82 Prophylaxis of Healthcare Workers in an Influenza Pandemic

S. M. Moghadas

Abstract: The threat of an imminent influenza pandemic has galvanized global efforts to identify effective preparedness strategies and consider securing health resources. As the nations prepare to meet this threat, public health interventions are being carefully gauged within the context of influenza epidemiology, populations, and healthcare systems. A pandemic will place enormous demands on healthcare systems that include at the center of planning efforts the protection of healthcare workers. During an influenza pandemic, healthcare workers will be on the front lines delivering care to patients and preventing further spread of the disease. Protecting these workers from acquiring or transmitting infection in the hospital ward and outside the workplace is critical to containing a pandemic and limiting morbidity and mortality of the population. Several approaches to protecting healthcare workers include vaccination, antiviral ❯ prophylaxis, use of personal protective equipment, and adherence to other infection control practices. In the absence of vaccination, application of antiviral drugs has been rationalized as the first-line defense against the ❯ pandemic strain. While the treatment of ill individuals is top priority in most national contingency plans, the use of drugs as prophylaxis has been debatable. This chapter attempts to highlight the importance of a competent healthcare system in response to an influenza pandemic, and presents the conflicting issues that are surrounding an antiviral prophylaxis strategy. An overview of potential benefits and limitations, logistical constraints, and clinical and epidemiological consequences of healthcare worker prophylaxis is also provided.

List of Abbreviations: *ESP,* essential service personnel; *FAO,* Food and Agricultural Organization; *HCW,* healthcare worker; *WHO,* World Health Organization

1 Introduction

Influenza pandemics have occurred episodically for many centuries, with significant rates of morbidity, mortality and socioeconomic disruption (Potter, 2001). The 1918–1919 pandemic, the first of the three that occurred during the last century (❯ *Table 82-1*), proved the most devastating with an estimated 50 million deaths among countless infections worldwide (Taubenberger and Morens, 2006). There is mounting concern that the current avian strain H5N1, originated in Southeast Asia, may cause the next major global pandemic (Webster et al., 2006), with a toll that could exceed that of the 1918–1919 pandemic (Cox et al., 2003; Jennings and Peiris, 2006). The H5N1 strain has crossed the species barrier and shown the ability to replicate and cause fatal disease in humans (WHO Avian Influenza, 2008). Since populations are entirely immunologically naïve to this deadly virus, the conditions for a pandemic will be met through the emergence of a re-assorted viral strain that can sustain human-to-human transmission (American College of Physicians, 2006).

Given the uncertainties regarding the timing, origin, characteristics and virulence of a future pandemic strain, planning strategies for an effective response have become the priority of global public health efforts. Pandemic preparedness measures encompass disease surveillance, case identification and treatment, prevention of community-wide spread of disease, maintenance of essential services, research and evaluation (WHO Checklist for Influenza Pandemic Preparedness Planning, 2005). Specific approaches to influenza infection control include the use of pharmaceutical products (such as vaccines and antiviral drugs), and non-pharmaceutical measures (such as personal protective equipment and social distancing). During seasonal influenza epidemics, vaccination has proven the most effective strategy for

◘ Table 82-1

Influenza pandemics of the twentieth century

Pandemic	Virus strain	Estimated mortality
1918−19	A/H1N1 (Spanish flu)	50 million
1957−58	A/H2N2 (Asian flu)	2 million
1968−69	A/H3N2 (Hong Kong flu)	1 million

Influenza viral strains of pandemics in the twentieth century, with their estimated mortality worldwide (Potter, 2001; Taubenberger and Morens, 2006)

reducing the risk of infection and subsequent complications (Bridges et al., 2000; Nichol et al., 1995). However, the unknown characteristics of a pandemic virus pose major obstacles to developing new vaccine candidates, thereby limiting immunological control of the disease. Social distancing measures, including quarantine/isolation, school closure, cancellation of gatherings, and to some extent, travel restriction, have been considered as possible strategies during a pandemic (Inglesby et al., 2006). These measures have in general only limited impact on disease containment for several evidence-based reasons: (1) influenza viruses replicate rapidly to transmissible levels in a relatively short period of time, usually within the first day of exposure; (2) there is a pre-symptomatic stage associated with the disease, during which the virus can be shed before symptoms appear; and (3) a sizable portion of infected individuals may experience an asymptomatic infection, and transmit the virus (at a low rate) without being clinically recognizable (Baccam et al., 2006; Fraser et al., 2004). To overcome the existing limitations with these transmission reduction measures, response plans incorporate antiviral drugs as an important primary tool for prevention and treatment of pandemic infections (Democratis et al., 2006).

