Review Article

A Global Perspective on Avian Influenza

Adrian Ong,[1] *MBBS, Dip ABIM (Inf Dis), MPH*, Mary Kindhauser,[1] *MA*, Ian Smith,[1] *MB,ChB, MPH*, Margaret Chan[2]

Abstract

Global public health security is both a collective aspiration and a mutual responsibility that demands cooperative action at all levels. The expansion of the current H5N1 avian influenza enzootic and its incursion into human health presents a real and significant threat of an influenza pandemic. The world has for the first time an unprecedented opportunity for pandemic preparation. Current global efforts to tackle the H5N1 pandemic threat are centred around the framework of the International Health Regulations (2005) that requires countries to openly share disease intelligence including clinical samples, viruses and epidemiological information. Present international initiatives also seek to establish more equitable allocation and sharing mechanisms for developing countries, of therapeutic resources, public health interventions and other broad-based support in the event of a pandemic. To be sustainable, country preparatory efforts need to be integrated within wider national emergency preparedness frameworks and emphasise the strengthening of basic capacities in disease surveillance, outbreak response and health systems that can respond to a range of public health emergencies. Such capacity building represents permanent investments in health that will have enduring benefits beyond a pandemic. Preparations must also go beyond the health sector; greater promotion of intersectoral cooperation and an adoption of a whole-of-society approach to preparation is recommended. Broad collaboration is vital in addressing the complex challenge posed by influenza to our collective security.

Ann Acad Med Singapore 2008;37:477-81

Key words: H5N1, Health security, Pandemic, Public health

Introduction

The world is confronted by many important public health challenges, some of which constitute potentially devastating global threats. Prime among these is the threat of a influenza pandemic. It is a possibility made more real by the emergence and multi-regional spread of highly pathogenic avian influenza A (H5N1). This epizootic has captured the attention of the international community and alerted the world to the prospects of a potentially devastating human health challenge. Since its first appearance in humans in 1997,[1] the H5N1 virus has not gone away, nor has it become less lethal nor less widespread in birds. On the contrary, its evolving ecology and persistence in wild animal reservoirs represents a real and sustained hazard, increasing the possibility that it may mutate into a pandemic strain. As long as this virus continues to circulate in animals, the risk of an influenza pandemic is immediately present.

Our concern for a future influenza pandemic is founded on a strong historical base. Influenza pandemics are natural phenomena that have occurred periodically for centuries. Further, the conditions for the emergence and spread of novel influenza viruses have not abated. In the previous century, the world has experienced 3 pandemics. Of these, the great pandemic of 1918-1919 is regarded as the most deadly disease event in the history of humanity.

The geographic persistence of H5N1, its continued spread and wide host range is both unprecedented and worrisome. Never before has a highly pathogenic avian influenza caused outbreaks in so many countries at once; never before has the disease spread so widely and rapidly to affect such huge geographical areas. The H5N1 epizootic is the most visible and worrisome threat presently. The possibility, however, of other novel pandemic agents arising should not be overlooked. Another pandemic from a novel

[1] World Health Organization, Geneva, Switzerland
[2] Director-General, World Health Organization, Geneva, Switzerland
Address for Correspondence: Dr Adrian Ong, World Health Organization, 20 avenue Appia, 1211 Geneva 27, Switzerland.
Email: onga@who.int

H2, H5, H6, H7 or H9 subtype – remains possible and cannot be ignored.[2]

Given the recurring pattern of pandemic influenza, 2 certainties and 2 unknowns confront us. First, it is almost certain and realistic to assume that an influenza pandemic will recur in the future; secondly, knowing this, it is incumbent upon us to organise and prepare for this contingency. We have at hand an extraordinary situation – never before has the world watched as the conditions conducive to a pandemic unfold in real-time. This has given us an opportunity for pandemic preparation that is unprecedented in history; it is a chance the international community would be remiss to squander.

These 2 certainties are tempered by 2 equally large unknowns – the timeframe and the virulence of a subsequent pandemic virus. In the past, pandemics have behaved as unpredictably as the viruses that caused them with great variations seen in mortality, severity of illness and patterns of spread. Given these ambiguities surrounding when the next pandemic will occur and how deadly it will prove, contingency plans must be put in place now during this inter-pandemic period, that are sufficiently flexible to respond to different patterns of disease.[3] Efforts must continue during this afforded 'lull' to put in place the system capacities and resources needed to mitigate a future pandemic crisis.

