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Facing the Next Pandemic: Ready or Not

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ABSTRACT

Influenza pandemics generally occur at 30-40 year intervals and it has been nearly 40 years since the last one. A global pandemic will result in devastating social, economical, and health consequences. Preparedness is crucial to minimize the threat to hematopoietic stem cell transplant (HSCT) patients. Vaccines, antivirals, and infection control measures are important elements of prevention. Antivirals, often given presumptively, are the mainstay of therapy.
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KEY WORDS

Pandemic • Influenza • Emergency preparedness

INTRODUCTION

The severe acute respiratory syndrome (SARS) outbreak in 2003 reminded us of how globally interconnected we all are and the potential of infectious diseases to render all of us vulnerable to considerable threat. Recently, sporadic occurrences of type A(H5N1) influenza (avian flu) has emphasized the specter of pandemics to threaten not just individuals at risk but entire populations. Such fears of pandemics have been magnified by the laggard and uncoordinated emergency response to Hurricane Katrina and such an example teaches us of the importance of emergency preparedness and rapid response.

THE THREAT

Pandemics occur 3 or 4 times each century. In recent history, influenza pandemics occurred in 1918-1919, 1957-1958, and 1968-1969, and millions of deaths occurred worldwide with each instance. Even with wide availability of influenza vaccine and public health programs to encourage awareness and mass vaccination, each year 30 000-50 000 influenza deaths occur in the United States.

SARS, which is caused by a novel coronavirus, was first recognized in 2002-20023 in southern China and Hong Kong [1]. With global travel part of today's social fabric, this quickly became a pandemic. More than 8000 individuals in 29 countries became infected over a 7-month period, with a case fatality rate ranging from 6% to 17%. Despite modern medicine's molecular diagnostic tools, availability of rapid communication networks, and established public health ministries in virtually all affected countries, delays contributed to the spread of the disease. Remarkably, many victims were health care workers and transmission within hospitals and other health care settings was a major source of spread [2].

Today there is a substantial fear of the potential for avian influenza (H5N1) to cause a pandemic. Several avian influenza viruses have caused human illnesses over the years, but the H5N1 strain was first recognized to cause human infection in 1957 in association with a poultry outbreak in Hong Kong [3]. The case fatality rate was an alarming 33%. Multiple other poultry outbreaks have been noted in Asia in the past 3 yr [4]. More recently, spread of the virus has taken place by migratory bird populations [5]. More than 200 human cases have occurred, with a cumulative case fatality of approximately 50%. Although the current strains of H5N1 are poorly transmissible from human to human, reassortment of genes may occur to allow enhanced infectivity as has happened with other influenza strains and a pandemic could ensue [6]. The World Health Organization has warned that a global pandemic may be at hand.

A global pandemic will have serious social, economic, political, and health implications. Despite medical advances that could possibly mitigate an outbreak, there are many modern factors that will make spread a greater hazard today. Travel may spread the pathogen rapidly and to distant sites. Increasing concentrations of people in densely populated cities will

facilitate spread. There are much larger groups of highly immunocompromised patients who likely will have more severe disease and may shed larger numbers of virus particles and for longer durations, which could spread the infection more efficiently to others. These include patients who undergo HSCT and solid organ transplantation. The SARS outbreak had a profound effect on transplantation activities in the Toronto outbreak and necessitated cessation of transplantation activity [7]. It is highly likely that a global pandemic will have serious repercussions on HSCT programs and preparedness and rapid response are important to minimize threat to transplant recipients.

