Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
The spread of H5N1, an avian influenza A virus, to many countries and the direct infection of humans by this virus have increased awareness of the likelihood of a pandemic among humans. The potential impact of pandemic influenza on the safety of the blood supply should be small because of the limited viremia and the nature of respiratory tract infection of influenza viruses. However, the potential impact of pandemic influenza on the availability of the blood supply could be significant because of reduced donation from blood donors and reduced staff capacity at blood centers during a pandemic. On the other hand, there could be reduced hospital admissions and reduced transfusions, at least for certain blood products, which should result in reduced demand for blood products. Studies are needed to further assess the likely impact of a pandemic on the blood supply and also of the possible intervention options.

A 2006 Elsevier Inc. All rights reserved.

A INFLUENZA PANDEMIC is a global outbreak of disease that occurs when a new influenza A virus appears or emerges in the human population. Pandemics are different from seasonal outbreaks or epidemics of influenza. Seasonal outbreaks are caused by subtypes of influenza viruses that are already in existence among people, whereas pandemics are caused by new subtypes or by subtypes that have never circulated among people or that have not circulated among people for a long time. The subtypes differ based upon certain proteins on the surface of the virus (the hemagglutinin or the HA protein and the neuraminidase or the NA protein). The appearance of a new influenza A virus subtype is the first step toward a pandemic, but the new virus subtype must also have the ability to spread easily from person to person to cause a pandemic.1

Many scientists believe it is only a matter of time until the next influenza pandemic occurs.2 However, the timing and the severity of the next pandemic cannot be predicted. Modeling studies suggested that its effect in the United States could be severe. In the absence of any control measures (vaccination or drugs), a medium-level pandemic could cause 89000 to 207 000 deaths, between 314 000 and 734 000 hospitalizations, 18 to 42 million outpatient visits, and another 20 to 47 million people being sick. Between 15% and 35% of the US population could be affected.3 The numbers of health care workers (HCWs) and first responders available to work can be expected to be reduced; they will be at high risk of illness through exposure in the community and in the health care settings, and some may have to miss work to care for ill
family members (Centers for Disease Control and Prevention [CDC]. Influenza—fact sheet. Available at: http://www.cdc.gov/flu/avian/gen-info/pandemics.htm).

What will be the likely impact on the blood supply, both in safety and availability, should an influenza pandemic occur? There have been many review articles recently on pandemic influenza, among which some of the most recent ones have been published in the journal of Emerging Infectious Diseases.4-8 This review focuses on certain relevant aspects of pandemic influenza and its potential impact on the blood supply.

CURRENT STATUS OF HUMAN INFLUENZA

According to the most recent report from the World Health Organization (WHO), influenza A(H1N1), A(H3N2), and B viruses cocirculated and caused outbreaks worldwide between September 2004 and August 2005. Although most of the outbreaks (regional or widespread) were associated with influenza A(H3N2) viruses, influenza B viruses circulated widely and caused outbreaks in some countries in Africa, Asia, eastern Europe, Oceania, and South America. Influenza A(H1) viruses circulated to a lesser extent and caused outbreaks in a few countries in Africa, central Asia, and eastern Europe.9

Human influenza is extremely contagious and is transmitted from person to person, usually by the airborne route. In nursing homes, up to 60% of patients can develop disease. Infected persons are most contagious during the period of peak symptoms. The attack rate in children is 14% to 40% yearly and more than 30% in preschool age children. Children frequently infect their families. In the United States, annual averages of 94735 (range, 18908-193561) primary and 133900 (30757-271529) “any listed pneumonia and influenza hospitalizations” were associated with influenza virus infections. Annual averages of 226054 (54523-430960) primary and 294128 (86494-544909) “any listed respiratory and circulatory hospitalizations” were associated with influenza virus infections. Significant numbers of influenza-associated hospitalizations in the United States occur among the elderly, and the numbers of these hospitalizations have increased substantially over the last 2 decades due in part to the aging of the population. Influenza-associated hospitalization rates increased annually from 1979-1980 to 2000-2001 among persons aged 50 through 85 years and older.10 Influenza and pneumonia comprise the sixth leading cause of death in the United States overall and the fifth leading cause among adults 65 years and older. In the 1990s, influenza-related deaths increased to about 36,000 per year. The number of deaths can increase to 40,000 during epidemics.11

