Planning for pandemic influenza: effect of a pandemic on the supply and demand for blood products in the United States

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BACKGROUND: Influenza causes episodic pandemics when viral antigens shift in ways that elude herd immunity. Avian influenza A H5N1, currently epizootic in bird populations in Asia and Europe, appears to have pandemic potential.

STUDY DESIGN AND METHODS: The virology of influenza, the history of the 1918 pandemic, and the structure of the health care and the blood transfusion systems are briefly reviewed. Morbidity and mortality experience from the 1918 pandemic are projected onto the current health care structure to predict points of failure that are likely in a modern pandemic.

RESULTS: Blood donor centers are likely to experience loss of donors, workers, and reliable transport of specimens to national testing laboratories and degradation of response times from national testing labs. Transfusion services are likely to experience critical losses of workers and of reagent red cells (RBCs) that will make their automated procedures unworkable. Loss of medical directors, supervisors, and lead technicians may make alternative procedures unworkable as well.

CONCLUSIONS: Lower blood collection capacity and transfusion service support capability will reduce the availability of RBCs and especially of platelets. Plans for rationing medical care need to take the vulnerability of the blood transfusion system into account.

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Influenza is a major cause of death. In typical years, it kills 30,000 to 50,000 people in the United States.[1] In the pandemic year 1957, the death toll was 70,000.[2] In the great pandemic of 1918, it was estimated that 675,000 died in the United States, 50 million worldwide.[3] The recent emergence of the H5N1 strain of avian influenza, "bird flu," raises concerns of a possible new pandemic.[4] Worldwide, 258 people have been infected, and 50 percent of these have died.[5] Projections based on the 1918 pandemic suggest that a new pandemic might infect and disable 30 percent of the US workforce at one time.[6] Direct effects on health care would include the inundation of hospitals with patients needing care, the loss of medical personnel and support staff to illness and absences necessitated by the illness of their loved ones, and the degradation of supporting economic and social infrastructure.

Blood transfusion is a critical part of modern health care, enabling the management of premature infants, congenital anomalies, trauma and burns, obstetric complications, and many complications of aging. Modern blood product provision and management is a highly developed, just-in-time logistic system, orchestrated at both the regional and the national level. It is susceptible to the loss of personnel and transportation at many points.

Effective planning for patients who may need blood during an influenza pandemic will require an understanding of how the blood supply system works and the likely ways that it will fail under the stress of pandemic disease with high rates of morbidity and mortality.[6] Dealing with the demand for blood will require clinical knowledge of the effectiveness of blood products and the way that pandemic disease will modify that effectiveness in individuals and cohorts. The appropriate use of a limited blood supply needs to be empowered. Such triage will raise ethical concerns and lead to confrontations with desperate individuals. If the care system is going to respond in a more than reactive way, health care providers must learn from the past and plan for the future.

BACKGROUND

Influenza

The genus *Orthomyxovirus* encompasses three species, influenza A, B, and C. Influenza A causes the majority of

clinically severe infections, usually manifesting as acute rhinotracheobronchitis with striking systemic symptoms, including high fevers and myalgias.[7] Secondary bacterial pneumonias are common. Facilitating the spread of influenza is the rapid growth of the viruses in the respiratory mucosa and the infectivity of viral droplets expelled by infected persons while coughing or sneezing, even before symptoms suggestive of influenza are present. Although people of all ages contract the infection, mortality is generally highest in patients at extremes of the age range, in infants or young children and in the elderly.

Influenza A strains are named based on the hemagglutinin and neuraminidase proteins on their surface: 16 described hemagglutinin and 9 described neuraminidase subtypes have been identified.[2] Viral replication is characterized by poor fidelity of RNA transcription, resulting in frequent mutations in the hemagglutinin and neuraminidase proteins present on the surface of the virus, thus allowing the virus to avoid recognition and elimination by the immune system. This process is known as "antigen drift." The influenza viral strains that have caused the majority of the yearly epidemics are the result of mutations in the H and N proteins, with three H and two N types predominating.

