

Responding to the new influenza A (H1N1) 2009 pandemic: moving forward together

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The Singapore Medical Journal (SMJ) has published editorials accompanying the early descriptions of the Nipah virus,⁽¹⁾ the first published report of the severe acute respiratory syndrome (SARS) coronavirus,⁽²⁾ and now a consensus guideline by a group of infectious disease physicians, clinical microbiologists and public health physicians, forming the Influenza Working Group (Singapore),⁽³⁾ and an early report of the epidemiological, clinical and virological data on the first ten confirmed new influenza A (H1N1) patients in Singapore.⁽⁴⁾ In a decade since the 1999 Nipah virus outbreak, there has been tremendous progress in the field of infectious diseases in Singapore. During the Nipah virus outbreak, there were fewer than a dozen trained infectious disease physicians, a small number of dedicated virologists and public health physicians, and limited infrastructure for infectious disease surveillance, detection, molecular analysis and clinical studies. Much of the work on the Nipah virus had to be “outsourced” to international centres with the requisite expertise. When SARS arrived in 2003, the impact was devastating in hospitals but we had the beginning of a biomedical science research community which led to important scientific papers and a strong collaboration between clinical, public health and basic science communities. These led to the eventual control of the deadly nosocomial pathogen that is SARS, but not before more than 60 healthcare workers were infected, and six died in the line of duty.⁽⁵⁾

Since SARS, the world has been on the alert for pandemic influenza. In fact, early cases of SARS were isolated for possible avian influenza which had been reported in the Fujian province in February 2003. The SMJ among others was involved in the scientific preparation for the possible emergence of H5N1 avian influenza with the publication of an international practical guideline on management of avian influenza in humans.⁽⁶⁾ However, many of us were surprised when, instead of H5N1 acquiring mutations necessary for efficient person-to-person transmission, reports emerged from Mexico about a novel influenza virus that was killing young people. Soon, it became evident in the United States and Canada that a novel triple re-assortant influenza virus of swine origin had

caused widespread human-to-human transmission with significant morbidity and some mortality.⁽⁷⁾ Immediately, alarm bells began to ring in the halls of Atlanta, Geneva, London and wherever else health policy is determined. The World Health Organisation (WHO) rapidly raised its pandemic alert level from 3 where it had been for years to 4 and then 5. Singapore correspondingly raised our Disease Outbreak Response (DORSCON) level⁽⁸⁾ from Green 1 to Yellow and then to Orange. When the severity of the virus appeared much less than was feared, the WHO began considering a more measured approach to the pandemic declaration with a pandemic severity index⁽⁹⁾ that takes into account the virulence of the pathogen. Singapore was ahead of the WHO in that we rapidly scaled down to DORSCON Yellow on May 7, 2009 while maintaining vigilance in border control and enhanced influenza surveillance, and ensuring that laboratories, infection control measures and clinical management protocols were in place and constantly updated.

In 1976, there was a major outbreak of swine influenza with more than 200 soldiers from Fort Dix, New Jersey, infected with a novel strain of influenza A of swine origin. A decision had to be made by the United States Public Health Service on developing a new influenza vaccine and immunising the general public. During the decision-making process, many scientists and experts weighed in with different opinions based on evidence which related to similar viruses. But obviously, no expert had any experience with the novel influenza virus. The New England Journal of Medicine, then as now, the leading clinical medical journal published a landmark “Delphic study” in which a poll was conducted among leading scientists of the day on the costs versus benefits of large-scale vaccination against the novel influenza virus.⁽¹⁰⁾ The conclusion of the poll was not unanimous, but leaned towards vaccination, especially for those aged 25 years or older. The President of the United States of America convened a high-level expert panel that included Salk and Sabin, who had been bitter rivals in the oral versus inactivated poliomyelitis vaccine debate. Both were unanimous that the country was on the verge of a deadly 1918-like influenza pandemic and everyone had

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to be vaccinated. The New England Journal of Medicine had published earlier in May two editorials – one by the great Louis Weinstein, one of the founding fathers of clinical infectious diseases arguing strongly in favour of vaccination, with a contrasting one by Ingelfinger, provocatively titled “Thou shalt be vaccinated”.^(11,12) Ultimately, more than 40 million Americans were vaccinated against the novel influenza virus. Fortunately, there was no influenza pandemic. Unfortunately, there was a rise in the incidence of Guillain- Barré syndrome with several deaths in the weeks following vaccination with both the whole virus and the split virus vaccines.⁽¹³⁾ This led to the abrupt cancellation of the vaccination programme and major changes in how US vaccines are regulated and manufactured.

Recently, two senior public health officials involved in that decision, Sencer and Millar wrote: “When lives are at stake, it is better to err on the side of over-reaction than under-reaction. Because of the unpredictability of influenza, responsible public health leaders must be willing to take risks on behalf of the public. This requires personal courage and a reasonable level of understanding by the politicians to whom these public health leaders are accountable.”⁽¹⁴⁾ In the same issue of Emerging Infectious Diseases, Richard M Krause, who was the director of the National Institutes of Allergy and Infectious Diseases at the National Institutes of Health of the United States at the time of the decision, wrote about the “fog of epidemics”⁽¹⁵⁾ that clouds the ability of even the best scientists to make decisions.

The only certainty about emerging infectious diseases is that uncertainty abounds. With this new influenza A (H1N1) virus and modern biotechnology, we are fortunate in that we have a great deal of clinical information and several genetic sequences,⁽¹⁶⁾ and are much better prepared than our predecessors three decades prior. Unfortunately, there are many questions still unanswered, in particular in the areas of vaccine safety and efficacy, and therapeutic and infection control strategies. The Influenza Working Group (Singapore) recognises these knowledge gaps and has put together a careful review of currently-available scientific evidence; it is possible that it may rapidly be rendered out of date by rapidly-emerging data. It will be a useful document both to readers of the SMJ in their daily practice, especially the primary healthcare providers who are at the frontlines of the efforts to control influenza, and to policy makers who have to make difficult decisions that will affect the health of Singaporeans. This is particularly

timely and pertinent as the WHO declared the start of the 2009 influenza pandemic on June 11, 2009.⁽¹⁷⁾ We wish them every success and will help in any way possible with the skills and training that we possess, for the good of Singapore.

Note: This editorial is written in the authors’ personal capacity and does not reflect the views or opinions of any of the institutions to which they are affiliated.

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