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Avian Influenza: Are We Ready?

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With all of the advances in health care and medicine, it would seem that we would be prepared for a pandemic such as bird flu. However, in spite of the billion dollars the United States Congress has proposed for the flu budget, only part of the solution is being addressed [1]. The threat of an H5N1 influenza virus (avian flu) pandemic is substantial, and an effective response is contingent upon effective coordination among state and local public health authorities and individual health care providers [2]. It is imperative that health care workers take an active role in the plans to meet demands that will be placed on the health care system. This is accomplished by developing an understanding of the etiology and manifestations of the virus, and becoming familiar with recent advances in research that address the demands of a pandemic. Equally important are the ethical considerations our state of preparedness will pose on the health care system, the community, and health care workers, both professionally and personally.

Critical care nurses are in a pivotal role as it relates to planning for this potential pandemic. With projections of the impact, it is important to consider what would happen if 25% to 30% of the nurses, physicians, and support staff were too sick to come to work [3,4]. A study by the Congressional Budget Office estimates several consequences of a severe pandemic. The study indicates that 200 million people in the United States could be affected, with 90 million being critically ill and 2 million dying. It is estimated that a pandemic would decrease the gross national product by 5%, and the total approximate economic cost would be approximately 675 billion dollars [4]. As of August 23, 2006, the World Health Organization has reported 241 human cases of avian flu across 10 countries, with 141 deaths. This constitutes a 58% mortality rate for identified cases [5]. The missing link to a logical pandemic spread is the lack of human-to-human transmission whereby analysis shows near all cases have resulted from direct contact with poultry, although this is not exclusive [6]. With the low probability of human-to-human contact, complacency about the potential for a pandemic is not an option. Additionally, even if H5N1 proves to have a negligible impact, planning will raise awareness and improve preparedness for a future pandemic influenza strain or another public health disaster such as smallpox, anthrax, or severe acute respiratory syndrome (SARS) [6].

It is important to consider different aspects of a pandemic before it occurs so that there is a plan of action in place. As this plan develops and evolves, it is imperative critical care nurses contribute as informed health care. This can only occur when there is a deliberate effort to understand the virus, its implications, current research, and through considering the ethical issues this pandemic could pose.

Overview of the avian influenza

The avian influenza is an influenza virus that occurs naturally in many wild birds but does not...
usually make them sick and does not typically kill them. However, avian influenza is very contagious among birds and can cause illness in and/or kill some domesticated birds, including chickens, ducks, and turkeys. Infected birds transmit the virus in their saliva, nasal secretions, and feces.

In humans, influenza is transmitted by inhalation of infectious droplets or droplet nuclei, by direct contact, and possibly by indirect (fomite) contact, with self-inoculation to the upper respiratory tract, or mucosa of the conjunctiva [7–9]. For human influenza A(H5N1) infections, evidence to date is consistent with bird-to-human transmission, possible environment-to-human transmission, and most importantly, limited and nonsustained human-to-human transmission [9]. Because the virus has not mutated to facilitate efficient person-to-person contact since its discovery over 10 years ago, there are some who believe it will not mutate and will ultimately pose only a minimal threat. However, the H5N1 influenza virus could adapt and change as influenza viruses such as those that caused Asian influenza in 1958 and Hong Kong influenza in 1968 have done [6].

How avian influenza could become a human pandemic strain

Anatomically, each strain of influenza is named for the hemagglutinin (H) and the neuraminidase (N), which involves the subtypes. Currently, we know of 16 subtypes of hemagglutinin and 9 of neuraminidase for influenza A. Hence, the identification of strains is based on subtypes such as H5N1 [10].

There are two processes by which the current strain of avian influenza could become a human pandemic strain. Mutation is a process of evolution whereby the virus may alter its genes and antigenicity and acquire new surface antigens. These new antigens may allow the newly formed virus to bypass the human immune response. Reassortment is a synergistic process in which human flu virus and avian flu virus infect the same host simultaneously. The genes from the two strains interchange resulting in a new strain composed of genetic materials from the two original strains. The resulting virus—the new hybrid virus—possesses surface antigens that the human immune system may not recognize [10].