These messages have been widely iterated and well-heeded by the global community. Accordingly, there has been much global activity since the first sounding of this alert by the World Health Organization (WHO) just over a decade ago. Potential vaccines have been developed, antivirals have been stockpiled and national preparedness programmes developed. Yet much more remains to be done.

In addressing this complex threat, a few clear priorities and issues have become evident. First, we must not and cannot relent in our current response to human cases of H5N1 and the corresponding threat of an influenza pandemic. Present approaches require the sustained and long-term commitment of all stakeholders; this opportunity must be used wisely. Further, neither our knowledge nor our tools are currently adequate – many gaps still exist in our understanding of the virus and in the implementation of mitigation strategies. Improving our science and the global capacity for response is an urgent task. Finally, the scope of this threat demands the collaboration, at all levels, of diverse agencies and sectors beyond those of health alone. The international, public health, veterinary, agricultural and business communities are confronted with a multifarious virus that traverses multiple sectors and borders, requiring cooperative action between all and by all. It must be remembered that regardless of when a pandemic occurs and which virus causes it, all our present efforts in building capacities and systems to cope with such an event represent permanent investments in health that will have enduring benefits beyond a pandemic.

Keeping the Momentum

At the international level, the relationship between health and security faces many new challenges (and opportunities) in an increasingly globalised world characterised by the unprecedented speed and volume of international travel, the interdependence of businesses and financial markets, and the interconnectedness brought on by the revolution in information technology. Acute threats to human health posed by conflicts, disease outbreaks, natural disasters and zoonoses have become a larger menace in a globalised society. The 2003 outbreak of the severe acute respiratory syndrome (SARS) – the first severe new disease of the 21st century – demonstrated how much the world has changed in terms of its vulnerability to emerging diseases. It underscored the need for international solidarity against threats that can spread readily and widely – with highly adverse consequences for economies and societies as well as public health.

As the emergence of diseases is tied to fundamental changes in the way humanity inhabits the planet, more new diseases can be anticipated as this century progresses.[4] In particular, the behaviour of emerging and epidemic-prone diseases has made all nations acutely aware of their shared vulnerability and their shared responsibility for mutual self-protection. Global public health security is thus both a collective aspiration and a mutual responsibility.

Pandemics may be expected, albeit not predicted. Although the world is now far better prepared than ever to face the next influenza pandemic, this must not lead to complacency. Our present initiatives and response to avian influenza should not be viewed from the perspective of solely preparing for the next possible pandemic event; such an approach will inevitably lead to policy fatigue if the expected pandemic does not emerge soon and to a boom-bust policy cycle if it does. Instead pandemic influenza preparedness should be addressed as part of a sustained long-term programme aimed at strengthening health systems and collective global security, a win-win situation that will be beneficial even in the absence of a pandemic.

It is appreciated that pandemic preparedness activities take place within the context of competing national priorities and limited resources. Thus, a sustainable approach to preparation should see the integration of pandemic preparedness into general national emergency preparedness frameworks and activities; the strengthening of basic capacities required for diverse public health emergencies; and the use of preparedness activities to actively build upon

communication channels with communities to strengthen health education and information dissemination while building trust.

Assessment, preparedness and response constitute the 3 main elements of a comprehensive approach for addressing the threats posed before, during and after an influenza pandemic. Five essential action strategies put forward by WHO to reduce the risk of a pandemic focus on reducing human exposure, intensifying capacity for rapid containment, strengthening early warning systems and disease intelligence, rapid investigation of human cases and clusters and building general capacity for health.[5] A sixth strategy focusing on preparedness within the non-health sector is being developed. Other leading priorities include addressing global concerns over food safety, infection control and ensuring global resilience in influenza vaccine production capacity.[6] These and other strategies now under way must be sustained and intensified given the real and present danger posed by the current epizootic expansion of H5N1 virus.

Initiatives to address pandemic preparedness have also stimulated broad global debate on a number of related touchstone issues. Linked to the process of improving international cooperation and outbreak intelligence (including virus sharing for risk assessment), have arisen important considerations around global solidarity, distributive justice, trade, globalisation and intellectual property rights.

