptoms.3,55-60 Almost all patients had clinically apparent pneumonia. In some cases, gastrointestinal symptoms (e.g., vomiting, diarrhea, and abdominal pain), pleuritic pain, and bleeding from the nose and gums have also been observed early in the course of illness. In those who present for medical attention, the illness is rapidly progressive, with patients often complaining of chest pain and dyspnea, which is rarely associated with seasonal influenza, especially in young, otherwise healthy patients (Table 2). Under most circumstances, dyspnea is worrisome and should be properly evaluated, but in the context of a rapid rising fever, it should sound an alarm for avian influenza or other serious infection.3,11-15 Avian influenza can have an extrapulmonary impact, including the central nervous system, causing seizures or encephalitis. Although gastrointestinal symptoms may be more
common among children with seasonal influenza, young adults and other age groups may experience abdominal pain, nausea, vomiting, or diarrhea before or during the development of respiratory symptoms resulting from H5N1—again, symptoms not common with seasonal influenza in this age group. Unlike seasonal influenza deaths, which often result from secondary infections such as bacterial pneumonia, avian influenza seems to have some direct pulmonary effects that can cause noncardiogenic pulmonary edema and viral pneumonia.

**DIAGNOSTIC CONSIDERATIONS**

**HISTORY**

Diagnosing a potential case of avian influenza is based upon clinical findings. Of paramount importance is a thorough history, including symptoms, patient travel within 14 days (especially to countries suspected of having H5N1 disease), and occupation. Laboratory testing may be helpful to confirm H5N1 but should not delay initiation of infection control or other critical interventions.

**CLINICAL TESTING**

If H5N1 is suspected based upon symptoms, travel, and exposure history, the healthcare provider should collect respiratory samples, such as a nasopharyngeal swab or aspirate. Healthcare providers should also alert the local health department, which should be able to provide the most current information on sample collection, packaging, and transportation. In addition, the local health department should have access to the state laboratory or Laboratory Response Network (LRN), a federally sponsored initiative to provide advanced testing capabilities throughout the United States. If a local health official is not accessible, contact the Center for Disease Control and Prevention (CDC) Director’s Emergency Operation Center at (770) 488-7100.

Major findings on chest radiograph include extensive infiltration bilaterally, lobar collapse, focal consolidation, and less commonly interstitial lung infiltrates. Clinical deterioration associated with these findings is common.

In comparison to the 1997 Hong Kong avian influenza cases, several patients in the past year have demonstrated lower total peripheral white blood cell counts, which are more often lymphopenic and associated with fatality. Many patients presenting with pneumonia associated with H5N1 had abnormal liver function tests, gastrointestinal symptoms, and more than 30% had impaired renal function.

Based upon the 1997 experiences, Real Time Polymerase Chain Reaction (RT-PCR) has superior sensitivity and specificity compared with antigen detection. Commercial immunochromatographic membrane enzyme immunoassay tests are not specific for H5 and only have 70% specificity compared to viral culture. Nasopharyngeal aspirate or bronchial alveolar lavage followed by nasopharyngeal or throat swab placed in viral transport medium (VTM) should be collected with airborne precautions in patients suspected of having avian influenza. A stool or rectal swab also placed in VTM should be considered. If you suspect H5N1, alert the laboratory to take proper precautions.

On February 3, 2006, the US Food and Drug Administration announced the approval of a new laboratory test to diagnose patients suspected of being infected with avian influenza A/H5 viruses. The test is referred to as Influenza A/H5 (Asian Lineage) Virus Real-Time RT-PCR Primer and Probe Set. This test can provide preliminary results on suspected H5 influenza samples within 4 hours once sample testing begins at the laboratory. This is a major advance, given previous technology required 2 to 3 days for similar results. If the H5 strain is identified, further testing is conducted to determine the specific subtype, such as N1. The test will be distributed nationwide to LRN-designated laboratories to enhance surveillance and...
diagnostic capabilities. There are approximately 140 LRN laboratories throughout the United States. The CDC recommends if a clinician suspects that a patient may be infected with avian influenza, it is important to contact the local or state health department for assistance in accessing the LRN capabilities.13

