



# **Pandemic H1N1 2009 Influenza: Clinical Management Guidelines for Adults and Children**

*Guidelines for Adults and Children prepared by  
the Department of Health*

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# Summary

1. Most disease seen in children and adults with pandemic H1N1 2009 influenza is mild.
2. Differentiation from other viral and bacterial infections is difficult in children and may be more problematic this winter, especially in children under 1 year old.
3. Children and adults should be offered oseltamivir if H1N1 is suspected before the results of confirmatory tests are available.
4. Antibiotics should be considered in selected cases: signs of bacterial or respiratory tract infection, failure to respond to antiviral therapy, underlying diagnoses, or severe H1N1 disease.
5. Pandemic guidance is based on evidence about other similar conditions together with limited information on pandemic H1N1 2009 influenza. This means that clinical judgment must remain paramount.

# Introduction

1. This document serves as an update to provisional guidance provided in 2007 by the British Infection Society, British Thoracic Society and Health Protection Agency in collaboration with the Department of Health.<sup>1</sup>
2. Knowledge of pandemic H1N1 2009 influenza continues to increase and the majority of existing clinical guidance continues to be valid. This document has been produced in the light of clinical experience during the first wave and has been endorsed by the clinical subgroup of the Pandemic Influenza Clinical and Operational Advisory Group. It is issued together with an update on the clinical management of pregnant women with an influenza-like illness, severe influenza and complications.
3. These guidelines are only intended for use during the H1N1 2009 influenza pandemic.
4. These guidelines will be updated regularly. Users are advised to refer to the latest web-based guidelines at all times.
5. Separate documents have been produced as practice notes for the care of critically ill children and adults affected by pandemic H1N1 2009 influenza. These documents are hosted by the Royal College of Paediatrics and Child Health<sup>2</sup> and Royal College of Anaesthetists<sup>3</sup> websites. The adult document is prefaced with current Health Protection Agency guidance on the use of personal protective equipment.

## 1. Clinical epidemiology

The information is taken from various data sources including the First Few Hundred study undertaken by the Health Protection Agency (FF100), HPA case follow-up and the Influenza Clinical Information Network (FLU-CIN) database. Only data of immediate relevance to clinical practice is included here.

### In primary care:

1. The likelihood of infection with pandemic H1N1 2009 influenza is strongly influenced by age; the young are at most risk and those aged >60 years at least risk. Approximately 60% of patients with confirmed H1N1 influenza A virus infection are aged 16 to 64 years. However case fatality increases with age, apart from the youngest children where it is also high.
2. Antiviral use as early as possible, in particular within the first 48 hours of onset of symptoms, reduces the risk of serious illness.

### In secondary care:

1. Less than 1% of patients are admitted to hospital.
2. Most patients admitted to hospital (80%) have not previously been started on an antiviral drug.
3. 12 to 15% of patients admitted to hospital require Level 2 (High Dependency Care) or Level 3 care (Critical/Intensive Care).
4. The mortality rate for hospitalised adults is approximately 6%.
5. Patients with underlying co-morbidities fare worse. Very few hospitalised young children (<20%) have co-morbidities, but this rises to 40% in 5-14 year-olds. Asthma is the commonest co-morbidity in children and young adults. Almost all (90%) hospitalised adults >65 years of age have at least one co-morbidity.
6. The risk of both hospital admission and death are strongly influenced by co-morbidities. In hospitalised adults significant risk factors for fatal outcomes include COPD, diabetes and heart disease. Obesity appears to be a risk factor for requirement for critical care but not for death.
7. The presence of pneumonia on admission is not influenced by sex, age or underlying co-morbidity.

## 1.1 Predictive risk factors for ICU admission<sup>4</sup>

### These are:

- dyspnoea (strongly predictive of both death and ICU requirement)
- requirement for supplemental oxygen (strongly predictive of ICU care and death)
- pneumonia on admission (strongly predictive of significant complications after admission – including ICU multi-organ support and death)
- heart rate in adults (the higher the pulse the greater the chances of ICU care being required)

altered conscious level

## 1.2 Clinical features of H1N1 2009 influenza virus infection

1. The majority of children and adults with H1N1 have mild symptoms that resemble infections with other winter viruses.
2. Amongst schoolchildren and adults, most experience mild illness with 50% of patients recovering within 7 days of symptom onset and a further 25% within 10 days. In the first wave of the pandemic, the main symptoms reported were fever, fatigue, dry cough, sore throat and headache.
3. Severe gastrointestinal disease (nausea, vomiting, diarrhoea, abdominal pain) has been a feature of H1N1 infection in children and adults requiring admission.
4. Features of H1N1 2009 influenza in children include current or recent history of high fever (temperature > 38°C) and usually two or more of the following: cough, rhinorrhoea, sore throat, headache, widespread muscle and joint aches, vomiting, diarrhoea, otitis media and rarely cerebral irritability and/or seizures. Atypical features have also been observed in children including haematemesis, photophobia, chest pain, epistaxis, croup, apnoea, and rigors. Some very young children and babies can exhibit sudden severe collapse (apparent life-threatening episode).<sup>5</sup>
5. In children <1 year of age, apnoea, reduced tone and poor feeding can occur with or without the classical features of influenza.
6. Complications of H1N1 2009 influenza appear similar to seasonal influenza. Myocarditis has been observed, usually associated with a marked tachycardia. The prognosis is unclear, though influenza-related myocarditis usually has a good prognosis for recovery.
7. As with seasonal influenza, neurologic complications such as seizures and encephalitis with altered mental state can occur.<sup>6</sup> The prognosis for patients with isolated neurological symptoms which can be optimised without requirement for ICU admission appears good.