In addition, H5N1 avian influenza virus is not the only avian virus that has recently been found to infect humans. However, it is perceived as posing the greatest threat for a pandemic. Because the virus was only found in birds and a few other animals before 1997, the recent transmission, or “jump,” from bird to human represents cause for concern.

Human-to-human transmission

Human-to-human transmission of avian influenza has been suggested in several household clusters [11], and in one case probably through child-to-mother transmission [12]. In these cases, intimate contact without the use of precautions was implicated. No cases have been clearly identified as human-to-human transmission through small particle aerosols [9,10]. Some evidence suggests that the virus may be adapting to humans, but because of the small number of cases and the geographic distributions among them, more epidemiologic and virologic studies are needed for confirmation [9].

The concern about the avian influenza virus rests in its ability to mutate or re assort. Currently the virus is considered by the World Health Organization to be in phase three of six phases of alert for pandemic classification. It is not considered pandemic because of its current inefficiency in transmission from human to human. Once this transmission is efficient and sustained, we will be in the midst of a serious pandemic [4].

There is also current evidence to support the idea that human-to-human transmission of the virus is limited because H5N1 viruses replicate effectively only in the cells of the lower respiratory tract. The avian virus receptor is prevalent only in the lowest part of the human respiratory system. This impedes the transmission of the virus as opposed to viruses that flourish in the upper respiratory tract and are transmitted easily through coughing or sneezing [13].

Environment-to-human transmission

Because the avian influenza virus is virulent, as are most type A viruses, it can survive in the environment that may prove a mode of transmission. Ingestion of water where contaminated birds have been, or conjunctival inoculation from swimming in contaminated water, are also potential modes of transmission. Additionally, places where avian feces is used as agricultural fertilizer is another possible risk.
Clinical features of persons infected with avian influenza

The clinical picture of the patient infected with avian influenza is based on descriptions of hospitalized patients. Most cases have been previously healthy young children or adults [9]. It is estimated that the incubation period of this virus is longer than for other human influenzas. Varying cases indicate this incubation period can be from 2 to 5 days and up to 8 to 17 days.

Initial symptoms of H5N1 avian influenza infection include high fever (typically over 38°C/14°F) and influenza-like symptoms primarily affecting the lower respiratory tract. Lower respiratory tract symptoms are usually evident early and are often discerned at presentation. Respiratory changes, including dyspnea, crackles, and/or respiratory distress, are common. Radiologic findings have included diffuse or multifocal infiltrates consistent with pneumonia. Diarrhea, vomiting, abdominal pain, pleuritic pain, and bleeding from oral and nasal mucosa have been reported early in the course of symptoms for some patients [9]. Diarrhea is more watery than what is seen in persons affected by human viruses, and conjunctivitis with H5N1 avian influenza is rare (although it is sometimes seen in other forms of avian influenza). Sputum production is variable and sometimes bloody [9].

In Thailand, the median time from the onset of illness to the progression of acute respiratory distress syndrome was 6 days, with a range of 4 to 13 days [14]. Multiorgan dysfunction with signs of renal failure and sometimes cardiac compromise, including cardiac dilation and supraventricular tachyarrhythmias, have been common [11,14,15]. Other complications associated with H5N1 infections have been ventilator-associated pneumonia, pulmonary hemorrhage, pneumothorax, pancytopenia, sepsis syndrome without documented bacteremia, and Reye’s syndrome [9].

Management of the patient who has avian influenza

However, whereas the number of affected persons remains small and manageable, patients who have suspected or proven influenza A(H5N1) should be hospitalized [9]. In the hospital, patients can be isolated, monitored, and receive appropriate pharmacological therapy. Within 48 hours of admission to a hospital, most patients who have avian influenza A(H5N1) have required ventilatory support [11,14]. These patients have also required intensive care for multiorgan dysfunction and failure and in some cases hypotension. In addition, vigorous treatment with broad-spectrum antibiotics, antiviral agents, and, in some cases, corticosteroids have been used [9]. The efficacy of these warrants further study, late institution of the drugs has not had an appreciable effect on mortality rates. It seems early initiation of viral drugs produce the best outcomes [10,11,14].

