Planning for a pandemic: a view from the accident and emergency department

On 11 June 2009 the World Health Organization raised the pandemic alert level to Phase 6 and declared that a global pandemic was underway. The causative pathogen, an H1N1 influenza A virus, was a triple-reassortant combination of swine, avian and human influenza that initially appeared in Mexico earlier that year (Cao et al, 2009). In April 2009, the first US cases of H1N1 were confirmed by the Centers for Disease Control and Prevention (CDC) (Jain et al, 2009). Since then, many more clinical cases have been reported to the CDC and to public health authorities.

Based on the initial epidemiology and information regarding the pathogenesis of H1N1, the current pandemic appears to be relatively mild in terms of its overall severity and case fatality (Cao et al, 2009; CDC, 2009 **Aq is this 2009 a or b - see ref list?**; Jain et al, 2009; Louie et al, 2009). However, there are some unique and potentially concerning aspects to its pathogenesis that need to be addressed.

Prior pandemics

Influenza pandemics have occurred periodically throughout history (Cunha, 2004). However, the time from one pandemic to another varies and cannot be accurately predicted. Accordingly, the current pandemic was expected, as are future pandemics. The real questions have always been: when will the next pandemic occur and how severe will it be?

In the last century, there were three pandemics: 1918 Spanish flu H1N1, 1957 Asian flu H2N2 and 1968 Hong Kong flu H3N2 (Mareiniss et al, 2009). The most severe of these was the 1918 Spanish flu, which is considered one of the worst epidemiological catastrophes the world has suffered. It occurred in three distinct waves and resulted in an estimated 50–100 million deaths worldwide (Taubenberger and Morens, 2006); over half a million deaths occurred in the United States (Markel et al, 2007)**AQ I'm not sure this reference is necessary - can I remove it?**. An important and unusual aspect of this pandemic was that it predominantly caused morbidity and mortality in relatively healthy young adults (Cunha, 2004; Taubenberger and Morens, 2006). In contrast, the 1957–8 Asian flu and 1968 Hong Kong flu were much milder and more typical pandemics, with most morbidity and mortality among the very young, old and compromised patient populations (Kilbourne, 2006; Taubenberger and Morens, 2006).

The current pandemic: 2009 swine flu H1N1

From April until 14 November 2009, the CDC estimated that 34–67 million individuals in the United States were infected with the H1N1 virus (CDC, 2009a/b **AQ?**). Of these cases, the CDC estimated that 154 000–303 000 resulted in hospitalizations and that 7070–13 930 **AQ these are very wide ranges - why is this? How accurate are these figures?** resulted in deaths (CDC, 2009a/b **AQ?**). A significant peak in pandemic flu activity across the United States occurred from 18 October to 14 November 2009, with a high during the week ending 24 October (CDC, 2009a/b **AQ?**). The overwhelming majority of hospitalizations and deaths in seriously ill patients occurred in individuals younger than 64 years of age (CDC, 2009a/b **AQ?**).

Studies of hospitalized H1N1 patients confirm that the current pandemic is more problematic in younger populations: the median ages of admission in two studies were 21 years and 27 years respectively (Jain et al, 2009; Louie et al, 2009). This is in sharp contrast with seasonal influenza, where typically 60% of hospitalizations and 90% of mortality is among patients >65 years old (CDC, 2009a/b **AQ?**; Jain et al, 2009). The lower average age of admitted patients and apparent sparing of this older population may be the result of prior exposure or vaccination in the elderly population that has created some degree of pre-existing immunity (Louie et al, 2009). However, poorer outcomes have been seen among patients older than 50 years who are admitted with H1N1 infections (Louie et al, 2009. As a result, although the average age of admitted patients during this pandemic has been lower, clinical vigilance of older patients admitted with H1N1 infections is still vital.

There are also other important features of this pandemic. Similar to seasonal influenza, the majority of hospitalized patients appear to have had comorbid conditions (endocrine, pulmonary, cardiovascular, neuromuscular) that put them at risk for a severe clinical course. In one study of 1088 hospitalized patients with confirmed H1N1, 68% had comorbid conditions (Louie et al, 2009). A similar study found that 73% of hospitalized H1N1 patients had comorbid and underlying medical conditions (Jain et al, 2009). Of these conditions, asthma and COPD **Aq please write out in full?** were the most common in each study. Additionally, both pregnant and post-partum patients appear to be at increased risk for complications, as do obese and morbidly obese patients (Louie et al, 2009, 2010). However, further study of the obesity risk is likely needed. Severe disease has also been reported in healthy young adult patients (Jain et al, 2009; CDC, 2009b).