8. In contrast to adults, most children admitted in the UK with severe influenza or complications have no recognised pre-existing risk factors. Children aged <5 years, regardless of whether they have co-morbidities, may be at increased risk for complications and death, as is the case with seasonal influenza.<sup>7</sup>
9. Clinicians should be aware of the potential for severe bacterial co-infections among children and adults with severe influenza and treat accordingly. Invasive bacterial infections that have been reported in paediatric patients include *Staphylococcus aureus*, Group A streptococcus and *Streptococcus pneumoniae*.<sup>7</sup>
10. In children and adults, initial symptoms of rapidly-lethal infections such as meningitis, encephalitis and bacteraemia can resemble influenza.

### 1.3 Influenza-related pneumonia

1. Influenza-related pneumonia has occurred in 40% of hospitalised patients in the United States, usually with bilateral infiltrates apparent in the chest x-ray.<sup>8</sup> Amongst patients with H1N1 influenza admitted to ICUs in New Zealand and Australia, 49% had viral pneumonitis or ARDS and 20% had secondary bacterial pneumonia.<sup>9</sup>
2. One report from the US of post mortem samples identified a bacterial co-pathogen in 29% of cases<sup>10</sup> including *Streptococcus pneumoniae*, *S. pyogenes*, *Staphylococcus aureus*, *S. mitis* and *Haemophilus influenzae*. Bacterial pneumonia was not suspected prior to death in these patients.
3. The assessment of disease severity in patients with influenza-related pneumonia remains a matter of clinical judgement. Currently, no specific prognostic markers have been identified for H1N1-related pneumonia. Severity assessment tools widely employed in the context of community acquired pneumonia (CAP), such as the CURB65 score or the Pneumonia Severity Index (PSI), are heavily influenced by age. There has therefore been concern that these scores are less relevant to this pandemic as most hospitalised patients with H1N1 influenza infection are less than 65 years of age.

4. However, older age is an important adverse prognostic variable in H1N1 influenza infection. In addition, in patients presenting with an influenza-like illness (ILI) and features of pneumonia, it will not always be possible to distinguish between H1N1 influenza-related pneumonia and *non*-H1N1 related community acquired pneumonia initially. Therefore, calculation of CURB65 scores in such patients is still advisable given their utility in the management of pneumonia in general.

**BOX 1:** CURB65 score for severity assessment in adults with community acquired pneumonia

**CURB65 severity score** - 1 point for each feature present:

**C**onfusion (altered mental status or disorientation in person, place and time)

**U**rea > 7 mmol/l

**R**espiratory rate  $\geq$  30/min

**B**lood pressure (systolic < 90mmHg or diastolic  $\leq$  60mmHg)

**A**ge  $\geq$  65 years

5. High dose corticosteroids have been associated with prolonged viral shedding in seasonal and H1N1 influenza virus infections as well as increased mortality in H5N1 influenza-related pneumonia/pneumonitis. There is also a substantial risk of side effects with their use.

## 1.4 Antiviral therapy

1. In patients with seasonal influenza A infection, antiviral treatment is most effective if it is commenced as soon as possible and in any case within 48 hours of symptom onset. However, recent experience with hospitalised patients with pandemic H1N1 2009 influenza reveals that antivirals given more than 48 hours<sup>8</sup> and up to 7 days after symptom onset also confer benefit.
2. The neuraminidase inhibitors, oseltamivir and zanamivir, are both active against pandemic H1N1 2009 influenza. In comparison to oseltamivir, zanamivir given by inhalation is effective in the respiratory tract but does not reach effective levels

systemically. At the present time, oseltamivir-resistance remains rare and no onward transmission of resistant virus has occurred.

## 1.5 The Swine Flu Clinical Package

1. The swine flu clinical package is a set of tools for use by frontline healthcare professionals, in severe and exceptional circumstances, during a pandemic situation.<sup>11</sup> The package contains community assessment tools, a referral letter and hospital pathways.
2. The package is for use only when high healthcare demand leads to the need for strict hospital admission triage in affected areas. They should not be used when emergency departments and acute admissions units are working with their usual establishment of trained staff, and can operate their usual daily decision pathways, including provision of hospital beds for all those who normally require admission.
3. The assessment tools in the swine flu clinical package are not intended for patients who present for diagnosis and treatment of uncomplicated influenza at an emergency department. These patients should be directed to use the normal routes for obtaining antivirals in the community, such as the National Pandemic Flu Service, or to contact a primary care surgery or clinic.