**Transmission of Influenza Virus**

To date, the most important route of acquisition for H5N1 infection is through contact with infected birds or their excreta. However, hospital-acquired infection was also demonstrated in a retrospective study. Healthcare workers exposed to patients with H5N1 infection were more likely to be seropositive and this was not attributable to animal exposure.5,4,9,25,35,56,61-63 It is reasonable to assume that the route of infection for patients with avian influenza, like most patients with influenza, can be from inhalation of infective respiratory secretions and/or contact with virus-laden secretions and subsequent transference contact with mucous membranes.17,54,61 Studies suggest airborne transmission of influenza is possible, which would explain the sometimes numerically explosive nature of influenza epidemics.54,56,61,62 Although the true epidemiology is unknown, it is possible there is asymptomatic or mildly symptomatic infection by H5N1; perhaps patients presenting for care are representative of the most severely infected. The actual transmission rate per person is unknown; the basic reproductive number for influenza (the number of secondary cases produced by 1 primary case) varies from 1.68 to 20. Viral shedding starts within 24 hours before the onset of symptoms and peaks within 48 hours afterward.32,45,52,55 Therefore, the CDC recommends treating potential H5N1 patients as a contagion risk: respiratory/airborne, droplet, contact, and standard precautions should be instituted as infection-control practices for healthcare workers and healthcare facilities.15,16,31,43,55,57,61 Although H5N1 is inefficient at person-to-person transmission, it is likely to acquire this capability in the advent of a pandemic.56,7 Although not studied fully in all populations, the period of communicability of H5N1 can last for up to 3 weeks in children.

**Treatment Options**

**Current Antivirals**

There are 2 classes of antivirals available to treat influenza virus: the neuraminidase inhibitors oseltamivir (Tamiflu; Roche, Nutley, NJ) and zanamivir (Relenza; GlaxoSmithKline, Research Triangle Park, NC); and the M blockers amantadine (Symmetrel; Endo Pharmaceuticals, Chadds Ford, Pa) and rimantadine (Flumadine; Forest Pharmaceuticals, St. Louis, Mo), the former approved for influenza A and B viruses.3,4,6,22 Each is designed to take advantage of the influenza viral structure. Both classes can treat influenza viruses. However, the present circulating H5N1 genotype “Z” confers a residue on the M2 protein, making avian influenza intrinsically resistant to the M blockers.7 The neuraminidase inhibitors remain effective against seasonal and avian influenza but should be administered early—ideally within 48 hours of illness onset.4,6

When oseltamivir is administered for seasonal influenza, it is usually given at a dosage of 75 mg by mouth twice daily for 5 days. A higher dose, 150 mg given orally twice daily, has been recommended in clinical trials and associated with a larger reduction in viral load and shorter duration of illness. Whether a higher dose given over a longer duration would confer benefit in avian influenza remains to be further evaluated but should be considered in patients with significant pulmonary and gastrointestinal symptoms. Children older than 1 year of age can receive twice-daily oral dosing based upon weight: 30 mg per dose if 15 kg or less, 45 mg if 15 to 23 kg, 60 mg for 23 to 40 kg, and 75 mg for those over 40 kg. Resistance to oseltamivir is emerging.6,64

Oseltamivir can be used as a prophylactic chemotherapy for persons exposed to avian influenza. The World Health Organization (WHO) recommends healthcare workers exposed to H5N1 receive 75 mg orally once a day for at least 7 days.4 Vaccination against seasonal influenza is recommended if the healthcare worker has not been immunized.65,66

Zanamivir is an inhaled neuraminidase inhibitor, and has little systemic absorption; it may not be useful if extrapulmonary disease occurs. Data are lacking in terms of the effectiveness of zanamivir against H5N1 for acute treatment or as chemoprophylaxis, although experts consider it of value given the class effect of neuraminidase inhibitors.