Viral strains with other H and N subtypes are found in animal populations, particularly in avian species, with occasional human infections reported in people who are in close contact with birds. In the absence of mutations that allow human-to-human spread of infection, these viruses will not cause epidemics within the human population. The frequent mutations that characterize the influenza replication process, however, and the possibility of coinfection of an animal or person with two strains, one human and one nonhuman, with consequent gene resorting, result in periodic exposure of humans to influenza viruses which have become capable of human-to-human transmission and to which they have little or no immunity. These larger changes in viral proteins are known as "antigen shift." The H5N1 subtype has been causing disease in various avian populations for the past 10 years, and an increasing number of humans have contracted it, almost exclusively those in close contact with fowl.[8] Several possible instances of human-to-human transmission have been reported within families, but there is no suggestion that the virus has mutated to a form that would allow epidemic transmission. The lethality of the H5N1 strain and the known genetic instability of influenza viruses, however, have raised concerns that another devastating pandemic could be on the horizon.

Blood-borne transmission of influenza has not been reported. Isolation of the influenza virus from the blood is unusual, but has been documented.[9,10] The H5N1 strain of influenza has been isolated from serum of an infected child in Vietnam[11] and plasma from an infected child in Thailand.[12] Although the short window period between exposure and symptoms and the historical rarity of documented viremia make influenza contamination of the blood supply likely to be at most an uncommon event, the recently reported cases of H5N1 isolated from blood specimens are concerning.

Treatment of influenza has been largely symptomatic, but there are both vaccines and drugs to limit infection and symptoms. Drugs such as amantadine and rimantadine, used in the past for prophylaxis, no longer appear to be effective, but the oral neuraminadase inhibitor oseltamivir can decrease severity and duration of symptoms if started within 48 hours.[13] There are two types of vaccines currently in use. The trivalent split vaccines are made from three strains of virus grown on the allantoic sac of embryonated hens' eggs, which are purified, concentrated, and then inactivated by the use of a detergent to disrupt or "split" the viral coat. A more recent development is the use of a cold-adapted live attenuated vaccine for intranasal administration. The vaccine synthetic process is slow, resource-intensive, and susceptible to contamination. Current research efforts involve other vaccine strategies, such as whole virus formalin-inactivated vaccines and monovalent split H5N1 vaccines with novel adjuvants that might prove more effective, but the production and distribution of vaccines in a timely fashion continue to present enormous logistical challenges. Therefore, despite our considerable knowledge of the virus and the pathophysiology of the infections it causes in humans and animals, there may be little actual protection available in the event of an acute outbreak.

The 1918 pandemic

The 1918 to 1919 pandemic peaked in the United States over 10 weeks in Fall 1918 when 5 to 40 percent of individuals in military bases and large cities were infected and 1 to 30 percent of these individuals died. The resulting deaths, estimated at 675,000, overwhelmed both the ability to provide care and to gather up and bury the dead.[14] Much of business and most of organized social life collapsed as functioning individuals struggled to respond to the many civic and personal crises. In places where the herd immunity was even lower, such as Western Samoa, infection was almost universal and mortality was 22 percent for the entire native population in a period of approximately 6 weeks.[15]

The blood supply system

Approximately 14.5 million units of red blood cells (RBCs) are collected in the United States every year, as well as approximately 1 million units of apheresis platelets (PLTs).[16] All of these products come from volunteer donors who must be recruited and offered comfortable and convenient opportunities to donate. It takes almost 1 hour to

donate, and the process is most efficient if it can be broken down into pieces in the context of large donor centers or their mobile blood drives. Large donor centers also take advantage of economies of scale by contracting the testing of collected blood to a handful of national testing laboratories. The blood supply system is reasonably efficient, providing RBCs for approximately $100 to $200 per unit, and has considerable surge capacity, as was demonstrated after September 11, 2001, but it is labor-intensive and absolutely dependent on the ability to assemble donors, maintain equipment, and move specimens and product.