Currently, two classes of drugs with antiviral properties against influenza viruses are available: inhibitors of the neuraminidase, an enzyme on the surface of the influenza virus; and inhibitors of the ion channel activity of membrane protein on the virus. The former include amantidine and rimantidine, and the latter include oseltamivir and zanamivir [16]. The therapeutic efficacy of amantadine is unclear in human influenza because of limited studies, but there have been reductions in fever and illness by one day seen in adults and children [17]. Currently, the optimal dose and duration of treatment with neuraminidase inhibitors are uncertain. Neurotoxicity and a rapid development of drug resistance are major disadvantages of amantadine, whereas rimantidine is less neurotoxic but is not available in most parts of the world [16].

Both zanamivir and oseltamivir have proven efficacy in the treatment of human influenza when started early during the course of the illness or as a postexposure prophylaxis [14]. Zanamivir is administered through inhalation because of its poor oral availability and has been used against various human influenza viruses, but has limited use in the elderly because it may cause bronchospasm. Oseltamivir can be given orally. Drug resistance has been identified as a potential development for both of these drugs because of the mutations of the hemaglutinin or neuraminidase in the virus [16]. It is important to reiterate that data are scarce on these medications in human cases of influenza H5N1 because most of the studies have been done on animal models.

Risks for health care workers

Caring for patients who have avian influenza poses a risk to health care workers. The obvious risk is exposure to the virus, that without vaccination, people are considered universally immunologically naive. Universal precautions with particular attention to droplet precautions are currently recommended for the care of
patients infected with human influenza. Because of the uncertainty as to which modes avian influenza may first transmit between humans, additional precautions for health care workers involved in the care of patients with documented or suspected avian influenza should be instituted [18]. Health care workers should also be alert to: “patients with a history of travel within 10 days to a country with avian influenza activity and are hospitalized with a severe febrile respiratory illness, or are otherwise under evaluation for avian influenza, should be managed using isolation precautions identical to those recommended for patients with known Severe Acute Respiratory Syndrome.” [18] Specific guidelines for precautions are outlined in Box 1.

Those providing care for patients who have avian influenza should monitor their temperature twice daily and report any elevations over 38°C immediately for diagnostic testing. In addition, if health care providers feel unwell for any reason, they should not be involved in direct patient care until an alternate cause is identified. If an alternative cause is not identified, they should be treated immediately with oseltamivir on the assumption of influenza infection [9].

Combination guidelines from the World Health Organization, and Center for Disease Control and Prevention indicate that for persons who have had possible exposure to infectious aerosols, secretions, excretions, or other body fluids due to a lapse in aseptic technique, consideration for postexposure prophylaxis is appropriate with oseltamivir for 7 to 10 days at 75 mg once a day [9]. Health care workers involved in high-risk procedures should also be considered for pharmacologic prophylaxis [9,10]. However, as with new strains of bacteria, there is a risk of promoting the emergence of neuraminidase inhibitor-resistant viruses. As such, the indiscriminate use of these drugs should be discouraged [19].

In addition, current recommendations from the Center for Disease Control and Prevention indicate health care workers involved in the care of patients who have documented or suspected avian influenza should be vaccinated with the most recent seasonal human influenza vaccine. This not only provides protection against the predominant circulating influenza strain, but also will reduce the likelihood of a health care worker being co-infected with human and avian strains, whereby genetic rearrangement (reassortment) could take place, leading to the emergence of potential pandemic strain [18].