During a pandemic, there will almost certainly be extreme scarcity of countermeasures especially in the short term. Resources will be limited and unevenly available. Even wealthy countries may lack sufficient means for protecting their own citizens. It will, however, disproportionately negatively impact socially and economically disadvantaged populations as well as developing countries,[7] where limited resources and immediate healthcare needs hamper their ability to implement adequate pandemic responses.[8] Many hospitals in developing countries are already close to the brink of collapse with beds full with AIDS, tuberculosis (TB) and malaria patients; home isolation recommendations would be of little value in extended African and Asian families that often live under one roof. Further, the next influenza pandemic would be the first after the emergence of HIV and the potential effect that it would have on the approximately 35 million people currently infected with HIV – more than two-thirds of whom live in sub-Saharan Africa – is concerning.[9]

Yet developing countries comprise an integral part of the global health security framework through their provision of disease surveillance, outbreak response and research. It is thus important that the benefits derived from this collective mechanism necessarily extend to developing countries, providing them with more equitable allocation and access to therapeutic resources, public health interventions and other broad-based support in the event of a pandemic. The universal nature of the pandemic threat calls for universal preparedness, or at least greater fairness in preparedness.

In recognition of this need, critical reviews of international cooperative frameworks and mechanisms around virus and benefit sharing,[10] and to research and innovation[11] are presently being undertaken. These processes have broad application to many other areas of public health where issues of equitable access to finite resources and the benefits of modern science are also central. As critical as these current appraisals are, however, they should not impede existing mechanisms, especially in the area of seasonal and pandemic influenza surveillance, that must necessarily continue to function in the interim.

Closing the Gaps

A future pandemic will throw into sharp relief the strengths and weaknesses of infrastructures designed to protect the public on a daily basis. To ensure global health security, 2 interrelated strategies are required: a significant strengthening of public health within both developed and developing countries and the establishment of mechanisms that facilitate the collaborative action of countries. The Global Outbreak Alert and Response Network (GOARN), which proved instrumental in the response to SARS, is one such mechanism. The revised International Health Regulations (IHR) are another. These Regulations, which came into force in 2007, include key provisions for surveillance and notification to WHO of "events which may constitute a public health emergency of international concern" which include cases of a new subtype of influenza.[12] It is within the framework of the IHR that current global efforts to the tackle the H5N1 pandemic threat are being centred. Strong international mechanisms for responding to emergencies, however, can never fully compensate for weak national capacities in health.

During a pandemic, one may envision in many countries not only shortages in countermeasures, but a more general situation of distress throughout the medical system. An influenza pandemic is a classic surge crisis and health systems in many countries, already under-resourced and under-staffed, will struggle to deal with the extra stress imposed. Equipment, facilities and essential personnel will be in short supply. Moreover, a prolonged effect on individuals and communities beyond the immediate period of disease will be expected to weigh upon local organisations and services.

Substantial progress in pandemic preparedness has been made during the years since the H5N1 virus first appeared. We need now, however, to shift some of our efforts from a

crisis mode of identifying and dealing with avian outbreaks, to greater emphasis on building long-term health capacity so that we can be better prepared to respond – nationally, regionally, and globally – to any pandemic, as well as to a broader range of emerging infectious disease threats. Such essential activities encompass improving primary healthcare services, respiratory disease surveillance and laboratory diagnostic capacities within countries. It also necessitates closing the gaps in health systems, mitigation protocols and the availability of therapeutics (including vaccines) that will be required to support a comprehensive and timely response to a pandemic.

Current global capacity to produce a vaccine to respond to an influenza pandemic is insufficient to meet the overall anticipated need. Experts now predict that global production capacity will rise to 6.2 billion pandemic immunisation courses per year in 2010.[13] Although this is significant progress, it is still short of the targeted 6.7 billion immunisation courses that would be needed in a six month period to protect the whole world. The WHO Global Pandemic Influenza Action Plan to Increase Vaccine Supply provides a strong framework for response to this shortfall.[6] Its implementation, however, must be accelerated and underpinned by strong political impetus and financial support, to further bridge the still substantial gap between supply and demand.

WHO has also developed a protocol outlining how the first emergence of a pandemic virus might be rapidly contained before it has spread widely[14] and given guidance on pre-pandemic national and community preparatory activities.[15] Most countries have accordingly developed national pandemic preparedness plans. Many states are considering how best to implement various public health measures during a pandemic and some countries have strategic stockpiles of antibiotics, antivirals, human H5N1 influenza vaccine and personal protective equipment. Yet, great variations exist in these plans and very few are fully tested and operationally credible.[16,17] What is needed now is testing and action to fill the operational gaps. For example, cross-border aspects of pandemic preparedness are conspicuously absent from many national plans as are the practical implementation aspects of social and other non-pharmaceutical measures.