The blood supply system is closely regulated by the US Food and Drug Administration. This oversight is designed to ensure that the production and shipping of blood components is conducted under current good manufacturing practices (cGMP), and compliance is enforced by the power of law. Blood collection services maintain staffs of quality control and compliance certification specialists who must know both blood banking and the intricacies of compliance, a process that consumes the time and efforts of many of the field's best workers.

Transfusion services

Collected blood is administered to approximately 2 million individual patients a year in the course of 3.8 million hospital visits and in outpatient infusion centers, dialysis centers, and home settings. The inventory management, final testing, and issuing of these blood products is the function of transfusion services. The transfusion service of the authors' hospital employs 40 technologists to provide round-the-clock coverage for a busy trauma center, a large transplant program, specialty surgery, a cancer center, and all of the other activities of a metropolitan university hospital.

The labor-intensive nature of transfusion services and the lack of pools of trained technicians are already problems for hospitals across the country. Highly skilled technicians are needed to cross-match blood, manage inventory, contact suppliers for products in demand, evaluate patients with antibodies, prepare further-modified products, and deal with the regulatory burden. National failure to educate an adequate number of technicians means the available pool is just adequate in the best of times. Automation of information and mechanical processes is slow, tied to evolving national standards, and poorly capitalized despite general recognition of system vulnerability.

The short shelf life of blood products means that inventory must be closely linked to immediate planned use. The size of local inventory is a compromise between ongoing day-to-day use and anticipated emergency need, with freshness sacrificed to build inventory and wastage the direct result of any lag in the demand for, or delivery of, blood products. In this sense, the management of liquid-stored cellular blood products is like that of fresh seafood or cut flowers.[17] Liquid storage systems can be made more effective, allowing somewhat longer storage and reducing losses, but the benefits are small.[18] Frozen storage is possible, but is expensive and labor-intensive and limited by process losses and low throughput.[19]

Transfusion medicine

In the United States, the use rate for RBCs is approximately 50 units per 1000 population.[20] Data concerning the recipients of the blood products are more difficult to obtain. A population-based study in Olmstead County covering the period from 1989 to 1992 found that 52 percent of RBC units were transfused into surgical patients.[21] More recent studies have suggested that medical patients are receiving a greater share of the transfused blood. Wells and coworkers[22] examined blood use in the north of England during two 14-day periods in 1999 and 2000 and found that 52 percent of RBCs were transfused for medical indications, with 41 percent for surgical patients and 6 percent for gynecologic or obstetric patients.[22] A study conducted of 175 randomly selected hospitals in France in 1997 revealed that 53 percent of patients receiving transfusions were on the medical wards including 30 percent on hematology wards.[23] Patients with neoplasms used 76 percent of PLT transfusions.

The academic specialty of transfusion medicine developed during and after World War II. As it has solved the technical problems of gathering and administering blood products, it has become more concerned with indications and safety. Recent attention has focused on the indications for RBCs, PLTs, and plasma and generally found that such products are overtransfused. Thus, Hebert and his colleagues[24] in the Transfusion Requirements in Critical Care (TRICC) study showed that the historic RBC transfusion trigger of 10 g of hemoglobin or 30 percent hematocrit (Hct) could be safely lowered in hemodynamically stable critical care patients with a 50 percent savings in blood product use and no worsening in mortality or morbidity. Studies have demonstrated a similar effect for PLT transfusion during leukemia induction therapy.[25,26] Dzik and Rao[27] have shown that plasma is administered frequently to prevent bleeding with invasive bedside procedures when the prothrombin and partial thromboplastin times are only mildly increased and that when plasma is administered, there is only rarely an improvement in the coagulation parameters.[28] In aggregate, these data suggest that many patients are exposed to blood products in situations in which they are unlikely to benefit. Enforcing blood use guidelines has worked best in conjunction with clear national standards, intensive education, and practice monitoring.