1.1 Antiviral Drug Use

Two groups of antiviral agents are currently available for the initial response to a pandemic (Hayden, 2004): M2 ion channel inhibitors (amantadine, rimantadine) and the more recent agents of neuraminidase inhibitors (zanamivir, oseltamivir). These drugs differ greatly in their clinical pharmacology, protective and treatment efficacy, and resistance selection profiles. The M2 inhibitors have been shown to provide partial protection as prophylaxis and to alleviate symptoms when used for early treatment, without affecting viral shedding (Jefferson et al., 2006). However, incidence of ❷ drug-resistance to M2 inhibitors has been associated with an increasing rate in seasonal epidemics, possibly through widespread or indiscriminate use of the drugs (Bright et al., 2005). The use of neuraminidase inhibitors in interpandemic influenza has been shown to be effective for both prevention and treatment (Halloran et al., 2006). They are also less prone to selecting for resistant mutations than M2 inhibitors (Moscona, 2005), and therefore offer a better option for pandemic preparedness.

A major concern of public health is the strategic use of antiviral drugs during pandemic influenza. One plausible policy, as considered in most pandemic plans (FAO United Nations, 2008; WHO, 2008), would be to focus primarily on the treatment of ill individuals and hospitalized patients in order to reduce morbidity and mortality of the population.

However, public health authorities are also concerned with questions related to delivery of adequate care and maintenance of key services and public order (American College of Physicians, 2006). To address these questions, a number of countries have included prophylaxis of healthcare and other essential community workers in the formulation of pandemic policies, which would require massive quantities of antiviral drugs to be stockpiled for the duration of a pandemic. The use of drugs for treatment or prophylaxis leads to subtle, yet very significant policy differences. While the inclusion of prophylaxis as a protective measure attempts to maintain surge capacity in the healthcare system, it entails a prohibitively expensive public health policy. Other factors that would significantly influence decisions regarding prophylaxis include the severity of the pandemic strain, the availability of antiviral drugs, and the impact of other intervention measures. Nevertheless, in the absence of vaccines, antiviral prophylaxis has the potential to offer a protection comparable to that induced by vaccination.

2   Surge Capacity in a Pandemic

The needs for pandemic preparedness are extensive and expensive, and appear to be beyond the response capacity of many countries. Even in non-pandemic times, healthcare systems in many parts of the world are stretched in meeting the need for regular services. While the demand for healthcare services will substantially increase during a pandemic, health resources will be more quickly depleted and there may be fewer healthcare workers available. Assuming a viral strain with 25–35% clinical attack rate over the estimated 8–12 weeks of a pandemic wave, a sizable portion of healthcare workers may become infected during the early stages of disease outbreaks (Gardam et al., 2007; Lee and Chen, 2007). The consequence is clear: a critical shortage of health personnel and care providers. While healthcare organizations often face staff-shortage during a natural disaster, the healthcare system may experience much higher absenteeism rates in the event of a pandemic. Considering the potentially reduced capacity of the healthcare system, and the lack of appropriate resources that is likely to arise, health professionals may be called upon to assume responsibilities outside their normal scope of practice. Such responsibilities may involve further exposure to the disease, and require strict adherence to infection control practices. In such circumstances, it is vital to ensure that healthcare workers are adequately protected and barriers to their participation are eliminated, especially in the presence of other potentially competing obligations that need to be addressed.

The diversity among healthcare workers and facilities makes preparation and response to a pandemic especially challenging. Healthcare facilities are magnets for individuals with influenza-related illness, and are at high risk of disruption during a pandemic, primarily due to hospital outbreaks of influenza that affect both patients and staff (Salgado et al., 2002). Such outbreaks can have serious consequences for a sustainable healthcare response: staff shortages can result or be exacerbated; admission maybe curtailed; and increased costs may be incurred. Published studies clearly demonstrate these outcomes (Horcajada et al., 2003; Lundstrom et al., 2002; Malavaud et al., 2001; Munoz et al., 1999; Sartor et al., 2002; Stott et al., 2002), and therefore preventing ❯ nosocomial spread of influenza is crucial for mitigating the impact of a pandemic on the population. While responding to the care of influenza patients, other health needs will continue and cannot be ignored during pandemic phases. Conventional wisdom considers access to inpatient and outpatient care to be central to any pandemic response. Were modern healthcare resources unavailable, ill individuals would not

be able to access antiviral drugs, antibiotics, oxygen therapy, intravenous therapy, intensive care, and other therapies. These modern options are essentially irrelevant without personnel, and their application requires a competent healthcare workforce, professional experience, and practice in order to minimize possible unintended health consequences.