**Newer Treatments**

Studies are under way evaluating a new neuraminidase inhibitor, peramivir. When compared to other neuraminidase inhibitors, it showed promise against influenza.13 Other drugs being investigated to treat seasonal and H5N1 include long-acting neuraminidase inhibitors, the antiviral ribavirin, and interferon alpha.22,24,53,66-68

**Other Treatments**

It is important to avoid aspirin-containing products as a precaution against Reye’s syndrome, especially in patients younger than 16 years of age and rarely in adults.3,28,67 In addition to early administration of antiviral therapy, respiratory support and intensive care are critical during the acute stage of H5N1 pneumonic illness. The physician should also be aware of alternative and unproven methods that claim to prevent or cure
avian influenza, including herbal remedies containing natural "antiviral" properties. Most of these products are untested and likely create a false sense of security, in addition to posing a risk for adverse effects.

VACCINATION STRATEGIES

Vaccination remains one of the most effective ways to reduce the spread of infections. If met, the goals of the initiative Healthy People 2010 to improve influenza vaccination rates among institutionalized elderly, high-risk persons, and the general public, would significantly reduce the current mortality in addition to the enormous burden faced by patients and the healthcare system.63-65

Nationwide influenza immunization rates are disappointing, especially among children and healthcare workers.28-31,43 National Health Interview Survey data show only 36% of healthcare workers are immunized against influenza each year.54 Medical literature suggests unimmunized healthcare workers are a serious problem and can be a potential cause of influenza outbreaks in a variety of healthcare settings. Primary care physicians must lead by example. Immunization of healthcare workers not only reduces the risk of outbreaks but has also shown to reduce morbidity and mortality among geriatric patients in long-term facilities. Stock annual influenza vaccines and encourage staff, colleagues, and patients to obtain the influenza shot or inhaled vaccine.

Even during years when the concordance between the influenza vaccine and circulating virus is not high, there remains significant value to receiving it; promoting vaccines is an essential stay-healthy practice that all healthcare providers should partake in and encourage. Seasonal influenza vaccines can be provided to persons over the age of 6 months old. Occupations that place individuals among crowds, such as fire rescue, law enforcement, healthcare, care giving (especially those assisting the elderly or patients with chronic illnesses), and emergency medical services, should be particularly encouraged to obtain annual vaccinations. Although the seasonal vaccine will not confer direct protection against H5N1, reducing influenza prevalence may decrease the likelihood of both viruses intermixing if an individual is exposed to seasonal and avian influenza.64,65 This may decrease the chance of viral genetic assortment and the emergence of new avian influenza capable of human-to-human transmission.67

There are currently 2 forms of seasonal influenza vaccines: the flu shot, which contains killed virus; and the nasal spray Live Attenuated Influenza Vaccine, which is made with live but

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<th>Table 3. Guidelines for Infection Prevention and Control in the Physician’s Office, 2004</th>
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<tr>
<td><strong>Routine Infection Control Practices</strong></td>
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<td>Routine infection control practices are to be used with all</td>
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<td>patients, at all times, regardless of presumed infectious status or diagnosis. Routine Infection Control Practices include:</td>
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<tr>
<td>• The separation of infected, contagious patients, including those with respiratory symptoms from uninfected patients.</td>
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<tr>
<td>• Hand cleaning should occur before and after every patient contact. Wash hands with soap and warm water for 15 to 30 seconds. Waterless (alcohol-based) hand antiseptics are also effective. Soap and water should be used if hands are visibly soiled.</td>
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<tr>
<td>• Gloves should be used as an additional measure, not as a substitute for hand washing.</td>
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<td>• Personal protective equipment, such as gowns, masks, and eye protection, should be worn during patient care activities likely to generate splashes or sprays of blood, body fluids, secretions, or excretions.</td>
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<td>• Mouthpieces and resuscitation bags should be available for performing cardiopulmonary resuscitation.</td>
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<td>• Safe handling and disposal of needles and other sharp devices.</td>
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<tr>
<td>• Appropriate sterilization and disinfection of reusable equipment and office surfaces (eg, counters and furniture) must be routine.8</td>
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<td><strong>Preventing Transmission</strong></td>
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<td>Preventing the transmission of infectious diseases spread by airborne or droplet routes poses a significant challenge in the outpatient setting. Special arrangements for patients with a suspected respiratory infection can reduce this risk. These include:</td>
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<td>• Screening patients at the time the office visit is scheduled.</td>
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<td>• Making efforts to see these patients at the end of the day.</td>
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<td>• Quickly triaging these patients out of common waiting areas.</td>
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<tr>
<td>• Closing the door of the examining room and limiting access to the patient by visitors and staff members who are not immune to the suspected disease.</td>
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<td>Preventing the transmission of infectious diseases spread by direct contact, such as antibiotic-resistant organisms (eg, MRSA and VRE), requires special attention to decrease the likelihood of spread. Patients may harbor resistant bacteria as part of their respiratory or gastrointestinal tract flora for an extended period. Precautions include:</td>
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<td>• Disinfecting surfaces and equipment that have been in direct contact with the patients immediately after a visit.</td>
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<td>• Patients known to be carriers of these organisms should have this indicated in their medical record to facilitate recognition on subsequent visits.</td>
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* Outpatient settings include, but are not limited to, ambulatory care clinics, physicians’ offices, walk-in clinics, and community health centers. MRSA = methicillin-resistant Staphylococcus aureus; VRE = vancomycin-resistant enterococci.