It is also often overlooked that without public support and confidence, no preparedness plan can be successfully implemented. The most immediate problems caused by a pandemic will probably arise not from death or sickness, but from uncoordinated efforts of individuals to avoid infection, as happened with SARS. The costs of public panic to nations are magnified by misinformation and result in the loss of trust in governments. Effective communication is the key to mitigating any public health crisis and is a fundamental part of risk management. It also promotes individual empowerment by allowing the public to exercise their personal responsibilities for planning and preparation.

As with other aspects of pandemic influenza preparedness, governments and public health authorities should adopt a proactive and strategic approach to communications planning. Initiatives that simply disseminate advice based on technical decisions will be insufficient given the complex risks and perceptions associated with an influenza pandemic. To close this gap in communication, public health agencies must instead incorporate the perceptions, attitudes, knowledge and cultural traditions of the public into risk planning and social mobilisation.

Preparedness planning also involves balancing potentially conflicting individual and community interests. In emergency situations, the enjoyment of individual human rights and civil liberties may have to be limited in the public interest. However, efforts to protect individual rights should still be part of any policy. In balancing competing interests and values, policy-makers can draw on ethical principles as tools for weighing conflicting claims and for reaching appropriate decisions.[18]

Promoting Intersectoral Cooperation

Preparedness is a continuous and integrated process resulting from a wide range of activities and resources rather than a distinct health-sector activity. Recent outbreaks of Ebola haemorrhagic fever, bovine spongiform encephalopathy, avian influenza and other zoonoses remind us that human and animal health are intimately connected – three quarters of new human diseases have arisen from animal reservoirs.[19] This convergence of animal and human disease threats and the likelihood of continued propagation of new zoonotic diseases suggest an urgent need for a corresponding convergence of animal and public health officials, professional organisations, and partners to meet these challenges. Achieving such a consilience of human, domestic and wildlife health is necessary given the multidimensional challenges posed to health security from zoonoses.

As an example, the primary risk factor for H5N1 human infection continues to be exposure to infected poultry, the vast majority in backyard flocks.[20] Five years after the widespread emergence and spread of H5N1 in Asia, the virus is now entrenched in domestic birds in many countries and regions. Thus, controlling H5N1 among poultry is essential in reducing the risk of human infection, and in preventing or reducing the severe economic burden of such outbreaks. This requires not only education about handling poultry and a fundamental change in cultural attitudes towards human-animal interactions but also husbandry

practices in many parts of the world. To achieve this, coordination across multiple agencies in the fields of public health, agriculture, social science, food safety and veterinary services are required.

While many countries have made substantial efforts to prepare for the health consequences of pandemics, not all countries have given sufficient attention to preparing for the societal, humanitarian, economic and governance consequences. Given that a pandemic will have significant consequences for entire communities, it is essential that a whole-of-society approach be adopted. Early planning beyond the health and medical boundaries, focusing on sustaining critical infrastructure, private-sector activities and the movement of goods and services across the country and the globe is essential.

The failure of businesses to sustain operations would also add to the economic consequences of a pandemic. The World Bank has estimated that a pandemic could cost the world economy between 800 billion dollars and 2 trillion dollars, depending on the virulence of the virus.[21] Other potential disruptions may include the threats to the continuity of vital services, increased work absenteeism and shortages of goods and services. Some business sectors will be especially vulnerable with severe demand shock anticipated for services sectors such as tourism, mass transportation, retail sales, hotels and restaurants.

Beyond the economic costs, such failures especially in basic utilities such as water or electricity, will have significant implications for the ability of the health sector to function and severe humanitarian consequences for vulnerable populations. Certain groups in society are likely to suffer more than others. Only through the development of robust preparedness plans and intersectoral cooperation can we aim to mitigate such social, health and economic impacts.

Conclusion

Although there is no certainty that an H5N1 pandemic will occur, history suggests that there will be future influenza pandemics, unpredictable in timing and severity and that this is beyond our control. At the moment the threat is still in the future; however, this is the best time to invest in an insurance policy. For it is within our control to strive to our utmost to minimise the impact of a future pandemic through cooperation, planning and research. The potential cost in human lives and suffering and the economic consequences should be sufficient incentive.[22]

