

Clinical characteristics of paediatric H1N1 admissions in Birmingham, UK

Our experience of the first wave of paediatric H1N1 swine-origin influenza admissions in Birmingham, UK, shows that presentations can be atypical, severity is often associated with underlying disease, and rates of secondary bacterial infection are low. We reviewed the 78 available case notes of 89 children positive for H1N1 influenza by PCR admitted to hospitals across our three Trusts between June 5 and July 4, 2009.

The median age of admission was 5.7 years (range 0.1–16.3); 50 of 89 were male. 29 of 71 patients did not fulfil the H1N1 influenza case definition as described by the UK's Health Protection Agency (HPA)¹ (temperature $\geq 38^{\circ}\text{C}$ or a history of fever and two other symptoms of cough, sore throat, rhinorrhoea, limb or joint pain, headache, vomiting or diarrhoea, or a severe or life-threatening illness).

12 of 64 did not have a temperature of at least 38°C or a history of fever. After fever, cough (49/67) and rhinorrhoea (45/73) were the most common symptoms (figure). Other symptoms included haematemesis, photophobia, earache, preseptal

cellulitis, chest pain, apparent life-threatening episode, epistaxis, croup, rigors, apnoea, and acute abdomens (appendicitis and intussusception). 31 of 77 patients had significant pre-existing disorders including asthma, chronic lung disease, developmental delay, neuromuscular disease, immunodeficiency, prematurity, recurrent chest infections, and metabolic and endocrine disease.

Median length of stay was 24 h, irrespective of any underlying disease. Six children required high-dependency or intensive care; all had pre-existing disorders. Ten of 63 had possible or probable bacterial infections (one otitis media, six respiratory-tract infections, one preseptal cellulitis, one appendicitis). Antibiotics were prescribed in 22 of 61 patients, reflecting recent changes in HPA guidance. Oseltamivir was given to only 26 of 65 patients.

To have followed the HPA algorithm would have meant that 40% of children with H1N1 influenza would not have been diagnosed. Low numbers of suspected and confirmed bacterial infections suggest that uniform co-administration of empirical antibiotics is inappropriate.

Both H1N1 influenza and common respiratory viral infections are likely to spread commonly this autumn and winter in children, making clinical diagnosis of influenza more difficult.

Clinicians should consider H1N1 influenza in the differential diagnosis of children with pre-existing disorders who present acutely to health services even if HPA diagnostic criteria are incomplete or an alternative diagnosis is suspected, especially if there are severe symptoms or underlying disease.

It is imperative that further data are collected prospectively on the clinical presentations and predictors of severity in H1N1 influenza.

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1 Health Protection Agency. Human swine influenza: information for health professionals. <http://www.hpa.org.uk/webw/HPAweb&Page&HPAwebAutoListName/Page/1240812234677?p=1240812234677> (accessed Aug 12, 2009).

Swine-origin influenza virus H1N1, seasonal influenza virus, and critical illness in children

The effect that the swine-origin influenza virus (S-OIV) H1N1 will have on global child health is currently unknown. Attempts to extrapolate from knowledge of related viruses and adult data^{1,2} provide approximations, but these should be revised with developing clinical experience. An early understanding of the patterns of organ failure that predominate and of which children are most at risk of critical illness with S-OIV H1N1 will assist with planning responses.^{3,4}

With parental consent, we summarise our experience with critically ill children in four UK intensive-care units with S-OIV H1N1 (table). We

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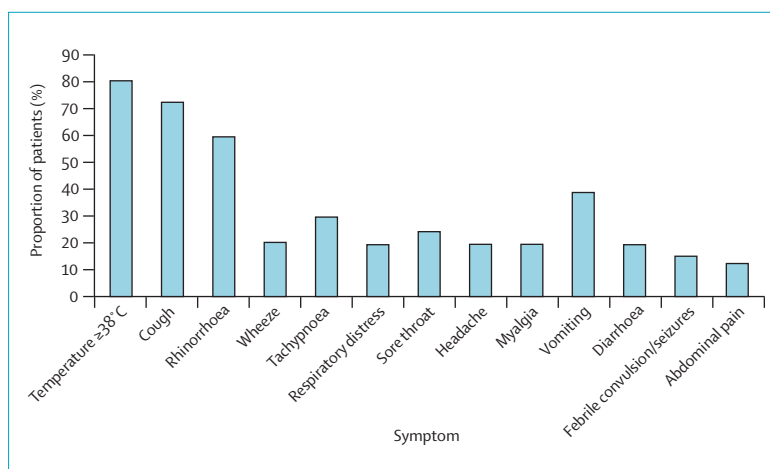


Figure: Proportion of patients with each symptom

also offer preliminary comparisons with the seasonal influenza cases 2004–07 identified in the Paediatric Intensive Care Audit Network (PICANet) dataset. PICANet collects prospective severity of illness, case-mix, interventions, and outcome data on all children admitted to paediatric intensive-care units in the UK.