Epidemiological and evaluation studies of seasonal influenza outbreaks provide convincing evidence that healthcare workers are central to any containment policy (Bridges et al., 2003), in particular to treatment and prophylaxis strategies. Given the potentially devastating health, economic and social consequences of a pandemic, preserving the capacity to deliver adequate, uninterrupted care to the ill is an unavoidable priority for preparedness strategies. Defining essential staff and services is an important component of pandemic planning, and should be integrated with the development of infection control protocols for triage, evaluation, prevention, and follow-up after exposure to disease.

3   Preventive Measures

Studies of the efficacy and effectiveness of influenza vaccines during seasonal epidemics reveal substantial benefits (❯ *Tables 82-2* and ❯ *82-3*), including reduced illness, mortality, hospitalization, absenteeism, costs of healthcare, and antiviral use (Bridges et al., 2000;

◘ Table 82-2

Effect of vaccination on healthcare personnel illness and absenteeism

Randomized trial 1 (Saxén and Virtanen, 1999)	Vaccinated	Controlled	Reduction (due to vaccination)
Days of lost work (due to respiratory infection)	1	1.4	28%
Days felt unable to work (whether on or off duty)	2.5	3.5	28%
Randomized trial 2 (Wilde et al., 1999)	Vaccinated	Controlled	
Days of lost work (due to illness)	9.9 (per 100 persons)	21.1 (per 100 persons)	53%
Total respiratory illnesses	28.7 (per 100 persons)	40.6 (per 100 persons)	29%
Incidence of influenza	1.7%	13.4%	87%
Cross-sectional survey (Lester et al., 2003)	Vaccinated	Unvaccinated	
Days of lost work (due to influenza-like illnesses)	63 (per 100 persons)	69 (per 100 persons)	0.08%
Influenza-like illnesses	42 (per 100 persons)	54 (per 100 persons)	22%
Days of illness	272 (per 100 persons)	374 (per 100 persons)	27%

The impact of influenza vaccination on healthcare personnel illness and absenteeism was evaluated in two randomized, placebo-controlled, double-blind trials (Saxén and Virtanen, 1999; Wilde et al., 1999), and a cross-sectional survey (Lester et al., 2003)

◘ **Table 82-3**

Cost-effectiveness of influenza vaccination of adults aged <65

Cost-effectiveness studies	Cost reductions
Healthcare provider visits	13–44%
Days of lost work	18–45%
Days of working with reduced efficiency	18–28%
Antibiotic use for influenza-like illnesses	25%

Cost reductions of influenza vaccination of adults aged <65 years associated with direct medical costs and indirect costs due to work absenteeism (Bridges et al., 2000; Nichol et al., 1995, 2003; Nichol and Mendelman, 2004)

Lester et al., 2003; Nichol et al., 1995, 2003; Nichol and Mendelman, 2004; Saxén and Virtanen, 1999; Wilde et al., 1999). However, the extent to which vaccination is successful depends largely on the antigenic match between the vaccine composition strains and the circulating viral strains (Bridges et al., 2000). The impact of vaccines on a pandemic can potentially be very significant, yet it remains to be proven in practice. While efforts are being made to shorten the delay in vaccine availability, retarding the progression of the first pandemic wave is essential for preventing excessive deaths and social disadvantages.

Without a pandemic strain vaccine, protection mechanisms are limited to antiviral drugs and infection control practices. The World Health Organization (WHO) recommends the use of non-pharmaceutical public health interventions in its updated influenza pandemic plan, to protect healthcare workers while providing care (WHO Writing Group, 2006). This update emphasizes the maintenance of capability/capacity for infection control and staff competency in use of personal protective equipment, such as gowns, gloves, and surgical masks. Although the use of such equipment may decrease the risk of transmission, the sheer number of encounters with infectious patients over the course of a working day would likely still result in disease transmission. Even with excellent infection control precautions, attack rates of greater than 10% are likely to occur among healthcare workers in the absence of vaccination (Salgado et al., 2002). Additionally, evidence suggests that infected individuals with developing or weakened immune systems (such as infants, elderly, and immunocompromised subjects) may suffer from prolonged illnesses and shed virus for several weeks, which makes transmission of the disease even more difficult to control in healthcare facilities and the community (Salgado et al., 2002). In a pandemic scenario, this would mean that a large part of the healthcare system, and particularly healthcare workers, will be at risk of repeated exposure. It is well recognized that even if protected at work, healthcare workers are just as likely as the general population to become infected outside of the workplace.