STEPS OF PREPARATION

Pharmaceuticals (vaccines and antivirals) are important tools for influenza prevention [8]. During nonpandemic years, influenza vaccination of patients after HSCT, families and caregivers of patients after HSCT, and the HSCT program staff should be vigorously encouraged. Currently, there is no H5N1 vaccine available, although research is ongoing. There is a real possibility that early during a pandemic a vaccine will not be available. Accordingly, antivirals are other important tools for prevention and treatment. There are 2 classes of influenza antivirals [9]. The adamantine drugs (amantidine and rimantidine), M2 inhibitors, are effective against influenza type A (but not type B). Unfortunately, H5N1 strains are resistant to amantidine [10]. In contrast, the neuraminidase inhibitors, oseltamivir and zanamivir, are effective against influenza types A and B, including amantadine-resistant strains. The neuraminidase inhibitors have been used in transplant recipients, found effective for influenza infections, are well tolerated, and lack significant interactions with immunosuppressive regimens. However, emergence of resistance has been reported in patients after HSCT [11]. It is expected that the neuraminidase inhibitors will be important as chemoprophylaxis in the event of an outbreak. One cautionary note is the observation of resistance in some H5N1-infected patients who did not respond to therapy [12].

Nonpharmaceutical measures are probably even more important steps of prevention [13]. Travel may need to be highly restricted to avoid spread. Infected patients or those with symptoms suggestive of infection should be isolated. Visitors or family members who have symptoms of influenza should avoid contact with patients after HSCT. Isolation should be maintained until the threat of shedding dissipates. Health care workers with symptoms suggestive of infections should also avoid contact with patients. During outbreaks aggregation of groups of individuals should be avoided. This will affect waiting areas of clinics and hospitals. Personal protection measures should be emphasized. Such measures include hand washing, wearing of masks, and respiratory hygiene. Ordinary surgical masks may offer protection against droplet transmission (thought to be the major mode of transmission), whereas the high-efficiency N95 mask offers additional protection against airborne transmission (thought to also be a mode of transmission, although much less important). The health care staff is at high risk of infection and should be provided maximal protection measures to optimize their ability to function and maintain morale.

RESPONSE ACTIONS

At the onset of an outbreak, it is important for the HSCT team to review its emergency preparedness plan and coordinate plans with the infection control team of the hospital. A suggested framework for HSCT programs has been formulated [14]. Supplies of masks and antiviral medications should be surveyed and fortified, if possible. Dispersal of patients away from the center may need to be considered to minimize spread. Consideration for closure of the program may be necessary if the extent of involvement of staff and general community threatens the center's access to vital resources to provide essential care.

Guidelines for identification of patients with H5N1 infection have formulated (for a regularly updated listing of H5N1-affected countries, see the World Organization for Animal Health Web site and the World Health Organization Web site). Testing for avian influenza A (H5N1) is indicated for hospitalized patients with (a) radiographically confirmed pneumonia, acute respiratory distress syndrome, or other severe respiratory illness for which an alternative diagnosis has not been established plus (b) a history of travel within 10 days of symptom onset to a country with documented H5N1 avian influenza in poultry and/or humans. Testing for avian influenza A (H5N1) should be considered on a case-by-case basis in consultation with state and local health departments for hospitalized or ambulatory patients with (a) a documented temperature >38°C (>100.4°F) plus (b) cough, sore throat, and/or shortness of breath plus (c) history of contact with poultry (eg, visited a poultry farm, a household raising poultry, or a bird market) or a known or suspected human case of influenza A (H5N1) in an H5N1-affected country within 10 days of symptom onset (http://www.cdc.gov/flu/avian/professional/han081304.htm).

Antiviral therapy with a neuraminidase inhibitor is crucial to minimize morbidity and threat to life. Early start of antiviral therapy optimizes the therapeutic benefit. Because each 12-h delay after onset of initial symptoms compromises benefit, initiation of therapy should be presumptive based on symptom assessment.

Involvement of extrapulmonary organs can occur with severe infection, including liver, kidneys, and central nervous system. There is anecdotal experience suggesting that treatment with high doses of corticosteroids may be of benefit but this has not been formally studied. Bacterial superinfections are frequent and antibiotics may be necessary. Vigilance for fungal superinfections should also be maintained.

CONCLUSIONS

Every 30-40 yr an influenza pandemic occurs. With global travel and commerce, the risk that a local outbreak can rapidly become widespread is high. Mitigation of the threat of a pandemic will require coordinated efforts of multiple countries and health and governmental authorities. Locally, prevention and treatment measures must be planned for to minimize threat to transplant recipients.

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