In economically developed countries, mortality increases distinctly during winter months. A study analyzed monthly the mortality in the United States during the period 1959 to 1999 for 4 major disease classes. The authors isolated the seasonal component of mortality by removing trends and standardizing the time series. Peak months of mortality for ischemic heart disease, cerebrovascular disease, and diabetes mellitus coincided appropriately with peaks in pneumonia and influenza. The magnitude of the seasonal component was highly correlated with traditional measures of excess mortality and was significantly larger in seasons dominated by influenza A(H2N2) and A(H3N2) viruses than in seasons dominated by A(H1N1) or B viruses. There was an age shift in mortality during and after the 1968 or 1969 pandemic in each disease class, with features specific to influenza A(H3N2). These findings suggest that the cause of the winter increase in US mortality is singular and probably influenza. Weather and other factors may determine the timing and modulate the magnitude of the winter-season increase in mortality, but the primary determinant appears to be the influenza virus.12

Observational studies reported that influenza vaccination reduces winter mortality risk from any cause by 50% among the elderly. A study by Simonsen et al13 could not correlate increasing vaccination coverage after 1980 with declining mortality rates in any age group. They showed that for people aged 65 to 74 years, excess mortality rates in A(H3N2)-dominated seasons fell between 1968 and the early 1980s but remained approximately constant thereafter. For persons 85 years or older, the mortality rate remained flat throughout. Excess mortality in A(H1N1) and B seasons did not change. All-cause excess mortality for persons 65 years or older never exceeded 10% of all winter deaths. The authors attributed the decline in influenza-related mortality among people aged 65 to 74 years in the decade after the 1968 pandemic to
the acquisition of immunity to the emerging A(H3N2) virus. They concluded that observational studies substantially overestimate vaccination benefit.\textsuperscript{13} The study has provoked starkly different reactions and certainly indicates that there is room for improvement of influenza vaccines.\textsuperscript{14} A statement by CDC and National Institutes of Health clarifies that the Simonsen study in no way implies that the elderly should not receive influenza vaccine. Rather, the study concludes that the vaccine may prevent fewer deaths among the elderly than previous studies would have suggested. Vaccination remains the best available protection from influenza for people 65 years and older. It may be beneficial to vaccinate larger numbers of healthy persons, including children, to prevent transmission of influenza viruses to high-risk persons such as the elderly (CDC. Available at: www.cdc.gov/flu/).

AVIAN INFLUENZA AND THE NEXT POTENTIAL PANDEMIC

In 1997, outbreaks of highly pathogenic avian influenza virus A(H5N1) were reported in poultry at farms and wet markets and among humans in Hong Kong. Altogether, 18 cases (6 fatal) were reported in the first known instance of human infection with this virus (WHO. H5N1 avian influenza: timeline. Available at: www.who.int). Since 1997, there have been many incidents of transmission of avian influenza virus to humans.\textsuperscript{5} Increased surveillance may have increased the detection rate, but there is support for the notion that H9N2 influenza virus was not found in Asia in domestic chickens or in humans before the mid-1980s. The spread of H5N1 influenza virus throughout Asia in 2004 is undoubtedly a novel event. The H5N1 virus that infected humans in 1997 acquired all 8 gene segments from Eurasian avian sources. The virus was soon replaced by different genotypes that were highly pathogenic in chickens but not in ducks. These viruses were again replaced by additional genotypes in 2002. The most remarkable property of the H5N1 genotype from late 2002 was its high pathogenicity for ducks and other aquatic birds. In early February 2003, H5N1 virus reemerged in a family in Hong Kong. The strain was antigenically and molecularly similar to the antigenically drifted strain that was highly pathogenic for ducks and chickens.\textsuperscript{15} As of December 23, 2005, cumulative numbers of confirmed human cases and deaths from avian influenza A(H5N1) since 2003 are 93 and 42 from Vietnam, 22 and 14 from Thailand, 16 and 11 from Indonesia, 6 and 2 from China, and 4 and 4 from Cambodia (www.who.int).