Infection spread among healthcare workers can promote institutional outbreaks (Horcajada et al., 2003). Investigations of host factors responsible for such outbreaks show that, in addition to suboptimal adherence to institutional infection control procedures, many affected healthcare workers with subclinical or even full clinical disease continue to work, thereby risking disease transmission to patients and colleagues (Salgado et al., 2002; Weingarten et al., 1989). Peer pressure from overworked colleagues, strong work ethics, and concerns regarding financial and employment security may motivate healthcare workers to work despite illness. Maintaining worker and patient safety is therefore a major challenge that may not be overcome simply by increasing emphasis upon compliance and appropriate use of personal protective measures. For healthcare workers, this could interfere with professional skills and affect the quality of

work-related interactions. However, infection control precautions may not be adequate to prevent the spread of disease among vulnerable healthcare workers and patients. The use of antiviral drugs for prophylaxis has been shown to be highly (70–90%) effective in reducing susceptibility to the disease (Halloran et al., 2006; Hayden, 2004; Monto, 2003), and decreasing the infectivity (if infection occurs) and absenteeism due to illness or concern over exposure to infection in the hospital ward (Lee and Chen, 2007). Although not a substitute for vaccination, antiviral prophylaxis appears to be a valuable strategy that affords immediate protection for individuals. Compared to vaccination, the cost of prophylaxis is prohibitive, yet far more economical than hospitalized care.
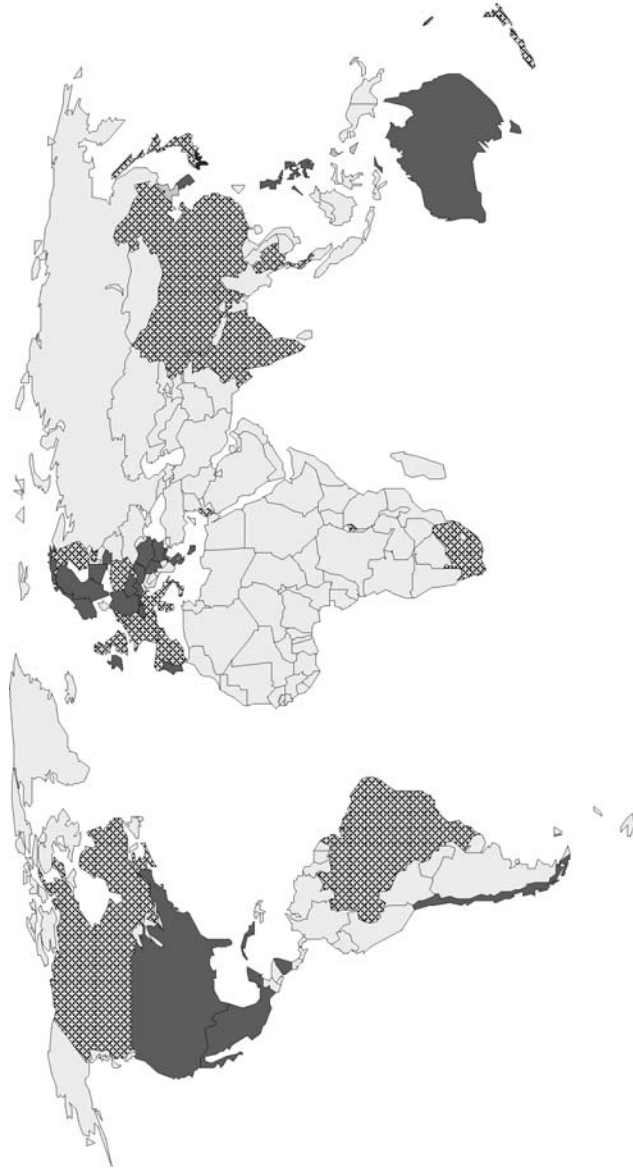
4　Prophylaxis of Healthcare Workers

For healthcare administrators and planners, key challenges for pandemic planning will include the degree of surge capacity necessary to maintain safe and effective delivery of healthcare, estimates of likely attrition among healthcare workers during a pandemic, and tradeoffs between worker and patient safety and health, such as those that may arise if antiviral drugs are used for healthcare worker prophylaxis rather than treatment of ill individuals. The latter issue has been a source of some controversy in preparedness strategies, as it is unclear whether hospitals would retain control over existing antiviral stockpiles in the event of a pandemic-related emergency. A recent study suggests that hospitals should consider stockpiling neuraminidase inhibitors for prophylaxis and treatment of healthcare workers (Cinti et al., 2005). While the proposed strategy focuses primarily on the treatment of ill healthcare workers, it emphasizes targeted prophylaxis of front-line healthcare providers. The outcome of this strategy may be potentially significant in mitigating pandemic burden, and two recent studies have addressed this effect through development of population dynamical models of influenza transmission (Gardam et al., 2007; Lee and Chen, 2007). Central to these models is the provision of antiviral treatment to the general population, by taking into account the availability of healthcare workers that is influenced by their reduced susceptibility to infection due to the protective efficacy of prophylaxis. Despite several limitations, these modeling efforts demonstrate that antiviral prophylaxis can substantially decrease absenteeism rates among key health personnel, and significantly reduce morbidity and mortality in the general population. However, both studies indicate that policy effectiveness depends critically on adequacy of the antiviral drug supply and the timely implementation of treatment and prophylaxis strategies.

