Pandemic Influenza A (H1N1) 2009 in Malaysia - The Next Phase

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In recent years, zoonotic RNA viruses such as Nipah, SARS coronavirus, avian influenza (H5N1) and Chikungunya have emerged with global impact. The latest has now been designated by World Health Organization (WHO) as pandemic (H1N1) 2009 virus. It was first reported as an outbreak in Mexico in April, and has now caused the first influenza pandemic since 1968. By July 11, 2009, there were 105,304 confirmed cases and 463 deaths in 143 countries, including 627 cases in Malaysia1. The rapid spread of the pandemic (H1N1) 2009 virus was first reported as an influenza pandemic since 1968. By July 11, 2009, there were 105,304 confirmed cases and 463 deaths in 143 countries, including 627 cases in Malaysia1. The rapid spread of the novel H1N1 strain not previously seen in humans, thus there is widespread susceptibility.

Influenza A is an enveloped RNA virus containing 8 genomic segments. The haemagglutinin (H) and neuraminidase (N) surface proteins are key virulence determinants and elicit the main host immune response. There are 16 H and 9 N, which determine the influenza subtype. The segmented nature of the genome facilitates swapping of genes between virus strains co-infecting a single host. As influenza is principally an avian virus, this reassortment process mainly involves a vast pool of avian strains, generating countless variants. For unknown reasons, certain avian strains successfully cross species barriers to infect mammals, including humans and pigs. Occasionally, a novel strain with efficient human transmissibility has caused pandemics in 1918 (H1N1), 1957 (H2N2), 1968 (H3N2), and now 2009. Since 1977, seasonal H1N1 and H3N2 have been circulating, and constantly mutating, which means the seasonal vaccines need to be changed annually. The current pandemic (H1N1) 2009 is a novel H1N1 strain not previously seen in humans, thus there is widespread susceptibility.

Epidemiological and clinical aspects

Clinically, pandemic (H1N1) 2009 infection resembles seasonal influenza. Most patients have fever, cough, sore throat, headache, dyspnoea, and myalgia, and some have diarrhoea and vomiting2. Most cases are mild. Deaths occur rarely, mainly due to severe pneumonia. About half involve previously healthy people. The rest have underlying conditions such as lung and cardiovascular disease, diabetes, immunosuppression, pregnancy, and, unexpectedly, obesity3. Although the current pandemic strain probably arose in pigs, the only documented swine infections with the pandemic virus to date occurred after the first reported human cases in April 2009, in Canada and Argentina4. The pandemic strain probably circulated undetected amongst pigs for some years in countries with no surveillance of swine influenza5. Pigs have tracheal cell receptors for influenza viruses which are similar to birds and humans6. Thus, pigs can be “mixing vessels” for reassortment of avian, swine and human influenza. However, influenza surveillance in swine has

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lagged behind that of humans and birds, as the disease in swine is mild and has little commercial impact. An opportunity to foresee a potential pandemic strain was missed. With the concurrent risk of a panzootic, or worldwide outbreak amongst swine, surveillance of pigs is now a priority. This is particularly critical, yet difficult, in countries with rudimentary pig farming, where pigs mix freely with birds.

The naming of the virus has been controversial, particularly the media-friendly term “swine flu”. This has been rejected by WHO as inaccurate and simplistic. The pandemic (H1N1) 2009 virus contains genes from swine, avian and human influenza sources. Furthermore, previous human infections with true “swine influenza” were rare, and involved direct contact with pigs, just as “avian” influenza (H5N1) is acquired from infected birds. Currently, swine play no active role in the ongoing pandemic. Although its recent genetic origin is swine-related, the pandemic (H1N1) 2009 virus is clearly behaving as a human influenza strain, as it transmits easily between humans.

**Situation in Malaysia**

The first case of pandemic (H1N1) 2009 in Malaysia was reported on May 15. The Ministry of Health (MOH) immediately responded with measures to contain disease spread. Containment focused on active case finding and robust control of contacts. Cases and contacts were placed under home quarantine orders, and given oseltamivir (Tamiflu). In accordance with WHO recommendations, no travel restrictions were made. Instead, travel advisories were issued regarding countries with extensive local spread, including USA and Australia. Some control measures, such as airport screening, have caused debate. They were perceived to incur unsustainable costs and social disruption incommensurate with the mildness of the disease. Also, there is a lack of data on their effectiveness. Nevertheless, it is likely that containment bought some valuable time. By delaying and flattening the inevitable epidemic peak, the nation made preparations such as training staff, and stockpiling antivirals, antibiotics, personal protective equipment, laboratory supplies, and so on.