A key feature of a potentially pandemic influenza virus is its ability to spread efficiently from infected to noninfected hosts (ie, its transmissibility). The molecular basis of influenza virus transmissibility remains unresolved.\textsuperscript{15} Like the 1918 virus, H5N1 influenza has unusually high virulence. Although the 2 viruses differ in their transmissibility among humans, there is concern that currently circulating H5N1 viruses will evolve into a pandemic strain by adapting to humans through genetic mutation or reassortment with human influenza strains. Fortunately, there has been no direct evidence of efficient poultry-to-human or human-to-human transmission to date.\textsuperscript{16} Nevertheless, probable person-to-person transmission of avian influenza A(H5N1) was reported. The index patient was an 11-year-old girl who lived with her aunt. She became ill 3 to 4 days after her last exposure to dying household chickens. Her mother came from a distant city to care for her in the hospital, had no recognized exposure to poultry, and died from pneumonia after providing 16 to 18 hours of unprotected nursing care. The aunt also provided unprotected nursing care; she had fever 5 days after the mother first had fever, followed by pneumonia 7 days later. Autopsy tissue from the mother and nasopharyngeal and throat swabs from the aunt were positive for influenza A(H5N1) by reverse transcriptase polymerase chain reaction. No additional chains of transmission were identified, and sequencing of the viral genes identified no change in the receptor-binding site of hemagglutinin or other key features of the virus. The sequences of all 8 viral gene segments clustered closely with other H5N1 sequences from recent avian isolates in Thailand. It was concluded that the disease in the mother and aunt probably resulted from person-to-person transmission of this lethal avian influenza virus during unprotected exposure to the critically ill index patient.\textsuperscript{17,18} However, a study from Vietnam showed a lack of H5N1 avian influenza transmission to hospital employees.\textsuperscript{19}

The incubation period in the reported cases seemed to be 2 to 4 days, similar to that in cases of human influenza, followed in most patients by fever, cough, and dyspnea. Diarrhea was variably
reported, and sore throat and runny nose were noted in some of the patients. A striking feature was marked lymphopenia in those patients who were severely ill. Unlike cases of human influenza, in the H5N1 avian virus cases, primary viral pneumonia was common, whereas secondary bacterial pneumonia has not been reported.20

An epidemic of avian influenza A(H7N7) occurred in The Netherlands in 2003, which affected 255 flocks and led to the culling of 30 million birds. To evaluate the effectiveness of the control measures, a study quantified between-flock transmission characteristics of the virus in 2 affected areas. The control measures markedly reduced the transmission of the virus. The study suggests that the containment of the epidemic was probably due to the reduction in the number of susceptible flocks by complete depopulation of the infected areas rather than to the reduction of the transmission by the other control measures.21 A recent report described the occurrence of infection with the virus in household contacts of human index cases, in the absence of contact with infected poultry, suggesting human-to-human transmission of the virus during the 2003 poultry epidemic.22,23 In 2004, an outbreak of highly pathogenic avian influenza A(H7N3) occurred in poultry in British Columbia, Canada. Surveillance identified 2 persons with confirmed avian influenza infection. Symptoms included conjunctivitis and mild influenza-like illness.24

Why is H5N1 of particular concern? Of the avian influenza virus subtypes, H5N1 is of particular concern for several reasons. It mutates rapidly and has a known propensity to acquire genes from viruses infecting other animal species. Its ability to cause severe disease in humans has now been documented. In addition, laboratory studies have demonstrated that isolates of this virus have a high pathogenicity and can cause severe disease in humans. Birds that survive infection excrete virus for at least 10 days, orally and in feces, thus, facilitating further spread at live poultry markets and by migratory birds. H5N1 variants demonstrated a capacity to directly infect humans in 1997, and have done so again in Vietnam and other countries since 2003. The spread of infection in birds increases the opportunities for direct infection of humans. If more humans become infected over time, the likelihood also increases that humans, if concurrently infected with human and avian influenza strains, could serve as the “mixing vessel” for the emergence of a novel subtype with sufficient human genes to be easily transmitted from person to person. Such an event would mark the start of an influenza pandemic.2