The coming pandemic: a projected scenario

The World Health Organization (WHO) has been following the H5N1 influenza activity in birds and people since the original outbreaks in Asia in the 1990s.[8] The disease has caused a high mortality in wild bird populations, has spread into domestic flocks, and has infected humans incidentally, in the context of close exposure to domestic poultry. In this form, it has infected 258 people over a decade and killed slightly more than half. There are no reports convincingly documenting human-to-human spread. The virulence of the virus might change if the virus evolves to allow efficient respiratory transmission in humans, but one could describe a likely clinical course based on past pandemics and the accumulated medical intelligence about the clinical course of the disease and the efficacy of drugs and vaccines.

The current planning model anticipates high infectivity, rapid worldwide spread in a matter of days to weeks, a broad range of severity of infection, rates of disability of 30 percent, and significant mortality. The basis for the model are described by the Interorganizational Task Force on Pandemic Influenza and the Blood Supply.[6]

Initial spread

The pandemic will probably start in Southeast Asia, where greater numbers of human beings live in close contact with domestic poultry than anywhere else on earth. There, national disease reporting systems may provide early warning and specimens for analysis by national and international reference labs. Attempts at quarantine may slow the spread of disease. Under the most optimistic of these scenarios, weeks might pass in a local epidemic phase, during which time knowledge of drug sensitivity might be established and some health care workers might be immunized with appropriate vaccines, with sufficient time to develop immunity. Under a less optimistic scenario, the virus might jump the species barrier and be transported in its human host on an airplane bound for the United States within a few days, causing a pandemic with very little warning.

Early response

With the recognition that an aggressive new influenza is threatening or active in the US, government, medical organizations, and the media will be deluged with questions and will be asked to provide information and guidance. Much of that guidance will be very general in nature, such as avoiding crowds, stocking up on canned food and water, and preparing for possible school closings and the reduced availability of goods and services. People who might have intended to donate blood will be presented with these other suggested activities and might be less willing to use potentially valuable gasoline to travel to a blood donation center or sit in a waiting room full of strangers.

Worsening crisis

As the number of individuals who are ill with influenza grows, two major effects will be seen. First will be an overwhelming utilization and depletion of hospital resources. Second will be the general social consequences of the accumulating loss of healthy workers.

Hospitals are the centerpieces of the national health care system, but a healthy population is only occasionally admitted to them and usually only for short stays. There were only 2.8 acute care beds per thousand members of the population in the United States in 2004.[29] More than 2000 hospitals were closed in the United States in the past two decades. By the time that one-half of 1 percent of the population needs medical care in an influenza pandemic, there will be two patients for every hospital bed in the country. Patients will be filling waiting rooms and lined up on gurneys in the emergency rooms, halls, and overflow areas of all public hospitals. There will not be enough staff to care for them, and medical and nursing students will be pressed into service to provide even minimal levels of care. Under these circumstances, it will not be possible to provide linens or remove waste. Caregivers will break down from exhaustion, frustration, and role confusion.

Hospital medical directors will have had to institute systems of triage. Care that can be deferred will have to be deferred. Care that is lifesaving and within the available resources will be undertaken. Care beyond the available resources should be deferred as well. Family members of patients can be expected to fight the decisions.

Blood donor centers will struggle to maintain donations of RBCs and PLTs. As increasing numbers of members of the population become ill or flee urban areas, regular donor roles will be decreased. Mobile blood drives to colleges will be lost as the education system closes, and blood drives to affinity groups such as churches will be limited as members' free time is filled caring directly for the sick. Mass media will still ask donors to come to blood centers, and moderate levels of donation will still go on. Getting blood tested for the usual infectious diseases will become more difficult as transportation and the productivity of regional reference laboratories degrades.

In the hospital transfusion services, maintaining staff for all work shifts will become increasingly difficult. Here, the loss of specific individuals, such as medical directors, supervisors, and lead technologists, will alter patterns of workflow that are written into policies and procedures and programmed into blood bank information systems. As remaining technologists are asked to assume responsibilities not usually their own, role confusion will occur. This will be especially evident in transfusion services

where a certain degree of obsessiveness is a basic job requirement, and the flexibility needed to deal with many kinds of stressful situations may be constitutionally lacking.