**Box 1. Precautions for health care workers engaged in the care of persons suspected to be infected with avian influenza (H1N5)**

**Standard precautions**
1. Engage in hand hygiene before and after all patient contact or contact with items potentially contaminated with respiratory secretions [18]

**Contact precautions**
2. Use gloves and gown for all direct patient contact
3. Use dedicated equipment such as stethoscopes, disposable blood pressure cuffs, disposable thermometers, and so forth [18]

**Eye protection (ie, goggles or face shields)**
4. Wear when within 3 feet of the patient [18]

**Airborne precautions**
5. Place the patient in an airborne isolation room. Such rooms should have monitored negative air pressure in relation to corridor, with 6 to 12 air changes per hour and exhaust air directly outside or have recirculated air filtered by a high-efficiency particulate air filter; if an airborne isolation room is unavailable, contact the health care facility engineer to assist or use portable high-efficiency particulate air filters to augment the number of ACH [18]
6. Use a fit-tested respirator, at least as protective as a National Institute of Occupational Safety and Health-approved N-95 filtering facepiece (ie, disposable respirator) when entering the room [18]

**Visitors**
7. Educate and limit number of visitors

Current status on vaccine for avian influenza

Although there is currently no commercially available vaccine to protect humans against H5N1 virus that is being seen in Asia and Europe, there are studies underway. An experimental vaccine
for avian influenza (H5N1) was produced from a seed of a virus isolated in Vietnam. Treanor and colleagues [20] studied an experimental vaccine in detail and conclude that it is possible to generate immunity with the “use of a purified, subviron vaccine administered in two relatively high doses.” The immunogenicity threshold for this study was set at an antibody titer of 1:40 or greater, which is typically thought of as seroprotective. Each of these two doses is six times the dose that is used in standard influenza immunizations. The experimental doses were found to induce immune responses in about half of the adults tested. The researchers suggest that there may be some dose-ranging approaches to enhance the efficacy of the vaccine. There have been several small studies that demonstrate the use of adjuvants such as aluminum [21], or the intradermal administration of the vaccine [22,23], as opposed to the typical intramuscular injection of influenza vaccines. An adjuvant that has been also found effective in influenza vaccination is an oil-based compound called MF-59, a compound primarily composed of squalene [24]. Additionally, recent demonstration of an experimental vaccine shows a substantial increase in immune response when administered to subjects 16 months after the initial priming series [24].

Pharmaceutical companies are reluctant to enter or remain in the production of vaccines. Unpredictable consumer demands coupled with lack of financial incentives make the production of vaccines somewhat risky. Currently the worldwide manufacturing capacity for influenza vaccine is estimated at 900 million doses at the dose level of 15 μg. Clearly with the requirement of two doses at 90 μg per person, only 75 million persons—less than 1.5% of the world’s population—could be fully immunized [4]. Based on the preliminary studies, only half of those would achieve seroprotection and it is not known whether this vaccine will offer cross-protection against other H5N1 strains of influenza. It is probable that more than one H5N1 vaccine will be needed.

There are live attenuated vaccines that are being developed that would produce more antibodies after one injection and would have several other advantages over inactivated vaccines in a pandemic [25]. One of the major disadvantages could be the reassortment of a virus if the vaccine is given too early. A reassorted virus could introduce the pandemic virus into the population.

There is discussion about a staged vaccine program. Once available and instituted, a maximum effect on reducing transmission of avian influenza would occur if children are vaccinated first, whereby school children have the highest rates of influenza transmission. The lowest impact on transmission will occur if elderly are vaccinated first [26].

Ethical considerations for an influenza pandemic

There is no certainty of an avian influenza (H5N1) pandemic. There are those who think the planning, thought, and finances that have gone into the potential for an avian influenza pandemic are pointless. However, the proposition is one that is “all or nothing” [1]. Who could have predicted the AIDS/HIV epidemic? There were fewer “warning signs” for AIDS than what we have seen historically with influenza epidemics. It stands to reason that overreacting will have a more beneficial effect in the long run on the health care system’s ability to serve most of the people in the world, rather than to ignore the lessons of history. It is important not only to know of the current state of avian influenza (H5N1), the current research on vaccines, and the current recommendations, but also to consider the ethics of health care as it relates to this potential pandemic.