The last century saw pandemic influenza viruses belonging to 3 subtypes (H1, H2, and H3), and indirect evidence suggests that H3 viruses were circulating from 1889 to 1918 and that H1 viruses were possibly prevalent before 1889. If this series of events over the last hundred years reflects a pattern, recycling of subtypes would be the norm in the human population, and the possibility for the emergence of new pandemics would be limited. On the other hand, if any subtype is able to thrive in the human population, a greater number of possibilities for novel pandemic strains would exist. Although H5N1 avian viruses were shown to cause death in humans, none of these strains were easily transmitted from human to human. Also, none of the H5N1 strains showed evidence of having acquired genes from circulating human influenza viruses. Whether this is a necessary requirement for a pandemic strain to be successful is not known. It would seem probable that such a reassortment event between an avian and a human influenza virus could have happened many times over, either in humans or in animals. It may be possible that infections of humans by avian influenza viruses have been ongoing for decades, and it is only the reporting that has improved in recent years. If this were the case, the present emphasis on the imminent pandemic outbreak would not be justified.25 However, the precursor of the severe acute respiratory syndrome (SARS)–associated coronavirus has been shown to have repeatedly crossed species barriers, probably for many years, before it finally acquired the capacity for human-to-human transmission, and its pathogenicity to humans was not attenuated.26 Because the H5N1 virus continues to evolve and spread, with additional human infections occurring in many countries, we cannot afford simply to hope that human-to-human spread of the virus does not happen, and that if it does, the pathogenicity of the virus will attenuate.8 What is warranted and where there is little or no disagreement among scientists is a continued surveillance of influenza viruses. Stockpiling of antiviral drugs and the development of new vaccines are highly recommended to be better prepared for a potential pandemic outbreak.25
Recent advances in recombinant technologies have shown the possibility of constructing premade libraries of vaccine strains, so that adequate preparations can be made for epidemics and pandemics. Cross-protection against multiple influenza A subtypes can be induced in animals by prior infection or vaccination. Multiple viral antigens and multiple immune effector mechanisms can participate. Mucosal vaccination induces different immune responses than systemic vaccination and is more effective at inducing broad cross-protection to multiple influenza A subtypes in animals. Broad cross-protection in humans is of unclear potency and duration, but epidemiological data suggest that it may have an impact. A variety of vaccines may induce broad cross-protection if administered appropriately. Imperfect vaccine protection is worth having, especially for a virus causing an acute (not latent) infection. It could provide a first line of pandemic defense to be augmented by subtype- or strain-specific vaccines when available. More recent articles also reviewed and discussed the development of cross-protective vaccines.

Both adamantanes (amantadine and rimantadine) and neuraminidase inhibitors (oseltamivir and zanamivir) were believed to be effective against a pandemic virus, although emergence of resistance has apparently occurred with adamantanes, and the more recent type A(H5N1) virus as well as some currently circulating seasonal viruses are not susceptible to this drug class. A recent study showed that stockpiles of neuraminidase inhibitors that cover 20% to 25% of the population would be sufficient to treat most of the clinical cases and could lead to 50% to 77% reduction in hospitalizations. Another study indicated that current stockpiling of oseltamivir appears to be cost saving under several treatment strategies, including therapeutic treatment of patients and postexposure prophylactic treatment of patients’ close contacts. In addition, antimicrobial agents can help control secondary bacterial infections, which could have been the cause of death among many patients during the 1918 pandemic.

In view of the threat of a potentially serious influenza pandemic, many governments have drafted pandemic influenza preparedness and response plans. The US draft plan was posted in August 2004. The plan stressed the need for improved measures to safeguard the public. In particular, steps need to be taken in the areas of surveillance, vaccine development and production, antiviral stockpiling, research, and public health preparedness. A key part of the plan is to establish public safety measures and coordination with state and local levels. The formal plan was launched by the Department of Health and Human Services (Washington, DC) in November 2005 (www.dhhs.gov/pandemicflu/plan/). On April 1, 2005, the US government issued a directive allowing authorities to detain or isolate any passenger suspected of having avian influenza when arriving in the United States aboard an international flight. Under the directive, the Health and Human Services Department is given legal authority to detain or isolate any passenger suspected of having avian influenza to prevent the person from infecting others (Reuters, April 1, 2005).

In summary, the threat of a potential pandemic has become more likely following the widespread avian influenza epidemics and the direct infection of humans with these viruses. On the other hand, however, the current awareness, preparedness, vaccines, antivirals, and antimicrobials were not there or at least not to the same extent before or during the 1918 pandemic. Therefore, it is not expected that the next pandemic will result in the same fatality rates among those who will be infected. This is not to say that we should not be prepared. On the contrary, it is the preparedness that will probably make the difference this time around compared with what happened in 1918.