REFERENCES

1. Claas ECJ, Osterhaus ADME, van Beek R, De Jong JC, Rimmelzwaan GF, Senne DA, et al. Human influenza A H5N1 virus related to a highly pathogenic avian influenza virus. Lancet 1998;351:472-7.
2. Webby RJ, Webster RG. Are we ready for pandemic influenza? Science 2003;302:1519-22.
3. Cox NJ, Tamblyn SE, Tam T. Influenza pandemic planning. Vaccine 2003;21:1801-3.
4. Ong AK, Heymann DL. Microbes and humans: the long dance. Bull World Health Organ 2007;85:422.
5. WHO. WHO activities in avian influenza and pandemic influenza preparedness. World Health Organization; 2006; Available at: http://www.who.int/csr/disease/avian_influenza/WHOactivities avianinfluenza/en/index.html. Accessed 30 January 2008.
6. WHO. The Global Action Pln (GAP) to increase supply of pandemic influenza vaccines. World Health Organization. 2008. Available at: http://whqlibdoc.who.int/hq/2008/WHO_IVB_08.10_eng.pdf. Cited 20 April 2008.
7. Murray CJL, Lopez AD, Chin B, Feehan D, Hill KH. Estimation of potential global pandemic influenza mortality on the basis of vital registry data from the 1918-20 pandemic: a quantitative analysis. Lancet 2007;368:2211-8.
8. Ferguson N. Poverty, death, and a future influenza pandemic. Lancet 2007;368:2187-8.
9. UNAIDS. AIDS epidemic update: December 2007. Joint United Nations Programme on HIV/AIDS (UNAIDS) and World Health Organizations (WHO). Geneva: WHO, 2007.
10. WHO. Interim statement of the Intergovernmental meeting on pandemic influenza preparedness: sharing of influenza viruses and access to vaccine and other benefits. World Health Organization. Geneva. 2007. Available at: http://www.who.int/gb/pip/pdf_files/IGM_PIP-IntStatement-en.pdf. Cited 10 April 2008.
11. WHO. Draft global strategy and plan of action on health, innovation and intellectual property. Report by the Secretariat. Intergovernmental working group on public health, innovation and intellectual property. World Health Organization. Geneva. 2007. Available at: http://www.who.int/gb/phi/pdf/igwg2/PHI_IGWG2_2-en.pdf. Cited 10 April 2008.
12. WHO. WHA 58.3 Revision of the International health regulations. World Health Organization; 2007. Available at: http://www.who.int/gb/ebwha/pdf_files/WHA58/WHA58_3-en.pdf. Accessed 12 March 2008.
13. WHO. Business plan for the global pandemic influenza action plan, February 2008. World Health Organization. 2008. Available at: http://www.who.int/vaccine_research/diseases/influenza/Report%20McKinsey%20Business%20plan%20Flu.pdf. Cited 29 May 2008.
14. WHO. WHO Interim Protocol: Rapid operations to contain the initial emergence of pandemic influenza. World Health Organization; 2007. Available at: http://www.who.int/csr/disease/avian_influenza/guidelines/draftprotocol/en/index.html. Accessed 8 April 2008
15. WHO. Global influenza preparedness plan. World Health Organization, Geneva. WHO/CDS/CSR/GIP/2005.5. 2005. Available at: http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_5/en/index.html. Cited 10 April 2008.
16. Coker R, Mounier-Jack S. Pandemic influenza preparedness in the Asia-Pacific region. Lancet 2006;368:886-9.
17. Mounier-Jack S, Coker RJ. How prepared is Europe for pandemic influenza? Analysis of national plans. Lancet 2006;367:1405-11.
18. WHO. Ethical considerations in developing a public health response to pandemic influenza. World Health Organization, Geneva. WHO/CDS/EPR/GIP/2007.2. 2007. Available at: http://www.who.int/csr/resources/publications/WHO_CDS_EPR_GIP_2007_2c.pdf. Cited 8 April 2008.
19. Taylor LH, Latham SM, Woolhouse ME. Risk factors for human disease emergence. Philos Trans R Soc Lond B Biol Sci 2001;356:983-9.
20. Writing Committee of the Second World Health Organization Consultation on Clinical Aspects of Human Infection with Avian Influenza AV. Update on avian influenza A (H5N1) virus infection in humans. N Engl J Med 2008;358:261-73.
21. World Bank. Evaluating the economic cosequences of avian influenza. 2006. Available at: http://siteresources.worldbank.org/INTTOPAVIFLU/Resources/EvaluatingAIeconomics.pdf. Cited 10 April 2008.
22. Hampson AW. Avian influenza: A pandemic waiting in the wings? Emerg Med Australas 2006;18:420-9.