Among hospitalized patients, early treatment with antiviral medication (oseltamivir or zanamivir) seems important in limiting the severity of the clinical course. In a review of hospitalized patients, a multivariable model demonstrated that treatment with neuraminidase inhibitors within 48 hours of symptom onset was significantly associated with decreased intensive care unit admissions (Jain et al, 2009). A similar publication specifically demonstrated that early treatment with this type of antiviral medication within 48 hours of symptoms significantly decreased intensive care unit admission and death in hospitalized pregnant and postpartum patients compared to delayed treatment (Louie et al, 2010). However **Aq this implies that the next statement will be contradicting**

the previous one, whereas this seems to confirm it - is this correct? are you just emphasising that treatment after 48 hours is still worthwhile?, some observational data appear to indicate that antiviral treatment after 48 hours may reduce disease severity and mortality in hospitalized patients (Uyeki, 2009).

Emergency medicine issues

Given the apparent effectiveness of early antiviral treatment in preventing severe hospital courses and death in patients with H1N1, all patients with influenza-like illness who require hospital admission should be started on antiviral medication as soon as possible (Jain et al, 2009; Uyeki et al, 2009 **AQ should this be Uyeki, 2009 as in the reference list - if not please give full reference details?**). Further, patients with lung infiltrates and suspected influenza should be treated with both antibiotics and antivirals. Antiviral treatment should ideally begin within 48 hours of symptoms, as earlier treatment appears to limit the clinical severity, intensive care unit admissions and the risk of death in hospitalized patients (Jain et al, 2009; Louie et al, 2010). However, treatment after 48 hours is thought to be beneficial as well and is recommended (Jain et al, 2009; Louie et al, 2009; Uyeki et al, 2009 **AQ should this be Uyeki, 2009 as in the reference list - if not please give full reference details?**). Accordingly, emergency medicine physicians should consider starting empiric antiviral treatment as soon as possible for admitted patients (CDC, 2009b).

Logistically, timely antiviral treatment may be difficult in the emergency department because influenza outbreaks typically result in emergency department overcrowding. Such overcrowding may make timely administration of either antibiotics or antiviral medication difficult (Pines et al, 2007). In spite of this challenge, we must continue to proactively work to ensure that all potential H1N1 inpatients are rapidly identified and treated. We must also continue to use appropriate respiratory precautions with these patients while keeping them separated from other emergency department patients without influenza-like illness (Rothman et al, 2007 **AQ this is 2006 in the reference list - which is correct?**).

Although the current pandemic has been fairly mild, a significant portion of hospitalized patients have had severe clinical courses requiring intensive care unit care. Studies of hospitalized H1N1 patients have reported 25–30% patients treated in the intensive care unit (Louie et al, 2009; Jain et al, 2009). As a result, providers must be aware of their critical care resources in the event the pandemic becomes more severe (Mareiniss et al, 2009). The Task Force for Mass Critical Care, spearheaded by the American College of Chest Physicians, has provided several guidelines and recommendations for emergently expanding intensive care unit space in hospitals during times of infectious disease crises (Rubinson et al, 2008). This task force has also made recommendations regarding the proper allocation of intensive care unit beds and ventilators in the event that resources are severely limited (Devereaux et al, 2008). Although this eventuality is not currently expected, providers should be familiar with the above guidelines and recommendations as well as their local emergency response plans.