Although several countries have followed guidelines issued by the WHO for formulating national preparedness strategies (❯ *Figure 82-1*), there remain discrepancies in planning for antiviral use, distribution, and priorities for treatment and prophylaxis. Most responding plans consider immediate treatment of ill individuals upon diagnosis as a more efficient approach to the use of drug stockpiles, and give priority to healthcare workers, essential and public safety staff, and those who are at risk of severe complications or death. However, antiviral prophylaxis has been a matter of ongoing debate for both logistical concerns and clinical-epidemiological consequences of viral evolution and transmission (Democratis et al., 2006; Lipsitch et al., 2007; Regoes and Bonhoeffer, 2006). ❯ *Figure 82-2* summarizes the likely prophylactic use of drugs for target groups of healthcare workers and essential service personnel in national pandemic plans published in the official websites of the Food and Agricultural Organization of the United Nations and the WHO National Influenza Pandemic Plans (FAO United Nations, 2008; WHO, 2008). Although recent studies provide scientific and

■ Figure 82-1

Global map of pandemic preparedness. ■ Countries with national plans that indicate prophylaxis of healthcare workers and/or essential service staff as part of their pandemic responses. ■ Countries with no, or not yet determined, prophylaxis strategy in their national plans. ☐ Countries with no published/accessible pandemic plans through official websites of the Food and Agricultural Organization of the United Nations, and the WHO National Influenza Pandemic Plans

◘ **Figure 82-2**

Prophylactic use of antiviral drugs in national pandemic plans. Among fifty-one published contingency plans for pandemic responses (FAO United Nations, 2008; Straetemans et al., 2007; WHO, 2008), healthcare workers are identified as the priority group for pre-exposure (long-term) prophylaxis in 17 national plans (Australia, Bahrain, Republic of Bulgaria, Chile, Czech Republic, Germany, Greece, Hungary, Lithuania, Montenegro, Nicaragua, Norway, Republic of Serbia, Sweden, Switzerland, Timor Leste, United States), and for post-exposure prophylaxis in eight plans (Austria, Cuba, Ireland, Republic of Korea, Mexico, Philippines, Portugal, Singapore). Essential service personnel are given priority for long-term prophylaxis in seven plans (Republic of Bulgaria, Chile, Czech Republic, Greece, Nicaragua, Norway, Sweden), and for post-exposure prophylaxis in six plans (Australia, Montenegro, Philippines, Portugal, Republic of Serbia, Singapore). A number of these plans indicate that the decision on prophylactic use of drugs may be influenced by the availability of vaccines and the size of antiviral stockpiles, in addition to the severity of the pandemic strain. Twenty-five national plans (Belgium, Brazil, Canada, China, Republic of Estonia, Finland, France, Hong Kong, India, Italy, Japan, Luxemburg, Nauru, Netherlands, New Zealand, Nouvelle-Calédonie, Palau, Poland, Rwanda, Slovak Republic, South Africa, Spain, Thailand, United Kingdom, West Bank/Gaza) indicate no specific strategy for prophylaxis of healthcare workers or essential service personnel. Most plans suggest that the strategic use of drugs should be re-evaluated during different phases of the pandemic, so that necessary modifications to antiviral strategies can be made in a timely fashion
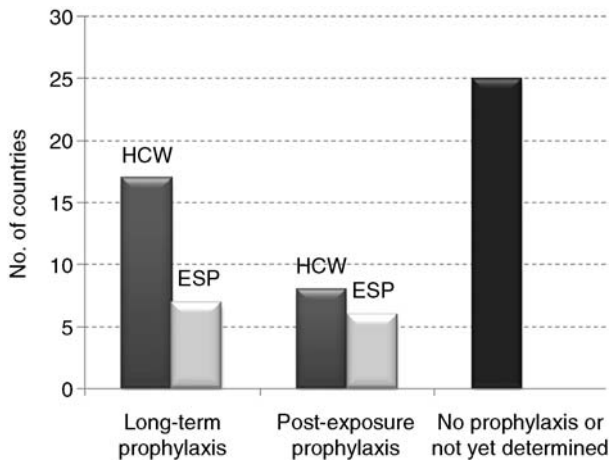
administrative frameworks for prophylaxis strategies that can effectively protect the healthcare workforce in the face of infectious disease threats (Cinti et al., 2005; Toner and Waldhorn, 2006; Xiong et al., 2007), precise planning for antiviral use is hindered by several unknowns – in particular, the transmissibility of the pandemic strain, effectiveness of drugs, and the impact of other curtailing measures. There is also much uncertainty about how a novel influenza strain would affect different populations with distinctly different mobility patterns, healthcare expenditures, and economic structures. The nature of the next influenza pandemic cannot be predicted with certainty, but the high mortality rates among younger adults in past pandemics compel us to consider maximizing the protection of healthcare workers by using available means of reducing disease transmission.