Bruce Gamage, BSN, BSc, RN, CIC, Infection Control Consultant, British Columbia Centre for Disease Control, Laboratory Services.

Trevor Cornell, BA, MD, MHSc, CCP, FRCPC, Clinical Associate Professor, Department of Health Care and Epidemiology, Department of Family Practice, University of British Columbia Faculty of Medicine.
Avian influenza

Weakened viruses. It is important for patients to have realistic expectations of vaccine response; it takes approximately 2 weeks after receiving influenza vaccine to produce sufficient antibodies to adequately protect against the flu, although some protection may develop earlier.

Although H5N1 vaccines are not available to the public, several are under clinical investigation worldwide. The US government is conducting clinical tests on a vaccine based upon the Vietnamese strain. Early data suggest the vaccine is safe for human use and is effective against the strain it was based upon.

Potential Magnitude of a Pandemic

Estimates vary, but an influenza pandemic could sicken upwards of 90 million people in the United States, including over one third of the healthcare workforce. Federal officials are concerned that 10 million influenza patients could require hospitalization for at least 1 night, including almost 1.5 million requiring intensive care and a possible 750,000 needing ventilator assistance.

Preparing Our Offices and Practices

Physicians and healthcare facilities should remain vigilant for severe respiratory illnesses. Severe acute respiratory syndrome (SARS) may reappear in addition to avian influenza, or other emerging threats.

Clearly, early diagnosis and rapid implementation of chemotherapy is a mainstay of containment.

The WHO established a set of guidelines for physicians for infection prevention and control (Table 3). These containment strategies rest largely upon early diagnosis, with efforts to reduce transmission to healthcare workers and other patients. They also depend upon clinicians maintaining a high index of suspicion, identifying patients who have traveled to affected areas, alerting the proper authorities, and initiating appropriate treatments, including antiviral medications, in a timely manner. The WHO also put forth 5 essential action strategies to reduce the risk of a pandemic (Table 4).

One study showed that unnecessary visits of the “worried well” could be prevented by offering patients information about effective interventions, including self-care. This information could be a 1-page brochure downloaded from the CDC Web site about avian influenza, obtaining flu shots, and respiratory hygiene tips.

It is important to ask patients if they are concerned about avian influenza. This is an opportunity to offer the influenza vaccine, in addition to teaching about the critical differences in symptoms associated with influenza, avian influenza, other severe respiratory infections, and the common cold (Table 2). Preventive strategies, including respiratory hygiene to ward off infection, should be discussed and implemented early. Given the high case-fatality rate of avian influenza and pneumonia in high-risk patients, a combination of contact, droplet, and airborne precautions are recommended. Whenever possible, separate well from sick patients in the waiting room.