On June 11, WHO raised the pandemic alert to level 6. At this point, Malaysia had 11 confirmed cases, all imported. Initially, most imported cases were from USA. In recent weeks, most imported cases have been from the Asia-Pacific region, mainly Australia, Indonesia, Thailand and Singapore. The first locally-acquired case was diagnosed on June 17. The incidence of total and locally-transmitted cases continued to rise (Figure 1). The two largest clusters of cases to date started in late June, at a conference in Penang (20 cases), and a school in Cheras, Kuala Lumpur (18 cases). By 9 July, the number of local transmissions had risen to 159 (27.7%) of 574 cases. With sustained community spread, and detection of new cases with no defined links with existing cases, it seemed that the disease could no longer be contained. On the same day, the MOH declared that Malaysia would be moving from containment to a mitigation strategy. Many other countries have also done this, in keeping with international guidance.

Mitigation focuses primarily on managing disease impact on health and society, rather than containing spread. The aims are to reduce disease-related morbidity and mortality, slow the spread of disease, and ensure running of essential services. Hospital admission, laboratory diagnosis and antivirals will be limited to selected patients with moderate or severe disease, and those at risk of severe disease. Mild cases will be managed at home, to prioritise healthcare resources for severe cases. Individuals will be expected to take responsibility and practice personal measures. These include social distancing (keeping one metre away from others, and avoiding crowds), cough etiquette, frequent handwashing, self-quarantine if ill, and household ventilation. Resource-intensive measures such as screening, tracing and quarantining contacts will be phased out. There will be continued monitoring of unusual clusters or severe cases which may indicate a change in viral virulence or transmissibility.

The restriction of antivirals to selected cases may be difficult for the public to accept. However, indiscriminate use of oseltamivir has led to the first oseltamivir-resistant strains of the pandemic (H1N1) 2009 virus. Up to 64% of seasonal influenza A (H1N1) viruses have a single neuraminidase mutation conferring oseltamivir resistance, including 44% of Malaysian isolates. As resistance is so easily acquired, the effectiveness of oseltamivir in this pandemic may soon be lost. Unfortunately, many countries, including Malaysia, have stockpiled oseltamivir. Pandemic (H1N1) 2009 virus is still susceptible to zanamivir (Relenza), which has the disadvantage that it is inhaled rather than taken orally. The most effective means of control is vaccination. However, an effective vaccine will not be available for several months. There is also insufficient manufacturing capacity for the whole world, and at least the first 600 million doses have been pre-purchased by developed countries. Thus, poorer countries may have limited access to vaccines, even in the medium term.

Some argue that the focus on the pandemic has detracted from other priority diseases such as tuberculosis and dengue. This is a difficult issue. The pandemic has an estimated

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<th>Gene</th>
<th>Recent origin</th>
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<td>PB2</td>
<td>North American triple-reassortant swine</td>
<td>avian H1N1</td>
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<td>PB1</td>
<td>North American triple-reassortant swine</td>
<td>human H3N2</td>
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<td>PA</td>
<td>North American triple-reassortant swine</td>
<td>avian H1N1</td>
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<td>H</td>
<td>North American triple-reassortant swine</td>
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<td>NP</td>
<td>North American triple-reassortant swine</td>
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<td>Eurasian “avian-like” swine H1N1</td>
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<td>NS</td>
<td>North American triple-reassortant swine</td>
<td>North American classical swine H1N1</td>
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PB2, polymerase PB2; PB1, polymerase PB1; PA, polymerase PA; H, haemagglutinin; NP, nuclear protein; N, neuraminidase; M, matrix protein; NS, nonstructural proteins.
reproduction number (R0), the average number of secondary cases arising from each case) of 1.4-2.0.22 This may result in cases arising from each case of 1.4-1.6, compared to estimates from previous pandemics of 1.4-2.0.22

Malaysia’s move to a mitigation strategy is acknowledged of the relentless spread of pandemic (H1N1) 2009. Mortality appears low amongst the healthy, so the focus is now on vulnerable at-risk groups. There will be possible shortages in effective antivirals and vaccines, two key components in pandemic control. Effective leadership and communication, particularly in view of rapidly evolving knowledge, will be critical as we face the challenges of this novel virus in the months ahead.

REFERENCES
17. European Centre for Disease Prevention and Control. ECDC interim guidance: Mitigation and delaying (or ‘containment’) strategies as the new influenza A (H1N1) virus comes into Europe. Stockholm: ECDC, 2009.