At some point early in the crisis, the FDA will issue guidance on how blood collection centers and transfusion centers may alter their function, because strict compliance with regulations and standards may no longer be possible. This was done at about midday on September 11, 2001, relaxing standards for training of individuals collecting blood, which allowed highly knowledgeable but not recently certified individuals to take part in blood collection.[30] The problem with such guidance is that it may not reflect the varied patterns of failure experienced by thousands of different transfusion services. It is difficult to imagine government guidance sufficiently broad to cover the situations of one hospital that cannot get a centrifuge repaired while another runs out of gloves.

At the height of the pandemic

By the time the pandemic reaches its peak, an estimated 30 percent of the population may be disabled by illness. Many more will be directly engaged in caring for ill family members. Emergency response personnel for other disasters (police, firefighters, electrical linemen, and communication workers) and regular workers involved in everyday commerce (production and transport of food and other basic supplies) will all be available in very reduced numbers. It will take longer to repair point failures in the electrical and telecommunications grids and water and sewerage systems. Secondary health crises will result. Even for healthy workers eager to do their duty, the increased demands of trying to find food and transport will degrade performance.

The blood system is very dependent on the rapid exchange of goods and services. Most notably, panels of reagent RBCs used for blood typing and antibody screening are collected by three companies in the United States and delivered under contract to thousands of hospitals every 3 weeks. It is likely that this part of the system will fail, that both blood collection centers and transfusion services would have to depend on forward-typing donor and patient cells with longer-lived monoclonal antibodies, and that the computer systems that manage labeling of blood products and routine blood typing will not work without this required data. The systems were often built without overrides for failures on such a basic level. The services will have to fall back on liquid cross-matching and paper records, more labor-intensive systems, precisely at a time when they are suffering from a severe labor shortage. PLTs are likely to be the first blood product where critical shortages are seen, but since PLT transfusions are given primarily to patients with hematologic malignancies, this will have its greatest impact on a subgroup of transfusion recipients.

Desperate situations frequently require desperate solutions, and it is often useful to know what other blood bankers have done in desperate situations in the past. In Sarajevo, during the siege in the early 1990s, artillery and sniper fire made the streets dangerous. Under these circumstances, citizens were instructed to send word to the blood center that they were willing to donate and teams of young people were trained to move quickly through the streets at night and collect individual blood units in basement shelters. Under such circumstances, the requirement for a predonation measure of the Hct was abandoned. The system worked well, providing the blood needs of citizens and the Bosnian defenders for 3 years (M. Haracic, NATO Blood Conference, 2000).

In Beruit, during the fighting in 1973 and again in 1982, the American University Hospital was isolated and cut off from supplies. Many workers could not get to the hospital because of the fighting, the bank was in danger of running out of blood bags, and gunmen were in the blood bank demanding rapid service for their comrades. Allam and his colleagues[31] describe the decision to collect only whole blood to reduce the use of bags and to issue group O un–cross-matched blood when workers were threatened.[31]

Finally, the US military has built up considerable recent experience with untested fresh whole blood in a variety of circumstances in Somalia, Bosnia, Kosovo, Iraq, and Afghanistan.[32,33] In Somalia, the force used its entire blood supply and needed more before resupply was possible. Blood was drawn from putative group O donors, type was confirmed by forward testing, and the blood given as fresh whole blood without further cross-matching. American soldiers are a relatively safe donor group in emergencies because they are routinely tested for human immunodeficiency virus and immunized for hepatitis B.