PANDEMIC INFLUENZA AND BLOOD SAFETY

An attempt to demonstrate viremia in cases of Asian influenza was reported in 1962. Twenty-four fresh blood pools containing 52 individual samples from 7 proved cases of Asian influenza were tested for the presence of influenza virus by amniotic inoculation of 10- to 11-day-old embryonate eggs. Fifteen pools containing 33 frozen samples from 4 of the cases were further tested for virus by incorporating chick embryo tracheal suspensions in the inocula used for the second and third blind passages. The samples were collected generally at 2- to 4-hour intervals over an 18- to 24-hour period from patients who had been ill 22 to 78 hours. Viremia was not detected. The experience of this effort indicates that in uncomplicated cases of acute influenza A, viremia cannot be demonstrated by the use of techniques that permit the ready isolation of virus from respiratory secretions.
However, a volunteer study showed viremia in Asian influenza. Nasal challenge with only 100 to 200 TCID$_{50}$ of the Bethesda 10/63 strain of influenza A$_2$ virus produced infection with viremia in 4 volunteers. Two of 11 others had a rise in the titer of serum antibody, but the studies were inadequate to confirm or exclude viremia. Virus was recovered from the blood within 24 hours after challenge and with decreasing frequency thereafter for the 3 days tested. Viremia preceded virus shedding from the nose and the onset of illness. Symptoms of infection were mild in 3 of the subjects with viremia, and the fourth remained completely asymptomatic. Proof of the human origin of the viruses recovered was gained by repeated reisolation from the original specimens, and infection was confirmed serologically. The virus isolates were confirmed as influenza A$_2$ with properties similar to those of the challenge strain. It was concluded that influenza virus infections may cause viremia during an asymptomatic incubation period, and that the course of viremic infection is not necessarily one of severe illness.37

In another report, a 31-year-old man who had undergone splenectomy 18 months previously because of hereditary spherocytosis suddenly became ill, with fever, vomiting, epigastric pain, and shock, and died 10 hours after the onset of his symptoms. Autopsy showed influenza viremia, pneumococcemia, and bilateral adrenal hemorrhage. The rapid course of the patient’s illness emphasizes the serious risk of sepsis for individuals who have had a splenectomy.40

The most recent report on influenza viremia was on an avian influenza A(H5N1) case that occurred in February 2004 in Vietnam. A 4-year-old boy presented with severe diarrhea, followed by seizures, coma, and death. The diagnosis of avian influenza was established by isolation of the virus from cerebrospinal fluid, fecal, throat, and serum specimens.41

Taken together, viremia can occur during influenza infection, including avian influenza infection, although the chance is low especially in asymptomatic infections, which are relevant to the blood supply. If it is assumed that the incubation period for avian influenza in humans is 2 to 4 days, similar to that in cases of human influenza, coupled with the result from a healthy contact in the 1968 Tehran Ghasr Prison study,38 it is likely that a period of 2 to 3 days of viremia could occur in humans infected with an avian influenza virus. In cases that develop symptoms, most of this period would lie before onset of symptoms, which could be significant for blood safety. What could be important, for which no data are available, is the transmissibility of influenza virus in blood transfused into a susceptible recipient. Influenza virus normally enters a human body through the respiratory tract and replicates there, which is different from West Nile
virus or any other currently known viral threats to blood safety. More studies are needed to further assess the threat of influenza virus to blood safety.

**POTENTIAL IMPACT OF AN INFLUENZA PANDEMIC ON BLOOD AVAILABILITY**

Although WHO believes the appearance of H5N1 signals that the world has moved closer to the next pandemic, it is impossible to accurately forecast the timing and the magnitude of the next pandemic. Experts' answers to the question of magnitude have ranged from 2 million to more than 50 million. Because of various factors, confidently narrowing the range of estimates cannot be done until the pandemic emerges. Even in the best case scenarios of the next pandemic, 2 to 7 million people would die and tens of millions would require medical attention (WHO). Estimating the impact of the next influenza pandemic: enhancing preparedness. December 2004; WHO. Avian influenza: assessing the pandemic threat. January 2005. Both are available at: www.who.int.