5   Benefits, Logistical Constraints, and Consequences of Prophylaxis

Considering the limited capacity of vaccine production that is concentrated in a very few countries (Fedson, 2003), antiviral drugs will likely be the primary control measure for several months following the emergence of a pandemic strain. Yet more frightening, antiviral therapy may be the only pharmaceutical option for many countries during the entire course of the pandemic. Stockpiling adequate supplies of drugs has therefore become a critical component of pandemic preparedness strategies. However, a major challenge is to define priority groups and formulate antiviral policies that are most likely to optimize the health of the greatest number of individuals in the face of an influenza pandemic.

In allocating antiviral drugs, it will be necessary to rate the relative importance of treatment and prophylaxis in avoiding complete coverage of the population, particularly when considering insufficient quantities of drugs, limited production capacity, and a surge in demand for antiviral therapy with the progression of a pandemic (Democratis et al., 2006). These contrasting factors highlight the importance of prioritizing public health policies that maximize both short-term population-wide benefits and long-term epidemiological effects of antiviral therapy. Published modeling studies suggest that the pandemic can be contained at the source if early treatment of diagnosed cases is combined with targeted blanket prophylaxis and social distancing measures (Ferguson et al., 2005; Longini et al., 2005). Significant assumptions are embedded in the core of such models, most of which are unlikely to be fulfilled in a real world environment, and therefore containment failure should be anticipated in devising effective preparedness countermeasures.

Clearly, targeted strategies are needed to optimize the use of available supplies of antiviral drugs, and precise planning should be based on pandemic-specific response goals for mitigating the overall disease burden. Long-term prophylaxis of healthcare workers and emergency service personnel may be beneficial in terms of reducing viral transmission between interconnected subpopulations with high levels of exposure, thereby preventing impending institutional outbreaks and staff demoralization, maintaining the quality and accountability of healthcare, and decreasing mortality of the general population. However, this strategy would require a prohibitively large drug stockpile, and delay the progression of the pandemic by the period for which prophylaxis is provided. Regardless of the level of stockpiles, substantial logistical challenges will arise for practical implementation of this strategy that need to be addressed, let alone its possible long-term epidemiological outcomes that may be disadvantageous to the control of disease. Key issues include, but are not limited to, determining target groups, potential regulatory barriers to dispensing, labor consequences that may arise from targeting specific sectors in healthcare and emergency departments but not others, and monitoring antiviral drug use, efficacy, and safety. Targeted ❯ post-exposure prophylaxis could provide significant benefits, but it would still require much greater stockpiles than currently provided.

5.1   Antiviral Resistance

Although antiviral therapy appears to be crucial in any containment strategy, the emergence of drug-resistance will impose significant threats to the effectiveness of drugs for both treatment and prophylaxis (Moscona, 2005). Early treatment largely inhibits generation of resistant viruses by suppressing viral replication, but results in a longer time for selection in favor of pre-existing resistant mutants (Moghadas et al., 2008). Prophylaxis blocks the

transmission of the drug-sensitive strain more effectively, but contributes to the emergence of resistance in the population by increasing the pressure for selection and spread of resistant viruses (Lipsitch et al., 2007; Regoes and Bonhoeffer, 2006). The interplay between these opposing effects appears particularly important for determining the advantages and disadvantages of population-specific antiviral strategies. Previous studies suggest that, in the absence of drug-resistant viruses, targeted prophylaxis of healthcare workers can substantially limit the community-level transmission of disease, by providing considerable protection to those who contribute to caring for influenza patients (Gardam et al., 2007; Lee and Chen, 2007). However, should resistance emerge during the early stages of a pandemic, this strategy may promote population-wide spread of drug-resistance through intense contacts with patients and colleagues in the healthcare setting and contacts outside of the workplace. As has been evident in the experience with outbreaks of Severe Acute Respiratory Syndrome (SARS) in 2003, hospitals and other healthcare facilities are particularly important resources for disease control, but they may also serve as "hot spots" for disease transmission, with subsequent hospital-to-community spread (Loutfy et al., 2004).

