the southern hemisphere (in late April 2009) that initially were successfully contained, it was a different case in Australia, where the virus entered without detection at a similar time and spread, especially in Victoria, well before the first official case was announced in Queensland on 9 May 2009[1]. Following the outbreak of the first influenza pandemic of the 21st century, a myriad of questions about the virus/disease emerged, such as the following: What is the severity of the pandemic? Who is at risk? How can we detect it? What is the attack rate? How does it relate to the currently circulating seasonal H1N1 viruses? Is it similar to the swine 1976 virus? Is it the same as previous pandemics? What vaccine do we need to make? Is the virus sensitive to existing licensed antiviral drugs? The transmission of the virus to swine from humans raised many more important issues to be considered and discussed. The authors of the articles contained in this issue were at the front line in responding to and answering many of these questions. The depth and skills of these and many other infectious disease specialists, scientists and public health officials have been tested over these past few years and will no doubt be tested further in years to come.

Australia is in a fortunate position to have on hand such a large pool of expertise and knowledge covering influenza and other potentially pandemic infectious diseases, a situation that one hopes will not be forgotten and will be retained in coming years as other health-related priorities arise. Governments and agencies will hopefully learn the most important lesson that influenza workers know from experience, that "influenza is a variable disease" and this applies to both human (seasonal and pandemic influenza) and animal influenza; hence, contingency plans and stockpiles should attempt to cover this range of possible outcomes, from mild to catastrophic. In this way it is hoped that we will have truly learned some valuable lessons from the 2009 influenza pandemic which will serve us better with future pandemics, which will assuredly come ... in time!

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Swine flu – lessons we need to learn

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Important lessons need to be learnt from the recent swine flu pandemic. Overall the population health effects of swine flu were less than a moderately severe seasonal influenza outbreak. A pandemic should not be declared unless we have both the spread of the virus but also when its virulence is above a predefined level. We need to ensure that we improve techniques to decrease the spread of infection both in the community and within our hospitals. This means improved infection control and hygiene with the use of masks, alcohol hand rubs and so on We also need to have a different approach to vaccines. Effective vaccines were produced only after the epidemic had passed and so had relatively little efficacy in preventing many infections. Mass population strategies involving vaccines and antivirals also misused large amounts of scarce medical resources.

In April 2009 a new H1N1 strain of influenza, with what appeared to be a high mortality rate (5%), was reported from Mexico. Worldwide, fear quickly spread that we might be about to see a recurrence of the "Spanish flu" of 1918–19, when tens of millions of people died. Internationally, pandemic plans designed to cope with new virulent strains of influenza such as the spread of "Bird flu" (H5N1) were triggered.

The "swine flu" virus (pandemic H1N1 2009) spread quickly around the world. However, by May 2009, data from the US and elsewhere showed that its virulence was considerably less than initially reported[1,2]. The case fatality rate was no greater than seasonal influenza and likely less than 1 in 10,000 people infected[1,2]. However, there remained concerns that enhanced virulence might still be seen during winter.

Large numbers of cases of infections occurred in Victoria in early winter 2009[1,3,4]. The mortality rate was low and similar to that already reported from the US and Canada. The elderly seemed to be relatively protected from getting infection (presumably as a result of previous immunity following previous H1N1 infections). Certain groups were more vulnerable[1-7] but in general were those more vulnerable during seasonal influenza (with underlying heart disease, lung disease and so on). The exception was pregnant women, who had a hospitalisation and death rates three to 10 times higher compared to other females of the same age[3,5,6].

In 2009, children and young adults had very high rates of infection, but their overall risk of death was very low. For those under 30 years and without risk factors, the chance of dying during the winter epidemic in Australia was less than one per million people[4,6].

The virus also had spread widely and much earlier than initially thought. In Victoria, this was likely weeks prior to it being first detected. It was circulating at the same time as first detected in the US[8]. In Mexico the spread may have also been occurring six months prior to its initial laboratory diagnosis[8].

Attempts to contain the virus did not appear to be very successful anywhere around the world. In Australia, when it became obvious that attempts at containment were unsuccessful, a newly defined PROTECT phase was developed[9]. This then, appropriately, focused our health resources on those who we knew to be at higher risk and thus more vulnerable to complications rather than the entire population. In practice, similar approaches were taken around the world.

Australia was one of the first countries to have a vaccine available for use in the general population. This was, however, only in early October 2009 – months after the epidemic had peaked (Figure 1)[4]. Our current vaccine technology does not have the ability to produce enough vaccine to protect large proportions of the population when a new form of influenza develops and spreads. We need to develop new influenza vaccines that are safe and effective that give protection against multiple strains of the virus (including newly emerging ones) for many years.