In the modeling conducted by Meltzer et al at CDC, 40%, 53%, and 7% of all cases were assumed to occur in the age groups of 0 to 19, 20 to 64, and 65 years or older; 6.4%, 14.4%, and 40.0% of the population in the age groups of 0 to 19, 20 to 64, and 65 years or older were assumed to be at high risk. They used gross attack rates (percentage of clinical influenza illness cases per population) of 15% to 35%. Outpatient visit rates for those that are not at high risk were assumed to be 16.5% to 23.0% for 0- to 19-year olds, 4.0% to 8.5% for 20- to 64-year olds, and 4.5% to 7.4% for 65 years or older. By applying the CDC model to the current blood donor population of the American Red Cross Blood Services, 8% to 19% of donors could be infected during a pandemic, assuming an attack rate of 15% to 35% and no intervention. Of those infected, 97% would need no hospitalization (unpublished data).

A study estimated the potential impact of a pandemic on the primary care medical workforce in New Zealand, also using the CDC model. The results showed that, using conservative baseline assumptions, the pandemic would lead to 1.2% to 2.7% loss of medical work time. For a more severe scenario, with inputs for greater health effect and time spent caring for sick relatives, 9% of medical workdays would be lost in the peak week and 3% over a more compressed 6-week period of the first pandemic wave. Most (64%) of the lost workdays would be due to illness, followed by caring for others (31%), hospitalization (4%), and then premature death (1%).

Enserink reviewed the current assessment of the impact of the next pandemic and suggested that pandemic influenza is unlikely to be contained using the old-fashioned public health measures that put the SARS genie back into the bottle, such as isolating patients and tracing and quarantining contacts. Severe acute respiratory syndrome has an incubation period of about 6 days, during which infected people do not seem to infect others, whereas influenza would have about 2 days on average. Moreover, SARS’s severe symptoms helped identify patients, whereas influenza can be as mild as the sniffles. The only exception may be very early on. When the virus is still struggling to replicate among humans, surveillance and quarantine, perhaps helped by aggressive use of antiviral drugs, might nip a pandemic in the bud—which is why WHO is exploring a plan to ship antivirals to the cradle of a potential pandemic. According to a study of the impact of travel on influenza spread, an outbreak in 2000 caused by the 1968 influenza strain would peak in most of the 52 major cities around the globe within 6 months. In the same model fed with the travel data from 1968—as well as in the actual pandemic—almost a year passed before the virus made it around the globe. Taken together with recommendations from WHO and the US government plan and directive, it is conceivable that, during a pandemic, there will nevertheless be increased isolation and quarantine of individuals as well as more people staying at home as advised during the SARS outbreaks.

Another study assessed HCWs’ ability and willingness to report to duty during catastrophic diseases through a survey of 6428 HCWs from 47 health care facilities in New York City and the surrounding metropolitan region. A range of facility types and sizes were represented in the sample. Results indicate that HCWs were most able to report to work for a mass casualty incident (83%), environmental disaster (81%), and chemical event (71%), and least able to report during a smallpox epidemic (69%), radiologic event (64%), SARS outbreak (64%), or severe snowstorm (49%). In terms of willingness, HCWs were most willing to report during snowstorm (80%), mass casualty incident (86%), and environmental disaster (84%), and least willing during SARS outbreak (48%),
radiologic event (57%), smallpox epidemic (61%), and chemical event (68%). Barriers to ability included transportation problems, childcare, eldercare, and pet care obligations. Barriers to willingness included fear and concern for family and self and personal health problems. The findings were consistent for all types of facilities.  

In summary, the potential impact of the next pandemic on the population would be highly relevant, especially the high outpatient visit rates for those who are not at high risk, 16.5% to 23.0% for 0- to 19-year olds, 4.0% to 8.5% for 20- to 64-year olds, and 4.5% to 7.4% for 65 years or older. Most of our blood donors and staff members are 20- to 64-year olds; illness with 0- to 19-year olds and 65 years or older may also impact on those of 20- to 64-year olds because they may need to care for those of 0 to 19 or 65 years or older in their families who are ill. Furthermore, what could be important but has not yet been fully assessed is the number of potential blood donors and even some staff members who would be afraid of coming out to blood centers to donate blood or perform blood collection or processing functions. Many people could be ordered to stay home because of potential exposure to the infection.

CONCLUDING REMARKS

In summary, the spread of H5N1 and the direct infection of humans by avian influenza virus have increased the likelihood of a pandemic, although the timing and magnitude cannot be predicted.