Ethical issues that would come to prominence during such a pandemic would involve surveillance issues, quarantine issues, resource allocation, justice, and issues of personal choice for health care workers [1]. These are core problems that will emerge in a pandemic that warrant careful consideration before the occurrence.

In our mobile society, surveillance is an important issue. This requires a system to detect and respond to the reports of an avian influenza outbreak so that supplies can be given to ameliorate the situation. Although the World Health Organization predicts the outbreak will occur in Asia, we must remain vigilant worldwide. There is a fine balance between surveillance and intrusive-ness that has been demonstrated by the myriad sexually transmitted diseases and other diseases. Issues of privacy will be particularly salient, particularly in an environment of fear and mass communication.

Quarantine procedures will need to be put in place at the first local outbreak of a pandemic to prevent the spread and amplification of the disease [1]. This poses numerous questions about who, where, how long, and what circumstances. Although there are recommendations in place from the Centers for Disease Control and
Prevention, there are many questions about who will enforce this quarantine: what will the effect be of potential pandemonium, and what of work loss or financial loss of the individual who is quarantined? The questions are extensive but warrant consideration.

Resource allocation is an issue in any crisis. Vaccine policy is driven larger by politics, in which vaccinations are given by categories or vulnerability rather than efficacy [1]. Who should receive vaccinations? What principles of justice guide these decisions? As stated by Zoloth and Zoloth [1], “Epidemics force us toward utilitarian conclusions, justifying the distribution schemes that favor the most useful over the neediest, so the most useful can best serve the overall telos of a functioning society.” Is this acceptable to the people of the United States, or the world? Allocation schemes pose inherent values. For example, look at the issue when anthrax prophylaxis was given to members of Congress before postal workers.

Additionally consider the increase in volume and expenses for not only pharmaceutical but also other supplies such as gowns, masks, and gloves. Consider how in the midst of the pandemic, supports from social service agencies and public services would be limited. Lastly, what occurs when all local hospitals are closed to new admissions? These questions should lead to practical planning for any health care institution.

Probably the most difficult question for critical care nurses and for most health care workers will be that of personal duty. An avian influenza pandemic would bring about a moral dilemma for health care workers in their competing roles as professionals versus family members [1]. Some states regard the obligation to treat during an emergency as a legal duty with criminal sanctions for those who refuse.

SARS provides a recent prototype of an example whereby the issue of personal duty has been demonstrated. A study involving 15,025 health care workers from nine major health care institutions in Singapore during a 2003 SARS epidemic yields results that might have implications for predictions in the event of an influenza epidemic [27]. Although personal risk was identified by 76% of the respondents, panic can be avoided by the implementation of simple protective measures based on sound hygiene and epidemiologic principles. This study, along with a study by Bournes and Ferguson-Pare’ [28] in the wake of a Toronto outbreak of SARS, focuses on principles that might ameliorate the personal affect that a comparable avian influenza outbreak might have on health care workers.

Summary

We cannot be certain when the next influenza pandemic will emerge, or even whether it will be caused by avian influenza (H5N1) or some unrelated virus. However, we can be certain that an influenza pandemic will occur [29]. The United States is leading the scientific effort to contain the pandemic through vaccine studies and antiviral studies. The need for pandemic influenza preparedness is extensive and expensive. Planning entails increased development of antivirals and vaccines, effective surveillance systems not only for people, but in agriculture, effective communication systems, plans to continue essential services, identification of health care priorities, and thorough guidelines for care. Critical care nurses, as well as all health care professionals, need to consider where their personal and professional obligations meet and end. There should already be discussions of contingency plan of the institution in which they are employed and the community in which they live. Additionally, a personal plan for their families with regard to economics, safety, and optimizing personal health outcomes during such a crisis should be considered. As many have said, “It is not a matter of if, but rather of when.” Although the pandemic might not be the avian flu, history has taught us that pandemics surface with little warning and can have devastating effects on human lives, and can over tax the already fragile health care system.

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