One essential issue, on which we need international consensus, is the trigger point for defining a pandemic. Whenever a "pandemic" is called, it will have major effects on the way governments and health departments allocate resources. It also will have profound effects on how society functions, particularly if it includes closing schools, work places and so on. The WHO definition of pandemic previously needs to re-incorporate a component that takes into account severity[2,10] as, appropriately, does one plan from the US[11]. If we define a pandemic (as was the case for swine flu) as merely being the spread of a new influenza virus strain around the world, we will be calling pandemics every few years. Unless the severity of the infection is much worse than what we see with seasonal influenza, it is inappropriate to invoke pandemic plans.

The value of drugs for therapy such as oseltamivir is controversial[12] but if there are benefits it is likely to be in the severely ill. However, even for those with underlying risk factors needing hospitalisation there were often considerable delays – in pregnant women a median of nine days before they received therapy after the onset of their symptoms[5].

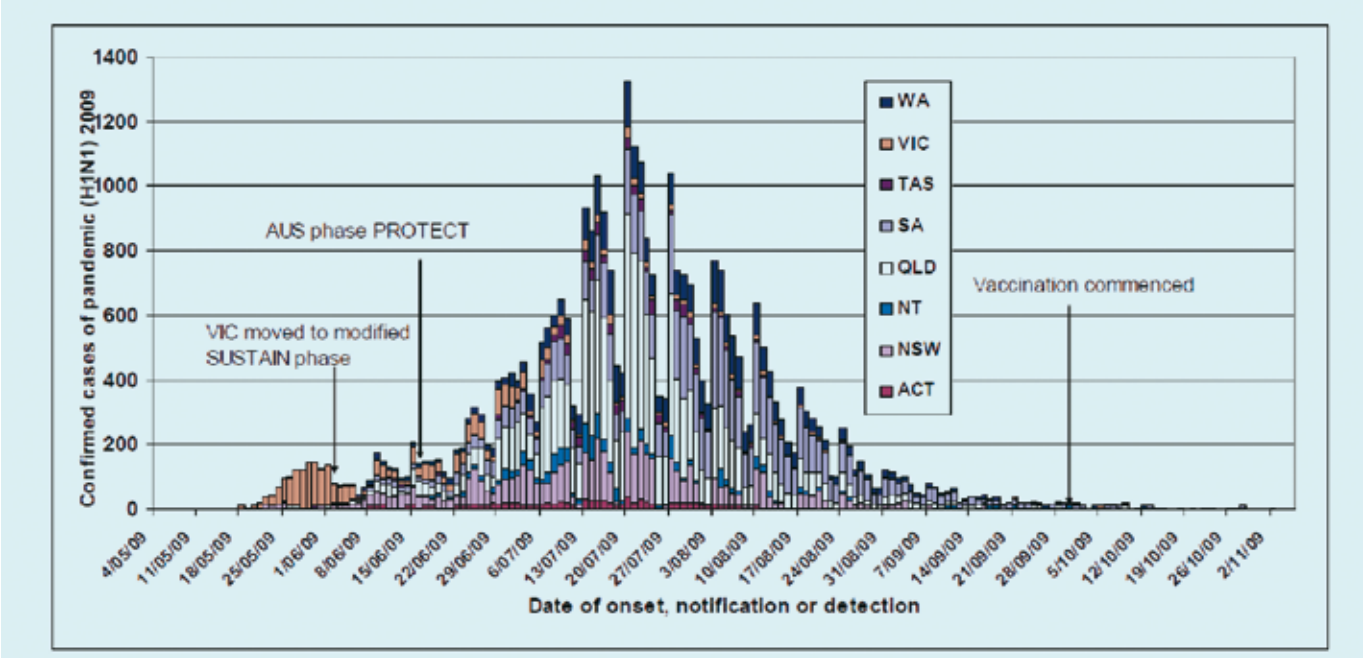

Figure 1. Laboratory confirmed cases of pandemic (H1N1) 2009 in Australia, to 6 November 2009. Taken from Australian Influenza Surveillance Summary Report No. 26, 2009, reporting period: 31 October 2009 – 6 November 2009[4]. *Source: National Notifiable Diseases Surveillance System, Australia, 2009 (with permission).*

The widespread media coverage as well as government press releases induced needless panic and fear in the population. This resulted in emergency departments and doctors' surgeries being overwhelmed with requests, especially for antivirals. The effect of this was those who were much more likely to be at risk for this infection were often not able to access medical advice or drugs. It also interfered with medical access for those with non-infective medical conditions. The vast majority of people who did not have risk factors just needed to stay at home and get better by themselves (usually within a few days) and only seek medical help if they developed symptoms to suggest that they developed a secondary complication such as bacterial pneumonia.

Given the inevitable delays in producing influenza vaccines, we need to re-examine how effective mass vaccination is ever likely to be[13], as well as its cost benefits. In the UK the swine flu vaccines had very poor cost benefits[14,15]. This was mainly because the vaccine was only available after the epidemic had peaked and this is likely to always be the situation. The other problem with mass population vaccination programs for swine flu was that the majority of those with risk factors were the elderly and they were already immune (and was evident early during the epidemic, as they were not getting infected). Vaccine and other studies also suggested that at least a third of those between the ages of 18 and 65 had protective levels of antibodies and that 70% had detectable antibodies[7,13,16].