Recovery

After the peak of the pandemic, assuming there is only modest mortality, many of the absent workers will be returning to work. There will, however, be many competing demands for their efforts in restoring services and infrastructure. Some services will be relatively easy to restore, such as schools, where the buildings will be largely intact. Some teachers will need to be replaced and the social needs of grieving children will need to be addressed, but the mere act of opening the doors contributes in a major way to normality. Other parts of the social network will be harder to restore. Among the most difficult parts of a social system to rebuild will be those activities that are highly dependent on the specific knowledge of many individual people.[34]

The donor side of the blood system will recover relatively quickly. Its historic problem has been attracting donors, and after the pandemic, many survivors will be highly motivated to give. The return of manufacturing and transport will bring donor centers most of the supplies they need and, at a national level, temporary alternatives will be approved for the items that are not immediately available.

The transfusion service side of the blood system will be harder to rebuild. The loss of critical individuals and key bits of equipment will be random and each of the thousands of transfusion services will have unique problems. The chronic shortage of trained workers will only become worse. The national collapse in the supply of immunohematologic reagent RBCs will take time to replace, making more and novel work for limited staff. Many hospital blood bank computer systems, programmed by consultants before the disaster, will not have the flexibility to respond to the changing circumstances.

The need for well-trained and broadly experienced transfusion medicine specialists and blood bank technologists will be larger than the supply during and after the pandemic. This will create opportunities to expand training.

WHAT CAN BE DONE TO MINIMIZE THE DAMAGE AND MAXIMIZE OUR RESOURCES?

Planning for maintaining a blood system during a major influenza pandemic needs to address protecting personnel, recruiting donors, assuring access to supplies, preserving the function of equipment and facilities, and keeping a functioning management system.[35] Protecting personnel is best accomplished by vaccination and working for the designation of blood system workers as critical medical personnel who will be immunized or given oseltamivir chemoprophylaxis and access to rationed gasoline. Recruiting donors will require a clear public message and convenient and safe opportunities to donate. Access to consumable supplies, both perishable and durable, will require rethinking the limits of just-in-time logistics. High-volume supplies, such as test tubes and gloves, and short-lived supplies, specifically immunohematologic testing cells, will run out if a national disaster continues for many weeks. Deferred maintenance will degrade blood bank equipment and facilities. Modifying blood bank computer systems to allow workers to bypass steps involving temporarily nonexistent reagents will reduce role confusion and allow technologists to use the residual systems to manage inventory even as processes change. Ensuring the continuity of management will require both a plan and the ability to respond to an evolving situation.

Protecting all blood-system personnel, donors, workers, and managers is a major goal, and masks, social distancing, vaccines, and chemoprophylactics are the available tools. The utility of masks is unknown, and social distancing will be hard to achieve in many crowded facilities.[36] H5N1 research vaccines are available in very limited quantities, and stockpiles of oseltamivir are sufficient for only 1 percent of the US population.[2] Therefore, planning must start with the assumption of the temporary loss of 40 percent of all classes of personnel.

Loss of donors can partially be addressed with limited overcollecting in the early stages of a pandemic while there are still relatively full staffs at donor centers. This would allow limited stockpiling of RBCs and plasma and the provision of PLTs to continue while the pandemic takes shape. Because liquid RBCs are licensed for 5 to 6 weeks of storage, which is more than half of the 6- to 8-week length of the height of the 1918 pandemic in any given community, the potential of early excess collections to ease later shortages should not be lost.[2]

There is information supporting the use of RBCs beyond their current outdate. AS-1 RBCs were originally licensed for 7-week storage and worked as well at the end of that time as currently licensed 5-week CPDA-1 RBCs.[37] AS-3 RBCs have been tested for 8-week storage and could potentially be used for extended times as well.[38] PLTs are good in conventional storage for at least 7 days and were at one time licensed for that period. In emergencies, extending storage should be accompanied by careful inspection of bags for hemolysis of RBCs and loss of "swirling" in PLTs. Emergency rules for not discarding RBC units that have been out of the refrigerator for a little longer than 30 minutes should also be considered.[39]

