

A novel strain of Influenza A H1N1

Over the past couple of weeks, both the traditional and new media have been inundated with reports and commentary on the influenza A(H1N1) epidemic. Popularly termed “swine flu”, this novel virus is suspected to have infected people from forty-three countries at the time of writing, with laboratory-confirmed cases in thirteen countries in four continents.

The World Health Organization (WHO) raised its influenza pandemic alert to Phase 5 Thursday morning Singapore time, and Singapore has correspondingly raised its alert level to Orange. The difference between WHO Phase 5 (imminent pandemic) and 6 (the ultimate level – pandemic phase) is likely to be a matter of time in this particular instance. Once local transmission has been established in another WHO region (such as the Southeast Asian Region, European Region, Western Pacific Region or African Region) outside North America, WHO will inevitably raise its pandemic influenza alert level again. Besides Mexico, United States of America (USA) and Canada (which belong to the WHO North America region), Scotland and Spain have reported possible cases of local H1N1 transmission. The bottleneck is at the level of confirmatory testing – currently, few laboratories outside USA have the capability for confirming the diagnosis of this novel influenza virus – but this will change in the coming days as both diagnostic kits and virus samples are distributed by WHO to national laboratories.

Many countries have activated pandemic preparedness plans and have independently taken steps towards limiting any potential outbreaks. In general, these have largely been similar: airport screening, public education, and stockpiling of masks and antiviral drugs. Singapore has initiated thermal screenings at airports and border checkpoints, and will start temperature checks at public buildings and events. Our hospitals have cut down on elective surgeries in a bid to free up bed capacity, stepped up use of personal protective equipment in hospitals and also limited visitation to reduce potential transmissions from visitors to patients and staff. Although many countries have instituted travel advisories for Mexico (and briefly, the European Union for USA as well), WHO has advised against travel restrictions and border closures. With so many countries already affected, it does not believe that such a strategy will be effective in the long term.

Although a pandemic – as well as local cases of influenza A (H1N1) – seems inevitable, the local and global impact remains unclear. This is because there are many details in this epidemic that are unexplained, the most important – for policy and clinical decision-making – of which is the difference in disease severity between cases within and outside Mexico. Mexico has reported 168 deaths to date at the time of writing on May Day, of whom 12 were confirmed to have influenza A(H1N1). This mortality rate is in excess of 5%, which is far higher than even the Spanish flu of 1918-1919. The rest of the world has only seen one death – that of a Mexican child in Texas – despite almost 200 confirmed cases.

Several hypotheses have been put forward to account for this difference: that there is a different influenza strain in Mexico (this has been disproved); that there is something different about the genetic make-up of Mexicans (remains to be proven); that the Mexican cases are co-infected with another viral or bacterial pathogen (possible); that the Mexican cases seek treatment too late (quite likely contributory). But perhaps the best explanation offered to date is that there has been substantial underestimation of cases in Mexico. This was suggested on Thursday night Singapore time during the WHO scientific teleconference when an official from the Mexican Ministry of Health mentioned the several thousand samples that were waiting for processing. It is also possible that poor Mexicans have limited access to the formal healthcare system thus perhaps only the more severe influenza cases were counted in Mexico. The mortality rate thus became correspondingly high as mild self-limiting cases might have been missed. Under-estimation will also explain why so many

travelers to Mexico have returned to their home countries with the virus – something one would not expect if there were only 2,000 or so cases in the entire country. But of course this is only speculation at this point in time.

There is no way to distinguish the symptoms of influenza A(H1N1) flu from other influenza-like illnesses at presentation, although early US reports suggest that diarrhea is a prominent feature in some cases. Because the virus remains susceptible to the neuraminidase inhibitors oseltamivir (Tamiflu) and zanamivir (Relenza), Roche and GlaxoSmithKline have stockpiles of their respective drugs – totaling in excess of three million doses – on standby and are in the process of making more. There is some concern that the novel strain of H1N1 influenza will acquire resistance genes from circulating seasonal H1N1 influenza that has become resistant to oseltamivir but remains susceptible to zanamivir. The major vaccine manufacturers have also declared that they will commence work on developing a H1N1 vaccine. The current seasonal influenza vaccines are not likely to provide protection against this new virus due to the fact that the H1N1 swine flu is a reassortant virus which is a hybrid of different pig viruses with sequences from previously circulating avian and human strains.

However, considerable caution will doubtlessly be exercised by world experts and governments in advocating vaccination with any new H1N1 vaccine that is developed, not least because the 1976 swine flu debacle at New Jersey, US, remains fresh in their minds. As has been described in recent newspaper reports, four severe viral pneumonias and one death attributed to a swine H1N1 (but of a different composition from the current virus) outbreak among healthy soldiers at Fort Dix in February 1976 triggered an emergency nationwide vaccination program later that year that resulted in deaths as well as cases of paralysis in vaccines who suffered from Guillain-Barre syndrome (disease in which the body damages its own nerve cells resulting in muscle weakness and sometimes paralysis). That particular outbreak ended as mysteriously as it appeared, leading to a public backlash against influenza vaccination and major implications for the vaccine industry. Now influenza vaccines have to meet stringent safety standards through a careful series of human and animal studies. While reassuring, they can delay deployment of new vaccines.

Comparisons between the current epidemic, SARS and the 1918 H1N1 Spanish flu pandemic are inevitable. SARS was caused by a totally different virus (a novel coronavirus) altogether. The mortality rate was far higher than even the 1918 H1N1 Spanish flu, but the SARS virus was not efficient at transmitting itself, therefore community transmission was rare and the epidemic burned itself out in a matter of months.

The 1918 pandemic influenza A virus was thought to be a “swine flu” initially but now we know that it was largely avian in origin, and it also belonged to the H1N1 subtype. The virus had also never been detected prior to the time of the outbreak. Liberal estimates suggest that up to 100 million people may have perished during the 1918 pandemic. Given the disturbing parallels between the two outbreaks (young and healthy affected, with deaths), one fear is that the current epidemic may result in a similar death toll, despite the low mortality outside of Mexico.

However, the world of 2009 is vastly different from 1918. For a start, there is no world war with young men in trenches. Furthermore, technology has advanced significantly. Ninety-one years later, we have effective drugs and the capability to develop vaccines rapidly. The care of critically ill patients has also progressed tremendously, and experience with both SARS and avian influenza has resulted in viable pandemic preparedness plans in many countries. It is probable that both transmission and mortality will be far lower this time round, even if the swine flu outbreak assumes pandemic proportions.

Information technology has made greater advances than medical technology in the last century. Multiple sources from the official websites of the World Health Organisation, US Centers for Diseases Control and Prevention, and Singapore Ministry of Health to informal sites, twitter updates, Google Maps and amateur epidemiologists provide a plethora of information for informed citizens to critically evaluate the data presented. More accurate information will be available in the coming weeks and the number of confirmed cases will undoubtedly jump as laboratories worldwide gain the capability to diagnose this infection.

The duration of this epidemic is unknown but it would not be unexpected if the virus continues to circulate for several months worldwide. In Singapore, the influenza pandemics of 1918, 1957 and 1968 were short and sharp with intense foci in schools. We have heard of school closures in New York and Texas. We should be prepared to adapt and live life as normally as possible despite the presence of the pandemic. To reiterate the Health Minister's advice yesterday, now is a good time to improve on personal hygiene – including cough etiquette and hand hygiene – and social responsibility when infected with a transmissible disease.

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