Intake staff should use reception prompts that identify potentially contagious patients and place them into an examination room rapidly to cut down on waiting room times. Sanitizing gels, tissues, and disposable masks in addition to appropriate information about influenza and other timely materials should be available in the waiting room. Although there is limited prospective research evaluating the practice of separating well from sick patients, emerging studies in aerobiology suggest that there is merit to the preventive measures practiced during the 1960s and 1970s, whereupon pediatricians encouraged parents to bring sick children with rashes and high fevers to the back door and directly to an examination room instead of the general waiting room.

Instances of measles transmission—not from direct contact but by the persistent virus left behind from an infected child—have been well documented.

Study data reveal that patients would be willing to wear a mask in a healthcare facility waiting area if one was offered to them. Those studies also reveal that, although masks would reduce the risk they posed to others, few patients were offered such preventive mea-

Table 4. World Health Organization

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<th>I. Reduce human exposure</th>
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<td>A. Advise patients about travel precautions to countries with endemic illness</td>
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<td>B. Promote respiratory hygiene or other contagion-reduction practices in the office/waiting rooms</td>
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<tr>
<td>C. Maintain an index of suspicion with patients presenting with symptoms consistent with unusual illness</td>
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<th>II. Intensify capacity for rapid containment</th>
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<td>A. Early diagnosis</td>
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<td>B. Rapid initiation of appropriate antiviral therapy</td>
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<td>C. Maintain an index of suspicion with patients presenting with symptoms consistent with unusual illness</td>
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<th>III. Strengthen early warning systems</th>
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<td>A. On a government level</td>
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<td>B. On a patient care/community level</td>
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<th>IV. Improvement in communications and capacity</th>
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<td>A. On a government level</td>
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<td>B. On a patient care/community level</td>
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<th>V. Building general capacity for health</th>
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<tr>
<td>A. This may depend upon diagnosing a community index case</td>
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Gloves should always be readily available. Otherwise, after glove removal, and use of restrooms, fluids, dirty materials, between procedures (invasive or otherwise), hands should be washed before and after contact with patients, body fluids, materials, between procedures (invasive or otherwise), after glove removal, and use of restrooms. Gloves should always be readily available.

**Travel Recommendations**

Patients planning to travel overseas for work, recreation, or humanitarian outreach should be able to do so relatively safely if precautions are taken. Encourage patients to allow as much advance preparation time as possible. Vaccines against diseases endemic to the new host region may need weeks to evoke an immune response. Special precautions should be taken when visiting countries where H5N1 infections are reported in birds, other animals, or people. This includes avoiding crowded places, farms, and marketplaces that have poultry and/or kill chickens on demand, and changing clothes if visiting any of the aforementioned.

Frequent hand washing and respiratory hygiene should be stressed. A referral to a travel medicine clinic or physician who specializes in travel medicine may be appropriate. The United States Department of State provides important information about nearly all countries, with timely alerts on emerging threats, political instability, or other risks for US citizens. Every 2 years, the CDC publishes Health Information for International Travel, also called “The Yellow Book,” which is a valuable travel health resource. Additionally, recommendations about vaccines appropriate to foreign destinations can be obtained through the CDC.

Although the incidence of imported infectious disease presenting to healthcare facilities is not well defined, it is well known that numerous patients present to medical facilities upon return from traveling with a variety of complaints, including respiratory infections. Studies suggest clinicians do a poor job of obtaining a travel history, including a general lack of awareness by physicians concerning the potential for nonendemic disease in the population that they attend. One study that evaluated whether a travel history was recorded in patients indicates that it was recorded in only 2% of patients presenting to this emergency department (ED), although 5.3% actually had the potential for a travel-related illness among the total number of patients presenting to the ED. Thus, there remains the risk that imported diseases such as avian influenza may be undiagnosed in the acute setting, lead to possible spread before containment can be implemented, and delay treatment.