Seasonal influenza was recorded in 58 children (median age 2.7 years, IQR 19 weeks–7.6 years; 33 male) who received intensive care between 2004 and 2007, of whom nine died. Most (48 of 58) presented with a respiratory illness and nine with new neurological symptoms. 32 patients and all nine who died had major

pre-existing diseases recorded, with neurological disease (12), chronic respiratory disorders (seven), and prematurity (five) being the most common. Inotropic support was given to 17 patients and three received extracorporeal membrane oxygenation. None was recorded as presenting with myocarditis.

	Age, sex, weight (kg), estimated risk of mortality (PIM2)	History	Known co-morbidity	Organ failures			Outcome
				Respiratory	Cardiovascular	Other, lymphopenia $<1 \times 10^9/L$, thrombocytopenia $<50 \times 10^9/L$	
June 26	6.9 years, female, 16 kg, PIM2: 40%	3 days fever, cough; rapid onset of respiratory distress, hypoxia, shock	Enteropathy: microvillus inclusion disease; chronic neutropenia	Four quadrant infiltrates. Day 1 PaO ₂ /FIO ₂ , 62, HFOV 9 h	Catecholamine- and steroid-resistant shock	Renal failure, Lymphopenia, Thrombocytopenia,	Died 9 h after admission
June 26	12 years, female, 35 kg, PIM2: 7%	3 days cough, fever, vomiting, lethargy; rapid onset of respiratory distress and hypoxia	None known	Progressive four quadrant infiltrates, PCV 4 days	Two inotropes for 48 h	Thrombocytopenia	Alive
June 27	11 years, male, 27 kg, PIM2: 7%	11 days painful crisis. 7 days fever, cough; respiratory distress and hypoxia.	Sickle-cell disease	Four quadrant infiltrates, PaO ₂ /FIO ₂ , 75, HFOV 8 days, PCV 2 days	Catecholamine for 24 h	Exchange transfusion for sickle chest crisis. Lymphopenia 48 h	Alive, discharged day 14
June 30	9 years, female, 25 kg, PIM2: 1%	3 days cough, fever; rapid onset of respiratory distress and hypoxia	Microcephaly, global developmental delay, epilepsy, severe kyphoscoliosis	Four quadrant infiltrates, PaO ₂ /FIO ₂ , 27.5, NIV×10 h, PCV 6 days	Catecholamine-resistant shock, Significant thoracic deformity		Died
July 1	9 years, male, 22 kg, PIM2: 2%	2 days fever, cough, vomiting; rapid onset of respiratory distress and hypoxia	Cerebral palsy, post-birth asphyxia, severe global developmental delay, profound kyphoscoliosis	Four quadrant infiltrates, PaO ₂ /FIO ₂ , 38, PCV 5-6 days	Catecholamine-resistant shock, Significant thoracic deformity	Possible secondary infection day 3	Died
July 5	5.5 years, female, 28 kg, PIM2: 4%	6 days fever, 2 days cough; respiratory distress and hypoxia	Encephalitis, autism, epilepsy	Four quadrant infiltrates, PaO ₂ /FIO ₂ , 76, PCV 9 days	Stable	Lymphopenia 48 h, thrombocytopenia	Alive, discharged day 10
July 5	1.3 years, male, 7 kg, PIM2: 15%	3 days fever, poor feeding, vomiting, lethargy; hypovolemic shock	Severe cerebral palsy secondary to hypoxic-ischaemic encephalopathy	Low-pressure ventilation, 48 h	Fluid responsive shock		Alive, discharged day 5
July 8	6 years, male, 20 kg, PIM2: 9%	2 weeks Intermittent fever and cough; progressive respiratory distress and hypoxia	Acute myeloid leukaemia	Four quadrant infiltrates, PaO ₂ /FIO ₂ , 2.56, HFOV 14 days, on-going	Stable	Encephalopathy, chemotherapy-induced lymphopenia and thrombocytopenia	Alive, discharged day 27
July 9	5.9 years, female, PIM2: 12%	2 days fever, tonsillitis, myalgia, abdominal pain; shock	None known	PaO ₂ /FIO ₂ , 190, PCV	Catecholamine-, steroid-, and milrinone-resistant shock	Streptococcal A co-infection	Progressive hypotension, died 10 h after admission
July 11	11 years, male, 38 kg, PIM2: 5%	5 days fever and cough; severe ketoacidosis	Newly diagnosed diabetes mellitus	Spontaneous ventilation, no respiratory support	Stable	Severe ketoacidosis	Alive, discharged day 3
July 14	9 years, female, 26 kg, PIM2 6.5%	2 days cough, fever, lethargy	Cerebral palsy, balanced chromosomal translocation, severe global developmental delay	Progressive four quadrant infiltrates, PaO ₂ /FIO ₂ , 44, PCV	Catecholamine responsive shock 8 days	Thrombocytopenia	Died
July 20	13 year, male, 40 kg, PIM2 2.6%	1 day cough, fever; respiratory distress	Well controlled asthma; no previous intensive-care admission	Low-pressure ventilation 12 h	Stable	Lymphopenia	Alive, discharged 22 h
July 20	10 year, male, 42 kg, PIM2 6.7%	Fever, lethargy, new-onset seizures; encephalitis	None known	Low-pressure ventilation 5 days	Stable	Diabetes insipidus. Cerebrospinal fluid negative for H1N1	Alive, discharged day 6

