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# Hot off the breath: the 2009 H1N1 flu pandemic may be gone but should not be forgotten

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The 2009 influenza pandemic was caused by the emergence of a new influenza virus, pandemic H1N1 2009 influenza A (pH1N1), to which many people had no pre-existing immunity. It caused unusual and extensive outbreaks of disease in the summer months in many countries and very high levels of disease in the winter months. The pandemic virus had almost complete dominance over other seasonal influenza viruses and was unusual in its clinical presentation because the most severe cases occurred more often in younger age groups. The WHO and the world's healthcare systems mobilised a massive healthcare resource effort to prepare for the potentially devastating effects of an influenza pandemic. In the UK there have been 474 deaths reported associated with confirmed cases of pH1N1 since the beginning of the pandemic. While this is almost certainly a sizeable underestimate, fortunately it is a figure much lower than some initial predictions.<sup>1</sup>

As of 10 August 2010, the WHO announced that the pandemic was over. In the southern hemisphere pH1N1 rates remain well below those observed during the same period in 2009 during the first pandemic wave. No large and unusual summer outbreaks have occurred in either northern or southern hemispheres. Indeed, the seasonal influenza A (H3N2) and

influenza B viruses are currently being reported in many countries. Based on this overall picture, the WHO believes that the evidence is strong that the recent influenza pandemic patterns are transitioning towards seasonal patterns of influenza.<sup>2</sup>

What has been learnt about pH1N1-induced respiratory failure from the 2009 experience? While pH1N1 disease is usually mild and often subclinical, it may cause life-threatening respiratory failure that evolves rapidly causing classical acute respiratory distress syndrome with a high incidence of other organ failures. Over the course of 2009, UK hospital admissions associated with influenza were increased sevenfold and, at the peak of the pandemic, almost 200 intensive care beds were occupied with influenza cases. Fortunately, perhaps because the patients were young, the ICU outcomes have been good with approximately 80% survival in multiple series despite the requirement for advanced support techniques including extracorporeal membrane oxygenation.<sup>3</sup>

Although roughly two-thirds of patients admitted to ICUs across the world had no longstanding health problems, several groups have been reported to be at increased risk of severe disease. The commonest comorbidities were asthma or chronic obstructive pulmonary disease, diabetes mellitus, heart disease and sickle cell disease.<sup>4</sup> A surprising proportion of critically ill patients were also obese or pregnant. While morbid obesity (body mass index >40 kg/m<sup>2</sup>) increased the risk of hospitalisation more than fourfold, an effect on mortality has not been demonstrated so far.<sup>5</sup> In contrast, infection during pregnancy or the postpartum

period was associated with a poor outcome from pH1N1, as has been shown for other forms of influenza.<sup>6</sup>

Predictions from experience with previous pandemics indicate that pH1N1 will continue to circulate for several years. Major concern remains in relation to the potential for the virus to mutate to a more lethal form. This concern is based on data suggesting previous influenza pandemics emerged after viral evolution<sup>7</sup> and with recent reports confirming that the pH1N1 virus has undergone genetic reassortment.<sup>8</sup> Indeed, there have been suggestions that mutant strains (notably D222G isolated from fatal cases in Norway) have a predilection for causing more aggressive disease, possibly because they bind preferentially to the glycan cell surface receptor that is highly expressed in the lower respiratory tract.<sup>9</sup>

While the rates of pH1N1 infection are now much lower, localised outbreaks may show significant levels of pH1N1 transmission. The risk of severe illness caused by pH1N1 remains, and with it a need for hospitalisation and critical care support. Indeed, within 48 h of the WHO downgrading the pandemic status, five patients with suspected pH1N1 were admitted to a hospital in the West Midlands. Two of these patients rapidly deteriorated with bilateral pulmonary infiltrates on chest x-ray requiring admission to the ICU and initiation of mechanical ventilation. The first case was a 44-year-old obese woman with a history of alcohol abuse and asthma who needed ventilation for 4 days. The second case was a 52-year-old man with treated vasculitis and a history of asthma and diabetes. Both patients met the criteria for acute lung injury upon intubation, with the second case progressing to ARDS on day 2 after intubation. Clearly, both these cases had more than one comorbid condition associated with severe pH1N1 infection.<sup>4</sup> These cases highlight the need for maintained vigilance, a high index of suspicion and a low threshold for empirical treatment of high-risk groups as we enter the seasonal influenza period.

Respiratory and intensive care clinicians are therefore reminded of the current Health Protection Agency clinical

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**Box 1 Diagnostic criteria for suspicion of H1N1**

Fever  $\geq 38^{\circ}\text{C}$  or a history of fever, influenza-like illness  
**PLUS** two or more of the following symptoms:  
 ► Cough  
 ► Sore throat  
 ► Rhinorrhoea  
 ► Limb or joint pain  
 ► Headache  
 ► Vomiting or diarrhoea  
**OR** severe and/or life-threatening illness suggestive of an infectious process.

diagnostic criteria for pH1N1 (see box 1).<sup>10</sup> Testing is recommended if patients are hospitalised for the control of infection in hospitals, or as part of 'spotter' surveillance schemes, or if there are unusual syndromes that are considered to have an infectious basis. Critically ill patients with suspected influenza should have samples taken from the lower respiratory tract as results from the upper airways are less reliable and may require repeating if negative.<sup>11</sup> Treatment should be continued if there is a high index of suspicion until repeated samples are negative.

It is also clear that delayed treatment with an appropriate antiviral agent

(oseltamivir or zanamivir) is associated with a poor outcome.<sup>12</sup> Treatment with oseltamivir should not therefore be delayed while waiting for sampling results. Careful attention to infection control procedures (hand washing, personal protective equipment, isolation where possible) should be maintained to limit cross-transmission among staff, patients and hospital visitors.<sup>13</sup>

In conclusion, the pH1N1 flu has taught us a lot about pandemic influenza without causing the devastating effects such as those seen with the 1918 influenza pandemic where millions of people died. The world's healthcare systems have learnt important lessons about dealing with a pandemic which will be invaluable for future major influenza outbreaks. Nevertheless, with H1N1 still causing serious disease outbreaks in the UK, although the pandemic may have gone the potential for H1N1 to cause disease should not be forgotten.

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