The unexpected very high seizure rates following vaccination with the CSL trivalent seasonal influenza vaccine in children in Western Australia, shows that we need better and more timely prospective surveillance systems in place[17-19]. We need to rapidly detect any unusual side effect profiles from the vaccine that has changed in composition from the previous season. Passive surveillance is usually the only way that influenza vaccines are monitored for safety but frequently greatly under-reports the number of adverse events that occur[20]. Passive surveillance resulted in the slow recognition of the increased problem with the swine flu vaccine in the US in the 1970s (Guillain Barré syndrome)[21]. In Australia, even though nine per 1,000 children developed febrile seizures after receiving a CSL trivalent vaccine containing a swine flu antigen, there were delays in recognising the problem and in actions to stop further vaccinations[17-19]. We need active prospective surveillance done through general practices and/or vaccine clinics to detect any untoward side effects occurring in, say, the first 3,000 to 4,000 adults and children vaccinated with any vaccine where the composition has been changed from what was used previously.

We also need better and timelier data on vaccine efficacy. The Canadians have done a commendable job in setting up such surveillance and this has also been done in Victoria[22,23]. Before we roll out any vaccine, we need to ensure that it is both effective and safe and not just rely on surrogates markers. Antibody levels often correlate poorly with immunity and protection in influenza[7]. We also need good active surveillance systems in place to detect side effects and/or efficacy issues, particularly those effects that are unexpected[17-23]. In Canada previous vaccination with seasonal influenza vaccine doubled the risk for an individual to become infected with the Swine flu virus[22].

The majority of deaths in the 1918–19 pandemic were from secondary bacterial infections – usually pneumonia[2,24]. Bacterial infections continue to play a major part in those who die. A large proportion of those dying after influenza infections have bacteria isolated from sterile sites[24,25]. If we continue to mainly focus just on the virus, through antivirals and vaccines, we are likely not to be targeting the best interventions that will prevent deaths. More effective may be identifying that small number of people who develop more serious complications resulting from influenza and then make sure that not only do we give them promptly antivirals but also antibiotics, as our ability to discriminate a viral from bacterial infections in those with more severe lung involvement is relatively poor[26].

This pandemic and other reviews show the importance of infection control and hygiene. We tend to have an undue focus on medical interventions such as drugs and vaccines. Overall oseltamivir may have caused more harm than good, as well as being an inappropriate waste of money for the vast majority of people who took them, especially otherwise healthy children[2,12,13]. The widespread use of oseltamivir had no obvious effect on the epidemic curves in any country compared to previous influenza seasons. Its use was, however, associated with widespread nausea and vomiting, especially in children and in whom the morbidity and mortality of influenza was very low. Infection control is relatively inexpensive and likely more effective in stopping the spread of viruses. A recent *Cochrane Review* suggests that if masks, alcohol hand hygiene and other approaches were used these would give good protection[27]. In Hong Kong during the SARS epidemic, the widespread use of masks and hand hygiene by the population resulted in a marked reduction in all respiratory illnesses[28]. This all suggests that there may be a lot more transmission by contaminated hands than we have previously recognised. The value of masks may be more to stop a person touching their own nose and mouth rather than decreasing the inhalation of any respiratory aerosols or droplets. This has had some significance as there was a lot of controversy as to what type of masks needed to be used, for example, surgical masks or N95 masks[26]. The available evidence suggests that using masks is protective compared to not using them. However, there is no great difference in regard to which type of mask is used.

Summary

In summary, there are important lessons for us to learn from the recent swine flu pandemic. Firstly, before we pull an international trigger to call a pandemic, we need to have appropriate trigger

points that involve not only the spread of the virus but also its level of virulence. This was not done over the last 12 months. We need to ensure that we improve techniques to decrease the spread of infection both in the community and within our hospitals. This essentially means improved infection control and hygiene and the use of masks, alcohol hand rubs and so on. We need to have a different approach to vaccines. The vaccines were produced only after the epidemic had passed and so have had and will have little efficacy in preventing many infections. Mass population strategies also misused large amounts of scarce medical resources. The large-scale uses of antivirals such as oseltamivir also appear to have been ineffective and very poor value for money on a population level.

Overall, our response to swine flu shows that we need to rethink how we declare and respond to pandemics. Even though around the world maximal attempts were made to try and contain the swine flu virus, these were unsuccessful. Overall they appear to have had little influence on the spread of the virus, despite the vast amounts of resources and effort expended. However, the virus in the vast majority of people infected caused only a mild illness and from which people made a full and rapid recovery and then developed immunity. Maybe it is time for a different approach. Australia changed to a newly defined PROTECT phase when it was realised the pandemic couldn't be controlled. Then the focus instead just went on to those who were known to be high risk and thus more vulnerable to complications. This may be a better international approach rather than trying to look at a whole of population approach using vaccines and antivirals.

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Biography

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