Concern for Blood Safety

Viremia can occur during influenza infection, including avian influenza infection, although the chance is low especially in asymptomatic infections, which are relevant to the blood supply. Further study is needed for the transmissibility of influenza virus in blood transfused into a susceptible recipient.

Implication for Blood Availability and Staff Safety

The potential impact of the next pandemic on blood donors and blood center staff could be significant. A proportion will be infected. Another proportion could be unable or unwilling to show up for donation or duty, although no data are available on the probable sizes of the proportions.

Potential Impact on Blood Demand in Hospitals

This is an issue that has not been addressed in this review but needs to be examined. During a pandemic, there could be reduced admissions to hospitals and therefore reduced number of patients who may need transfusion. Furthermore, there could be reduction in transfusion even for existing patients because of reduced hospital staff capacity or simply for contingency purposes. It will be important to know whether reduced demand in hospitals will out- or underperform reduced collection and delivery of blood products. Another important aspect of the potential impact of a pandemic on blood demand is the likely difference for different products such as whole blood vs platelets. Although the need for whole blood or plasma may decrease because of cancelled operations, the need for platelets may be unaffected or affected to a lesser extent.

Further studies are needed to further quantify the impact of a pandemic on blood availability and on the transfusion needs of recipients during a pandemic. In addition, there will be various intervention measures that may have an impact on the blood supply from blood centers and on the blood demand from hospitals. The likely impact of such measures on blood availability as well as on blood safety ought to be evaluated. Results from such studies will be able to help contingency planning and necessary actions.

ACKNOWLEDGMENTS

The author would like to express his gratitude to Drs Roger Y. Dodd and Chyang Fang of the American Red Cross for their guidance and for reviewing the manuscript. The author also appreciates the valuable discussions he had with Dr Earl G. Brown of the University of Ottawa, Ontario, Canada.