Conclusions

Only time will tell how this pandemic will evolve and eventually resolve. Until then, we must strive to quickly identify and treat hospitalized H1N1 patients with antivirals, continue to communicate new information and use our current understanding of H1N1 to better prepare for future waves of disease. Finally, as with all disasters, it is of paramount importance to maintain a high level of communication and coordination within the health-care setting. BJHM

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Cao B, Li X, Mao Y et al (2009) Clinical features of the initial cases of 2009 pandemic influenza (H1N1) virus infection in China. *N Engl J Med* **361**(26): 2507–17

Aq please confirm correct citation in text? Centers for Disease Control and Prevention (2009a) CDC estimates of 2009 H1N1 influenza cases, hospitalizations and deaths in the United States, April – November 14, 2009. www.cdc.gov/h1n1flu/estimates_2009_h1n1.htm (accessed 24 December 2009)

Aq please confirm correct citation in text? Centers for Disease Control and Prevention (2009b) Antiviral treatment options, including intravenous peramivir, for treatment of influenza in hospitalized patients for the 2009-2010 season. www.cdc.gov/h1n1flu/EUA/peramivir_recommendations.htm (accessed 23 December 2009)

Cunha BA (2004) Influenza: historical aspects of epidemics and pandemics. *Infect Dis Clin N Am* **18**: 141–55

Devereaux AV, Dichter JR, Christian MD (2008) Definitive care for the critically ill during a disaster: a framework for allocation of scarce resources in mass critical care from a Task Force for Mass Critical Care Summit Meeting, January

KEY POINTS

- On average, patients hospitalized with H1N1 are younger than the patients typically admitted for seasonal influenza. However, older hospitalized patients appear more likely to have poorer outcomes.
- Most patients hospitalized with H1N1 have comorbid conditions, but some severe clinical courses have been seen in healthy young adults.
- A significant percentage of hospitalized H1N1 patients with severe clinical courses have required ICU AQ please write out in full? admission.
- In hospitalized patients, treatment with neuraminidase inhibitors within 48 hours of symptoms appears to be associated with a decreased likelihood of ICU admission and death.
- All hospitalized patients with suspected H1N1 infections should receive empiric neuraminidase treatment as soon as possible. Such treatment should be initiated even if symptoms have persisted for more than 48 hours.

26-27, 2007, Chicago, IL. *Chest* **133**(5): ??? **AQ please give page nos for this ref?**

Jain S, Kamimoto L, Bramley AM (2009) Hospitalized patients with 2009 H1N1 influenza in the United States, April – June 2009. *N Engl J Med* **361**(20): 1935–44

Kilbourne ED (2006) Influenza pandemics of the 20th century. *Emerging Infect Dis* **12**(1): 9–14

Louie JK, Acosta M, Winter K (2009) Factors associated with death or hospitalization due to pandemic 2009 influenza A (H1N1) infection in California. *JAMA* **302**(17): 1896–902

Louie JK, Acosta M, Jamieson DJ, Honein MA (2010) Severe 2009 H1N1 influenza in pregnant and postpartum women in California. *N Engl J Med* **362**(1): 27–35

Mareiniss DP, Hirshon JM, Thibodeau BC (2009) Disaster planning: Potential effects of an influenza pandemic on community healthcare resources. *Am J Disaster Med* **4**(3): 163–71

Markel H, Lipman HB, Navarro JA, Sloan A, Michalsen JR, Stern AM, Cetron MS (2007) Nonpharmaceutical interventions implemented by US cities during the 1918-1919 influenza pandemic. *JAMA* **298**(6): 644–54

Pines JM, Localio RA, Hollander JE, Baxt WG, Lee H, Phillips C, Metlay JP (2007) The impact of emergency department crowding measures on time to antibiotics for patients with community-acquired pneumonia. *Ann Emerg Med* **50**(5): 510–16

AQ this is 2007 in the text - which is correct?

Rothman R, Irvin CB, Moran GJ et al (2006) Respiratory hygiene in the emergency department. *Ann Emerg Med* **48**(5): 570–82

Rubinson L, Hick JL, Hanfling DG (2008) Definitive care for the critically ill during a disaster: a framework for optimizing critical care surge capacity from a Task Force for Mass Critical Care Summit Meeting, January 26-27, 2007, Chicago, IL. *Chest* **133**: ??? **AQ please give page nos for this ref?**

Taubenberger JK, Morens DM (2006) 1918 influenza: the mother of all pandemics. *Emerging Infect Dis* **12**(1): 15–22

Uyeki T (2009) Antiviral treatment for patients hospitalized with 2009 pandemic influenza A (H1N1). *N Engl J Med* **361**: e110