Shortages of blood products will occur. Individual clinical services with the aide of blood bank medical directors will have to design triage schemes. Thus, a trauma service director might decide to set limits on which patients should be resuscitated given the restricted resources. In the United States, 10 to 15 percent of RBCs transfused are used in the setting of acute trauma.[20] A closer look at the recipients of these transfusions at one trauma center revealed that the majority of this blood was transfused into a very small fraction of the most critically injured patients: 3 percent of trauma patients received more than 70 percent of the RBCs transfused. Despite all efforts, the mortality for these massively transfused was 39 percent, half of this occurring in the first 24 hours.[40] In reduced circumstances of blood or nursing availability, mortality would be higher, care for such patients might be identified as futile, and resources could be directed elsewhere.

Chronic transfusion programs for genetic disease offer another example of a possible pattern for triage.

Individuals with thalassemia major do not make RBCs and need regular transfusions to survive. Efforts to transfuse them regularly need to continue through the crisis. On the other hand, individuals with sickle cell anemia on regular exchange transfusion programs to prevent stroke are exchanged monthly to reduce middle cerebral artery narrowing and increased flow velocity, which increased slowly when exchange was stopped.[41] More limited transfusion, rather than full exchange, would allow these individuals to get through a several-month-long critical period and free up blood and nurses for other efforts.

A significant fraction of blood products are given to patients with malignancies. The hematologic malignancies account for the majority of these products, in particular the PLTs. Slichter[26] has shown how the combination of lower PLT transfusion triggers and reduced PLT dosage can reduce PLT use by two-thirds. A UK study revealed that 33 percent of patients with solid tumors received at least one transfusion during the course of their therapy.[42,43] In the event of an influenza pandemic, careful consideration will need to be given to the risk:benefit ratio of cytotoxic chemotherapy with its attendant immunosuppressive effects. For instance, the result of adjuvant chemotherapy for Stage II breast cancer is a 9 percent net reduction in mortality in 5 years.[44] The acute mortality to be associated with being immunocompromised during an influenza pandemic is probably higher than that.

Transplant recipients, both solid organ and hematopoietic stem cell, are particularly susceptible to complications from influenza, with a relatively high rate of progression to viral pneumonia reported in some but not all series.[45,46] Because transplant patients are required to be in close contact with the health care system, more opportunities for exposure to the virus might exist. Infected transplant patients have been shown in some cases to shed viruses for extended periods. These safety concerns, both for the transplant patients and for the general population, might suggest to transplant program directors that a temporary suspension of transplant procedures would be in their patients' best interest. Given the likely shortage of hospital beds, health care workers, and ventilators in the event of a pandemic, this suspension would likely be encouraged by those in the health care system attempting to triage scarce resources. A temporary closure of the transplant program in Toronto was effected during the SARS epidemic, because of similar concerns.[47]

Transfusion service medical directors should make hospital medical directors and service chiefs aware of the limits of the blood supply. They should also reemphasize conservative blood use with its potential to prevent more than half of all transfusions. There are specific bits of knowledge that need to be reemphasized, such as the lack of benefit for RBC transfusion in helping patients get off of respirators and the evidence from a large consecutive series suggesting that lumbar punctures can safely be performed in children with low PLT counts.[24,48] Strict adherence to these guidelines will prevent the wasteful use of scarce resources, but there has been no effective educational intervention identified that will alter physicians' transfusion practices.[49] Empowering transfusion medicine experts to enforce these guidelines might be necessary so that blood products can be directed to those who need them the most.

In summary, influenza causes periodic pandemics. The H5N1 bird flu strain appears to be a potential agent for such a catastrophic event. Protection of the blood supply during a pandemic will require plans to protect donor center and transfusion service personnel, assure access to supplies and reagents, maintain equipment and facilities, and assure the continuity of management. Plans to manage blood use also need to be considered. Special attention needs to be given to the critical role of electronic information systems. The above insights on the nature of an influenza pandemic and on blood collection and use are offered as a contribution to the societal efforts that we collectively should be making to minimize the effect of a pandemic on public health and national welfare.

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