PCV=pressure control ventilation, HFOV=high-frequency oscillatory ventilation, NIV=non-invasive ventilation.

Table: Critically ill children with H1N1 influenza of swine origin in the UK in order of clinical presentation

Details of the S-OIV cases are summarised in the table. Most cases have occurred in children with known comorbidities including chronic lung disorders and immunodeficiency. The median age is higher than that for seasonal influenza (9 vs 2.7 years), but this could reflect transmission patterns in the early phases of a pandemic.

Eight of the cohort presented with shock: one was fluid-responsive, three responded to catecholamines, and four had catecholamine-resistant and steroid-resistant shock, one of which was associated with bacterial coinfection. Five children died. This fulminant course was not seen in the seasonal cohort.

There is a risk of selection and attribution bias in comparison of these contrasting cohorts with the current high level of interest and monitoring of S-OIV. However, the occurrence of fatal catecholamine-resistant shock in four of the 13 patients suggests an organ-failure pattern that might be different to that of seasonal influenza.

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Global responsibilities for global health rights

In his Comment on G8 responsibilities for global health and health systems strengthening, Julio Frenk (June 27, p 2181)¹ argues that the concept of "health security" (ie, the health components of human security) should include a "truly universal package of guaranteed benefits or entitlements, comprising [a] set of essential services applied to all in the world."

This notion is consistent with a human rights approach to health: there are core obligations arising from the right to health, and if some countries are too poor to fulfil them, the obligation shifts to the global level. Countries in a position to assist must help countries in need of assistance.² It is also compatible with the idea of a global social protection floor³ and of global health governance to meet the survival needs of the world's least healthy people.⁴

At the risk of being immodest, we also think it is in line with our proposal of a World Social Health Insurance or Global Health Fund.⁵ We therefore believe the time has come to further explore these concepts and to move from concepts to reality. What is this universal package of entitlements, these core obligations arising from the right to health, this global social protection floor, and this response to survival needs? What do these concepts include exactly? What are the responsibilities of low-income countries and when can they claim assistance? What are the responsibilities of the G8 and the countries able to assist? Which countries are we talking about and how should they share the burden?

Unless these questions are answered convincingly, the "health social contract" as a "key component of human citizenship" will remain a distant dream. To start the move from concepts to practice, we will be holding an international workshop on global responsibilities for global health in Brussels, Belgium, on Oct 19-21, 2009.

We declare that we have no conflicts of interest.

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The science and ethics of primate research

Your Editorial about transgenic marmosets (June 6, p 1920)¹ is thoughtful and recognises that causing suffering to animals, particularly primates, when it is not for their benefit raises serious ethical issues. We applaud your call for greater transparency.

We have to be clear, however, that research even on primates, our closest evolutionary relatives, is highly problematic from a scientific point of view. History tells us that it is wrong to assume that it leads inexorably to cures for human diseases, or guarantees safety. For example: not one of the 85 or more candidate AIDS vaccines tested successfully on primates has worked in patients; more

For the Global Responsibilities for Global Health Rights Conference see <http://www.hdbf.org>