DOI:10.1111/j.1750-2659.2009.00092.x
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Editorial

The 'novel' influenza A(H1N1) enigma: is it a pandemic, how should we respond, what should we call it?

[Submitted 2 June 2009]

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Please cite this paper as: Hampson (2009) The 'novel' influenza A(H1N1) enigma: is it a pandemic, how should we respond, what should we call it? Influenza and Other Respiratory Viruses 3(4), 119–120.

On 24 April 2009 the World Health Organization (WHO) reported human cases of swine influenza A/H1N1 occurring in the USA and Mexico.[1] The number of recorded cases increased rapidly, there was clear human to human transmission,[2] and it appears that the outbreak originated in Mexico in mid-March or earlier.[3] This prompted WHO on 27th April to raise its pandemic preparedness from phase three, where it had been for some time as a result of the ongoing H5N1 virus epizootic, first to phase 4[2] and then 2 days later to phase 5.[4] Countries with national pandemic plans responded accordingly.

It might be argued that by the end of May the spread of this new virus has been sufficient for WHO to declare that phase 6, a pandemic, had been reached. However, most of the recent pandemic preparedness planning has been initiated and refined in the face of the perceived threat of a severe outbreak due to a virus such as the H5N1 subtype. In fact most such plans have an introduction or preamble explaining, for those less familiar with influenza, that there are two types of antigenic variation in human influenza, 'antigenic drift', due to small ongoing mutational changes and 'antigenic shift' when a novel influenza A subtype successfully enters and transmits in the human population and that this is when pandemic influenza results. True to the frequent description of influenza as enigmatic or unpredictable this new outbreak represents neither antigenic shift nor antigenic drift and whether this should truly be considered a pandemic is not yet clearcut.[5]

In this issue of Influenza and Other Respiratory Viruses there are a number of articles related to the current outbreak and to pandemic preparedness and response. Tracking the virus is clearly important in attempts to contain spread and the article by Hurt *et al.*[6] provides a preliminary assessment of rapid point of care tests for the detection of the novel H1N1 virus. Kelly *et al.*[7] demonstrate that the age distribution of outbreaks due to this virus to date, in the USA and Europe, is similar to that of seasonal A(H1N1) when compared with recent outbreaks in Australia and suggest that this may be an inherent property of A(H1N1) viruses. McCaw *et al.*[8] speculate that a variety of factors that influence both the susceptibility of populations and the fitness of circulating influenza viruses could explain the varying mortality rates experienced in the 1918–1919 pandemic. These may be important in responding to the current outbreak as continued out of season activity in the Northern hemisphere and ongoing geographic spread may be an indication that this novel H1N1 has true pandemic potential. As we move into the Southern hemisphere winter it remains to be seen whether season may influence the impact of the virus and whether certain populations are at increased risk as suggested by the initial, apparently greater severity in Mexico.

While WHO is yet to recommend commercial manufacture of a vaccine against the novel H1N1 virus, news reports indicate that many European countries, the USA and Australia have already placed orders for vaccine. The article by Hessel on behalf of the European Vaccine Manufacturers[9] reviews current progress in meeting the challenges of pandemic influenza vaccine manufacture, however, as has been frequently emphasised in the past and again recently in the context of the current outbreak,[10], the lead-time for influenza vaccine manufacture and global production capacity seem destined to fail global demands for both timeliness and quantity of supply for a pandemic occurring in the immediate future. The Holy Grail for influenza scientists has long been a vaccine that could produce heterotypic protection across all influenza A viruses. An encouraging approach targeting T-cell immunity with lipopeptide vaccines that may reduce the severity of disease and supplement the antibody-based approach to vaccination is reported by Ng *et al.*[11] If such vaccines are effective in practice their value globally will clearly be dependent on a number of factors including cost, duration of immunity and availability, particularly for developing countries.

The World Health Organization recommends that all countries should develop a pandemic preparedness plan as part of the implementation of the International Health Regulations.[12] However, web-based documents[13,14] provide evidence of only 45 such plans and it appears that some countries, particularly developing countries, have yet to complete a pandemic plan. Clearly, for those countries with little

capacity to directly source vaccines or antivirals as a part of their pandemic response, preparedness planning requires special considerations[15] including an emphasis on non-pharmaceutical interventions.[16] The current emergence of a novel virus, be it a pandemic virus or not, places additional emphasis on the need for pandemic preparedness planning and the article by Azziz-Baumgartner *et al.*[17] provides a valuable overview of a process for drafting a plan. In his review article, in this issue,[18] David Fedson observes that 'most of the world's people will not have access to affordable supplies of vaccines and antivirals' and that 'In the 21st century, science ought to be able to provide something better'. He proposes that understanding the system-wide effects of influenza on the host that are responsible for the severe consequences of pandemic influenza, particularly the increased mortality in younger adults, may provide a basis for ameliorating these effects with inexpensive generic agents that are readily available even in developing countries. The current outbreak may provide an ideal opportunity to test these and other approaches to minimising the impact of a pandemic. And we must remember that while we are distracted with the H1N1 outbreak the H5N1 epizootic continues and the number of human cases continues to rise, particularly in Egypt. Wouldn't it be a terrible irony if H5N1 suddenly achieved the ability to transmit readily in humans, possibly aided by widespread infection of H1N1 and increased opportunity for reassortment, with much of our resources already committed to H1N1. Influenza may yet hold more surprises.

As the World Health Organization and the scientific community ponder whether the current outbreak constitutes a pandemic and the appropriate level of response to it, an additional area of confusion has become apparent – how should we refer to it, particularly as it doesn't represent a novel subtype? Official communications and scientific reports, including those included in this issue of this journal, already contain a confusing array of nomenclature. These include 'swine influenza', 'novel swine-origin H1N1 influenza' and 'human-swine influenza'. Recently it seems that it is considered inappropriate to include the word 'swine' in referring to the virus and it has become 'novel influenza A(H1N1)' and currently 'influenza A(H1N1)v' (v for variant). The latter gives no hint as to its origin or uniqueness, is very bland and seems unlikely to resonate with the popular media many of whom, probably by analogy with referring to H5N1 as 'bird flu', continue to use 'swine flu' or 'pig flu' when reporting this outbreak. From a scientific standpoint there is, of course, nothing novel about the circulation of 'variant' influenza viruses.

The journal will continue to fast-track reports related to the current outbreak, the global response and pandemic preparedness and response generally, as it has for this issue and welcomes contributions.

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