6   Concluding Remarks

The impact of the next influenza pandemic may be catastrophic worldwide, particularly for nations with poor healthcare resources and fragile economies. Ongoing efforts may not be sufficient to combat it or prevent every single death, but the basic tenet of pandemic preparedness is not to miss the unprecedented opportunity provided by the increased awareness of the potential devastation of the next influenza pandemic. To a large degree, it will run its course; however, the healthcare system and society will need to prepare for a rapid and effective response by developing system-wide contingency plans that accommodate the full spectrum of harms related to pandemic influenza and benefits related to control activities. Historical precedent, from both seasonal influenza epidemics and the 1918–1919 influenza pandemic, suggests that an emergent influenza strain with high ❯ pathogenicity would severely tax existing health resources, and force healthcare administrators and providers alike to make difficult decisions that may include rationing of scarce resources (e.g., antiviral drugs, intensive care beds, and ventilators) and decisions that violate the autonomy of the individual (e.g., forced quarantine or isolation of individuals). The ethical framework of such decisions is complex; however, evaluation of the potential benefits, costs, and limitation of competing strategies, as well as the resources and practices required to achieve best outcomes, will allow planners and providers to balance the protection of community health against individuals' rights and freedoms in the context of influenza infection control.

Summary Points

- Effective protection of healthcare workforce during an influenza pandemic is an essential priority of pandemic preparedness endeavors, and should be based on scientific knowledge and evidence of disease transmission, prevention, and mitigation. Such protection must address the diversity of institutional activities with varying degrees of exposure to the disease.
- Considering the nature of interaction between ill individuals and healthcare workers, the lack or poor administration of preventive measures will leave healthcare workers highly vulnerable to the infection, and therefore the surge capacity required to treat influenza patients could be severely impaired.

- Prophylaxis of healthcare workers is an essential protective mechanism that can maintain the capacity to cope with the increased demand for healthcare, prevent nosocomial outbreaks and further spread to the community, and reduce morbidity and mortality of the general population.
- An effective vaccine may not be available for several months following declaration of a pandemic. Preparedness efforts should therefore include securing antiviral supplies, particularly when prophylactic use of drugs is planned for limiting disease propagation locally as well as globally.
- Significant logistical challenges lie at the heart of prophylaxis strategies for healthcare workers and essential service personnel that must be addressed. Scarce supplies of antiviral drugs create ethical dilemmas of distribution priorities and target groups. These ethical considerations must be taken into account for rationing of limited stockpiles.
- Antiviral treatment can induce a massive selective pressure on the drug-sensitive pandemic strain, resulting in the clinical outcome of developing drug-resistance. Prophylactic use of drugs can substantially enhance the spread of drug-resistance in the population due to a significant reduction in susceptibility to the drug-sensitive strain.
- In order to prevent unintended epidemiological consequences of drug therapy, antiviral strategies should be re-evaluated during the progression of the pandemic and necessary adaptations should be rapidly implemented to prevent subsequent outbreaks of drug-resistant infections.
- In order to identify more tangible antiviral strategies with a global perspective, similarities and differences in pandemic plans with respect to the use of antiviral drugs and priority groups for treatment and prophylaxis should be carefully examined.
- Development of appropriate mathematical models for disease management can help evaluate the potential impact of various public health intervention strategies, optimize health policy decisions, and maximize population-wide benefits of scarce health resources.

References

American College of Physicians. The Health Care Response to Pandemic Influenza. Philadelphia, American College of Physicians, 2006.

Baccam P, Beauchemin C, Macken CA, Hayden FG, Perelson AS. (2006). J Virol. 80: 7590–7599.

Bridges CB, Kuehnert MJ, Hall CB. (2003). Clin Infect Dis. 37: 1094–1101.

Bridges CB, Thompson WW, Meltzer MI, Reeve GR, Talamonti WJ, Cox NJ, Lilac HA, Hall H, Klimov A, Fukuda K. (2000). JAMA. 284: 839–844.

Bright RA, Medina MJ, Xu X, Perez-Oronoz G, Wallis TR, Davis XM, Povinelli L, Cox J, Klimov AI. (2005). Lancet. 366: 1175–1181.

Cinti S, Chenoweth C, Monto AS. (2005). Infect Control Hosp Epidemiol. 26: 852–854.

Cox NJ, Tamblyn SE, Tam T. (2003). Vaccine. 21: 1801–1803.

Democratis J, Pareek M, Stephenson I. (2006). J Antimicrob Chemother. 58: 911–915.

FAO United Nations. (2008). http://www.fao.org/avian-flu/en/national.html

Fedson DS. (2003). Clin Infect Dis 36: 1552–1561.

Ferguson NM, Cummings DAT, Cauchemez S, Fraser C, Riley S, Meeyai A, Iamsirithaworn S, Burke DS. (2005). Nature. 437: 209–214.

Fraser C, Riley S, Anderson RM, Ferguson NM. (2004). Proc Natl Acad Sci USA. 101: 6146–6151.

Gardam M, Liang D, Moghadas SM, Wu J, Zeng Q, Zhu H. (2007). J R Soc Interf. 4: 727–734.

