Influenza A (H1N1) 2009 Pandemic Virus: Learning from the First Wave, Preparing for the Second

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In a short period of two months, the novel influenza A/H1N1 virus has circumnavigated the entire planet leaving behind in its wake approximately 3000 reported deaths worldwide. Fortunately, in many areas around the world, September 2009 brought a lull in the number of new H1N1 infections. This brought welcomed relief in many countries that had earlier experienced high respiratory disease activity in their communities. However, based on previous influenza pandemics, this reprieve may well be short-lived. As the Northern hemisphere approaches its winter months, many experts are now predicting a second wave of influenza A/H1N1 infections. This prediction maybe well placed as all 3 influenza pandemics in the last century reported second or even subsequent waves of new infections, all of which appeared to be more severe than the primary event (ref). The timing of these second waves have varied from 6 months to 3 years and invariably seemed to be linked to the winter months. It is unclear precisely what changes caused the increased severity seen during the second waves; one possibility is the progressive adaptation of the novel influenza virus to its new human host [1]. Molecular analysis, for example, suggests that the 1918 Spanish influenza virus that emerged during the second wave had undergone changes in the hemagglutinin binding site that increased the binding specificity for human receptors[2]. This is thought to have increased the replicative capacity and hence, the pathogenicity of the virus. It is also evident that as the H1N1 2009 pandemic virus continues to spread, opportunities for adaptation that increases virulence will also increase. Nonetheless, the changes needed for such adaptation and for increased virulence are unpredictable and by no means inevitable [3].

It is thus prudent that we now take stock of our experience accrued during the initial wave of the 2009 pandemic virus and explore more effective ways of handling the virus in the second and subsequent waves. Lessons learnt may come in positive ways (what has worked well) or from negative outcomes (what has not worked well). This should not just cover the clinical and therapeutic areas but should also include critical components like public health, community education and risk communication.

It is evident from experiences around the world that the pandemic 2009 H1N1virus generally causes a mild, self-limiting illness in a large majority of patients. Nonetheless, individuals with certain risk factors or co-morbidities have an increased risk of developing complications when infected with the virus. These high risk groups appear to be similar to those identified with seasonal influenza. Two risk groups do stand out for specific mention in relation to influenza A/H1N1 i.e. pregnant women especially those in the 2nd and 3rd trimester and those who are obese (body mass index > 30). Treatment guidelines universally recommend prompt empirical therapy with influenza antiviral agents when patients from these high risk groups develop influenza-like illness (ILI). There is also good consensus that patients with moderate-to-severe influenza and those who are experiencing rapid progression of symptoms would benefit from early and prompt treatment with anitvirals [4]. Hence, an effective treatment delivery system with strong emphasis on antiviral accessibility and trained personnel should be an integral component in any country's influenza pandemic preparedness plan. This will ensure not only prompt, consistent and appropriate treatment but will also reduce the risk of antiviral drug resistance, something that has been reported by the World Health Organization [4].

Another critical issue in controlling the H1N1 pandemic was limiting its spread in the community. The awareness and cooperation of the entire population was an important factor in the successful control of this outbreak. Educating the public about the dangers of the infection without causing general panic involved a fine balancing act which required good risk communication strategies. Clear and practical instructions and advice was essential in allaying anxiety and provided a sense of empowerment to the individual and society at large; that they too could make a difference to the situation. Innovative messaging involving all forms of media were utilized during this pandemic; bringing the message of cough etiquette, hand hygiene and social distancing to very large numbers of people in a very short period of time5. This was critical as it was clear that the H1N1 influenza virus frequently caused an explosive and rapid outbreak. In Malaysia, the Ministry of Health formed a national task force chaired by the Director General of Health which had a multi sectoral composition involving both government and non-governmental agencies. This facilitated cooperation and collaboration across various sectors so as to ensure an effective and cohesive public messaging strategy.

Another aspect that needs to be factored into the response to the H1N1 pandemic is the use of the H1N1 vaccine. Since October 2009, the H1N1 vaccine have begun to leave the production line and into the market for human consumption, albeit at varying speed. It is evident that the production has not been able to keep up with the demand even in the developed countries of the world. It is estimated

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that the access to the vaccine will continue to be poor in the more economically challenged nations in the immediate future. Nonetheless, as the availability of the H1N1 vaccines improves the world over, there have been concerns that the vaccines may not have fulfilled the quality and intensity of scrutiny to ensure maximal safety. The memory of the events of 1976, where there was a small but statistically significant association of a swine-origin influenza virus vaccine with Guillian Barre syndrome (attributable risk of 1 per 100,000 vaccinees) has highlighted the issue of vaccine safety. The reason for this association remains unknown. However, vaccine production has changed since 1976, with increased use of vaccines which are treated with solvents to produce split-virus vaccines, or with detergents to produce subunit vaccines, resulting in fewer adverse reactions. Since then, the safety of seasonal influenza vaccines have been well established [6].

The Joint Commission and The Centers for Disease Control and Prevention (CDC), USA has endorsed the safety of the current H1N1 vaccines approved for use in the US market. The US Food and Drug Administration (FDA) has approved the H1N1 2009 influenza vaccines from at least 4 different manufacturers. All 4 manufacturers are using similar processes in vaccine production as for seasonal influenza vaccines, which have a long safety track record. Up till the current time, the global vaccine safety vigilance program has not reported any unexpected adverse effects despite millions of doses being given [7]. It would appear that based on all available evidence at this point in time, the H1N1 vaccines are safe for use and should be prioritized for those with highest risk i.e. those with high risk co-morbidities and the healthcare workers who are working in the frontlines. It has been reported that the Ministry of Health, Malaysia has purchased 400,000 doses of the Influenza A H1N1 2009 vaccine; the stock of which have begun to arrive since late November 2009. The vaccines have been prioritized for frontline healthcare workers as well as the priority risk groups. While the vaccine delivery mechanism for healthcare workers has been well tested, it would remain a small challenge to implement an effective, equitable and timely system to reach the target groups in the community. As the seasonal influenza vaccines in 2010 will also provide coverage for the H1N1 virus, it would be prudent to encourage all those with high-risk co-morbidities to get vaccinated when the vaccines become available.

There have been many lessons learnt during the first wave of the influenza pandemic of 2009. We have collected substantial scientific data and information of the novel H1N1 virus in a fairly short period of time. This has been made possible due to the high level of commitment demonstrated by international agencies, national governments, the scientific fraternity and communities around the world. On many fronts, the level of cooperation and collaboration shown has been unprecedented. Although there is now significant agreement on how best to manage this pandemic, there remains gaps in our knowledge bank in many areas. Whether we have learnt enough to be prepared for the second wave remains to be seen.

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