**Discussion**

Chronic diseases such as coronary disease and diabetes have replaced acute infections as the leading cause of mortality in persons older than 65 years in the United States, with outbreaks of contagious infectious diseases remaining uncommon. With such rarity comes concern and a lack of knowledge about illnesses that have not caused widespread sickness in the United States since the early 20th century but persist in other parts of the world.

The dramatic changes in the top-leading causes of death from infection related to chronic disease could give the false sense of victory that we have conquered pathogens in the United States. However, we remain vulnerable because many nations still endure poverty, overcrowding, and unsanitary conditions that include sleeping near livestock such as poultry or swine, lack of immunizations, or antivirals. “Victory” is better exchanged for the term “stalemate” with infections—possible only as long as we practice the sound infection control practices that led to the changes in mortality from 1900 to 2000. Inattention to these practices may account for the death rate from infectious diseases rising 58% between 1980 and 1992 (making them in the aggregate the third leading cause of death in the United States). Influenza and pneumonia remain responsible for 5.5% of the deaths of people 65 years old and older (95 640 in 1997), with an increase in infection-related deaths among older persons from 1980 to 1992. Additionally, the combined death rate from influenza and pneumonia for all age-race-sex groups has increased.

Evidence suggests hand hygiene can reduce healthcare-associated infection rates, whether using soap and water or other waterless interventions such as alcohol-based hand rubs. Failure to perform appropriate hand hygiene is a leading cause of healthcare-associated infections, the spread of multidrug-resistant organisms, and contributes to outbreaks. Approximately 1 in 20 patients contracts an infection in hospitals across the United States. Approximately 2 million patients acquire nosocomial infections each year in US hospitals; therefore, the war against infectious diseases is clearly not over.

Overcrowded waiting rooms, in addition to healthcare facilities lacking surge capacity and filled to the point of overflowing, provide less time for proper sanitation. Healthcare workers not adhering to good hygiene practices contributes to the rising infection problem. Overcrowding in the absence of an epidemic only portends a system-wide failure in the presence of a highly transmissible virus. Recent ED closures in the face of increased patient volume and lack of affordable resources for uninsured persons contribute to diversions and overcrowding. Lack of hospital beds exacerbates the problem. Because influenza occurs seasonally and predictably, exerting profound effects on the population,
causing over 36,000 deaths annually and 200,000 hospitalizations, widespread influenza activity in a region can severely strain already overburdened healthcare facilities. Physicians and healthcare facilities must prepare now and identify solutions in anticipation of an epidemic—H5N1, SARS, or another emerging pathogen.

CONCLUSIONS

Although no cases of human avian influenza are reported in the United States, being alert for this or other emerging threats is good medical practice and may facilitate early intervention of other potentially dangerous illnesses imported through immigrants, visitors, or travelers. Concern about H5N1 provides opportunities to discuss with patients good respiratory hygiene practices and influenza vaccinations.

If and, perhaps more reasonably, when the first human cases of avian influenza arrive in the United States, the primary care physician may be in the position to identify the index case, initiate proper antiviral treatment, and alert authorities, setting off a cascade of events, including public health containment strategies.

The healthcare community is concerned with its ability to handle a pandemic. The high case-fatality rate of more than 50% in selected countries of avian influenza H5N1 is worrisome. The ability of H5N1 to rapidly overcome species barriers, sicken birds normally not overcome by avian influenza viruses, and travel West quickly, coupled with the propensity of influenza viruses to undergo genetic reassortment, adapt, and mutate, argue for this strain to be a likely candidate for the next human pandemic.

Rapid diagnosis and early treatment are critical to containment and preventing an outbreak from becoming an epidemic of global proportions. All treatments must be given early in the course of illness. Of 4 antivirals known to treat influenza virus A infection, only 2 at the present time are potentially useful as chemotherapy and chemoprophylaxis against H5N1: oseltamivir and zanamivir. Oselamivir has been approved for both indications, but resistance is emerging. Peramivir holds promise as a new neuraminidase inhibitor, but it is still in clinical trials. Avian flu vaccines may become available in the future.

Whether diagnosing the index case in the United States or called upon to perform in an epidemic, the primary care physician has an important role in local preparedness efforts.

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