REFERENCES

1. WHO: Avian influenza and human pandemic influenza—Summary report on the avian influenza meeting held in Geneva, Switzerland in November 7-9, 2005. www.who.int
2. WHO: Avian influenza—Current evaluation of risks to humans from H5N1 following recent reports. Wkly Epidemiol Rec 79:265-268, 2004
3. Meltzer MI, Cox NJ, Fukuda K: The economic impact of pandemic influenza in the United States: Priorities for intervention. Emerg Infect Dis 5:659-671, 1999
4. Dowdle WR: Influenza pandemic periodicity, virus recycling, and the art of risk assessment. Emerg Infect Dis 12:34-39, 2006
5. Fauci AS: Pandemic influenza threat and preparedness. Emerg Infect Dis 12:73-77, 2006
6. Kilbourne ED: Influenza pandemics of the 20th century. Emerg Infect Dis 12:9-14, 2006
7. Taubenberger JK, Morens DM: 1918 influenza: The mother of all pandemics. Emerg Infect Dis 12:15-22, 2006
8. Webster RG, Peiris M, Chen H, et al: H5N1 outbreaks and enzootic influenza. Emerg Infect Dis 12:3-8, 2006
9. WHO: Summary of influenza activity, September 2004-August 2005. Wkly Epidemiol Rec 80:353-355, 2005
10. Thompson WW, Shay DK, Weintraub E, et al: Influenza-associated hospitalizations in the United States. JAMA 292:1333-1340, 2004
11. Zimmerman RK: Recent changes in influenza epidemiology and vaccination recommendations. J Fam Pract 54:S1-S8, 2005
12. Reichert TA, Simonsen L, Sharma A, et al: Influenza and the winter increase in mortality in the United States, 1959-1999. Am J Epidemiol 160:492-502, 2004
13. Simonsen L, Reichert TA, Viboud C, et al: Impact of influenza vaccination on seasonal mortality in the US elderly population. Arch Intern Med 165:265-272, 2005
14. Cohen J: Influenza. Study questions the benefits of vaccinating the elderly. Science 307:1026, 2005
15. Lipatov AS, Govorkova EA, Webby RJ, et al: Influenza: Emergence and control. J Virol 78:8951-8959, 2004
16. Hien TT, de Jong M, Farrar J: Avian influenza—A challenge to global health care structures. N Engl J Med 351:2363-2365, 2004
17. Unchusak K, Auewarakul P, Dowell SF, et al: Probable person-to-person transmission of avian influenza A (H5N1). N Engl J Med 352:333-340, 2005
18. Monto AS: The threat of an avian influenza pandemic. N Engl J Med 352:323-325, 2005
19. Liem NT, et al: Lack of H5N1 avian influenza transmission to hospital employees, Hanoi, 2004. Emerg Infect Dis 11:210-215, 2005
20. Kaye D, Pringle CR: Avian influenza viruses and their implication for human health. Clin Infect Dis 40:108-112, 2005
21. Stegeman A, Bouma A, Elbers AR, et al: Avian influenza A virus (H7N7) epidemic in The Netherlands in 2003: Course of the epidemic and effectiveness of control measures. J Infect Dis 190:2088-2095, 2004
22. Du Ry van Beest Holle M, Meijer A, Koopmans M, et al: Human-to-human transmission of avian influenza A(H7N7), The Netherlands, 2003. Euro Surveill 10 (Electronic publication ahead of print), 2005
23. Nicoll A: Avian and pandemic influenza—five questions for 2006. Euro Surveill 10 (Electronic publication ahead of print), 2005
24. Tweed SA, Skowroński DM, David ST, et al: Human illness from avian influenza H7N3, British Columbia. Emerg Infect Dis 10:2196-2199, 2004
25. Palese P: Influenza: Old and new threats. Nat Med 10:882-887, 2004 (suppl 12)
26. Guan Y, Zheng BI, He YQ, et al: Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China. Science 302:276-278, 2003
27. Bardiya N, Bae JH: Influenza vaccines: Recent advances in production technologies. Appl Microbiol Biotechnol 67:299-305, 2005
28. Epstein S: Control of influenza virus infection by immunity to conserved viral features. Expert Rev Anti-infect Ther 1:627-638, 2003
29. Spier RE: On the need for, and the delivery of, cross-protective vaccines. Vaccine 23:2027-2029, 2005
30. Monto AS: Vaccines and antiviral drugs in pandemic preparedness. Emerg Infect Dis 12:55-60, 2006
31. Palese P: Making better influenza virus vaccines? Emerg Infect Dis 12:61-65, 2006
32. Thomas PG, Keating R, Hulse-Post DJ, et al: Cell-mediated protection in influenza infection. Emerg Infect Dis 12:48-54, 2006
33. Gani R, Hughes H, Fleming D, et al: Potential impact of antiviral drug use during influenza pandemic. Emerg Infect Dis 11:1355-1362, 2005
34. Balicer RD, Huerta M, Davidovitch N, et al: Cost-benefit of stockpiling drugs for influenza pandemic. Emerg Infect Dis 11:1280-1282, 2005
35. Hampton T: Government drafts flu preparedness plan: concerns about serious pandemic spur effort. JAMA 292:1671-1672, 2004
36. Minuse E, Willis PW III, Davenport FM, et al: An attempt to demonstrate viremia in cases of Asian influenza. J Lab Clin Med 59:1016-1019, 1962
37. Stanley ED, Jackson GG: Viremia in Asian influenza. Trans Assoc Am Physicians 79:376-387, 1966
38. Khakpour M, Saidi A, Naficy K: Proved viraemia in Asian influenza (Hong Kong variant) during incubation period. BMJ 4:208-209, 1969
39. Lehmann NI, Gust ID: Viraemia in influenza. A report of two cases. Med J Aust 2:1166-1169, 1971
40. Roberts GT, Roberts JT: Post-splenectomy sepsis due to influenzal viremia and pneumococcemia. CMAJ 115:299-305, 1976
41. de Jong MD, Bach VC, Phan TQ, et al: Fatal avian influenza A (H5N1) in a child presenting with diarrhea followed by coma. N Engl J Med 352:686-691, 2005
42. Wilson N, Baker M, Crampton P, et al: The potential impact of the next influenza pandemic on a national primary care medical workforce. Hum Resour Health 3:7-12, 2005
43. Enserink M: Looking the pandemic in the eye. Science 306:392-394, 2004
44. WHO: Nonpharmaceutical interventions for pandemic influenza, national and community measures. Emerg Infect Dis 12:88-94, 2006
45. Qureshi K, Gershon RR, Sherman MF, et al: Health care workers’ ability and willingness to report to duty during catastrophic disasters. J Urban Health 82:378-388, 2005