Halloran ME, Hayden FG, Yang Y, Longini IM Jr, Monto AS. (2007). Am J Epidemiol. 165: 212–221.

Hayden FG. (2004). Pediatr Infect Dis J. 23: S262–S269.

Horcajada JP, Pumarola T, Martínez JA, Tapias G, Bayasz JM, de la Prada M, García F, Codina C,

Gatell JM, Jiménez de Anta MT. (2003). Eur Respir J. 21: 303–307.

Inglesby TV, Nuzzo JB, O'Toole T, Henderson DA. (2006). Biosecur Bioterror. 4: 1–10.

Jefferson T, Demicheli V, Rivetti D, Jones M, Di Pietrantonj C, Rivetti A. (2006). Lancet. 367: 303–313.

Jennings LC, Peiris M. (2006). Inter Med J. 36: 145–147.

Lee VJ, Chen MI. (2007). Emerg Infect Dis. 13: 449–457.

Lester RT, McGeer A, Tomlinson G, Detsky AS. (2003). Infect Control Hosp Epidemiol. 24: 839–844.

Lipsitch M, Cohen T, Murray M, Levin BR. (2007). PLoS Med. 4: e15.

Longini IM Jr, Nizam A, Xu S, Ungchusak K, Hanshao-workakul W, Cummings DAT, Halloran ME. (2005). Science. 309: 1083–1087.

Loutfy MR, Wallington T, Rutledge T, Mederski B, Rose K, Kwolek S, McRitchie D, Ali A, Wolff B, White D, Glassman E, Ofner M, Low DE, Berger L, McGeer A, Wong T, Baron D, Berall G. (2004). Emerg Infect Dis. 10: 771–776.

Lundstrom T, Pugliese G, Bartley J, Cox J, Guither C. (2002). Am J Infect Control. 30: 93–106.

Malavaud S, Malavaud B, Sanders K, Durand D, Marty N, Icart J, Rostaing L. (2001). Transplantation 72: 535–537.

Moghadas SM, Bowman CS, Röst G, Wu J. (2008). PLoS ONE. 3: e1839.

Monto AS. (2003). Vaccine. 21: 1796–1800.

Moscona A. (2005). N Engl J Med. 353: 2633–2636.

Munoz FM, Campbell JR, Atmar RL, Garcia-Prats J, Baxter BD, Johnson LE, Englund JA. (1999). Pediatr Infect Dis J. 18: 811–815.

Nichol KL, Lind A, Margolis KL, Murdoch M, McFadden R, Hauge M, Magnan S, Drake M. (1995). N Engl J Med. 333: 889–893.

Nichol KL, Mallon KP, Mendelman PM. (2003). Vaccine. 21: 2207–2217.

Nichol KL, Mendelman P. (2004). Virus Res. 103: 3–8.

Potter CW. (2001). J Appl Microbiol. 91: 572–579.

Regoes RR, Bonhoeffer S. (2006). Science. 312: 389–391.

Salgado CD, Farr BM, Hall KK, Hayden FG. (2002). Lancet Infect Dis. 2: 145–155.

Sartor C, Zandotti C, Romain F, Jacomo V, Simon S, Atlan-Gepner C, Sambuc R, Vialettes B, Drancourt M. (2002). Infect Control Hosp Epidemiol. 23: 615–619.

Saxén H, Virtanen M. (1999). Pediatr Infect Dis J. 18: 779–783.

Stott DJ, Kerr G, Garman WF. (2002). Occup Med. 52: 249–253.

Straetemans M, Bochhols U, Reiter S, Haas W, Krause G. (2007). BMC Public Health. 7: 236–247.

Taubenberger JK, Morens DM. (2006). Emerg Infect Dis. 12: 15–22.

Toner E, Waldhorn R. (2006). Biosecur Bioterror. 4: 397–402.

Webster RG, Peiris M, Chen H, Guan Y. (2006). Emerg Infect Dis. 12: 3–8.

Weingarten S, Riedinger M, Bolton LB, Miles P, Ault M. (1989). Am J Infect Control. 17: 202–207.

WHO. (2008). http://www.who.int/csr/disease/influenza/nationalpandemic/en/index.html

WHO Avian Influenza. (2008). http://www.who.int/csr/disease/avian_influenza.

WHO Checklist for Influenza Pandemic Preparedness Planning. (2005). http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_4/en/

WHO Writing Group. (2006). Emerg Infect Dis. 12: 81–87.

Wilde JA, McMillan JA, Serwint J, Butta J, O'Riordan MA, Steinhoff MC. (1999). JAMA. 281: 908–913.

Xiong W, Hollingsworth E, Muckstadt J, Vorenkamp JVL, Lazar EJ, Cagliuso NV Sr, Hupert N. (2007). Infect Control Hosp Epidemiol. 28: 618–621.