# 2. Recommendations for primary care

## 2.1 Assessment and management of children in primary care

1. Mild fever, coryza, and new cough are common features of many viral respiratory tract infections and in most children can safely be managed by parents and carers with fluids and antipyretics such as paracetamol and ibuprofen.
2. The symptoms of influenza and serious bacterial infections, especially in children under one year old, may be confused and difficult to differentiate. For this reason, a general

practitioner should see all children under one year old who are unwell with fever or influenza-like symptoms.

3. Aspirin should not be given to children unless on the recommendation of a medical specialist.
4. Parents and carers should not use over-the-counter cough and cold medicines in children under 6 years old. There is no evidence that they work and they can cause side effects such as allergic reactions, effects on sleep or hallucinations.<sup>12</sup>

## **2.2 Assessment and management of adults in primary care**

1. Patients with clinically diagnosed uncomplicated influenza infection would be expected to make a full recovery. They require good symptomatic management, access to antiviral treatment as soon as possible, information about the natural history, and advice as to when to re-consult.
2. Symptomatic treatment includes:
  - treatment of fever, myalgia and headache with paracetamol or ibuprofen
  - good fluid intake
  - avoidance of smoking
  - rest
  - topical decongestants, throat lozenges and saline nose drops may be helpful
3. Patients with acute exacerbations of asthma should be treated according to established evidence-based guidelines for the management of asthma in addition to antiviral therapy.<sup>13</sup>

4. Patients with dyspnoea or recrudescence of fever not responding to treatment should be examined to assess the presence and severity of influenza-related pneumonia, and the need for hospital referral.

## **2.3 Antiviral therapy in children and adults in primary care**

1. Oseltamivir remains the drug of choice for the majority of patients.
2. Oseltamivir dosing should follow current national guidelines.
3. Doses and indications for antiviral therapy in young children are subject to change as knowledge of pharmacodynamics and efficacy advances.
4. In the UK, zanamivir is the antiviral of choice for pandemic H1N1 2009 influenza virus infection in:
  - a. Pregnant women who do not have severe disease unless they suffer with conditions such as asthma or chronic pulmonary disease, or may have difficulty with an inhaled preparation, when oseltamivir should be used.
  - b. Patients five years of age and older with renal failure.
5. Antiviral therapy may be offered to patients who are unable to mount a febrile response but have other features that are consistent with H1N1 2009 influenza infection. Such patients may include:
  - a. very elderly people
  - b. immuno-compromised patients.

## **2.4 Empiric antibiotics for children and adults in primary care**

1. Patients do not routinely require antibiotics if they have uncomplicated influenza and were previously healthy.

2. Adults and children with features of influenza complicated by lower respiratory tract signs, severe painful pustular tonsillitis/sore throat, severe painful cervical lymphadenopathy and significant acute suppurative otitis media who are not referred to hospital, should be offered empiric antibiotic therapy.
3. When antibiotics are indicated, children should receive co-amoxiclav or clarithromycin if penicillin/amoxicillin allergic. Adults should receive doxycycline or co-amoxiclav.
4. A five-day course of an oral antibiotic should be adequate for most patients deemed suitable for treatment in the community. Patients should be warned to seek further medical attention if symptoms persist or deteriorate.
5. Patients with pre-existing co-morbidities (such as chronic lung, heart, renal, liver or neuromuscular disease and immuno-suppression) who are therefore at high risk of severe disease and complications, and who present with an influenza-like illness, should be strongly considered for antibiotics in accordance with NICE guidelines on Respiratory Tract Infections.<sup>14</sup>
6. Patients presenting with an exacerbation of COPD should be considered for antibiotics in accordance with existing guidelines for the management of COPD.<sup>15, 16</sup>

## **2.5 Review and reassessment in the community**

It is inevitable that some children will develop significant flu complications and others a potentially serious non-flu illness.

1. When reviewing a child who is not responding to standard management clinicians should consider alternative diagnoses such as bacterial pneumonia, septicaemia, meningitis and encephalitis.
2. GPs must advise parents or carers to seek further medical advice without delay if their child develops a rash or their condition suddenly worsens.

3. All children whose parents or carers contact their GP under these circumstances require urgent face to face clinical assessment in a clinical setting.

## 2.6 Criteria for referral to hospital

1. Indicators for hospital referral are not exclusive but include:
  - a. signs of respiratory distress (dyspnoea, tachypnoea, and also in children, nasal flare, grunting, indrawing of lower chest wall and severe recession)
  - b. peripheral oxygen saturation  $\leq$  94% in air
  - c. dehydration or shock
  - d. any sign of sepsis
  - e. altered conscious level
  - f. seizures.
2. In all patients with a clinical diagnosis of influenza-related pneumonia, hospital referral and assessment should be considered for those with dyspnoea.
3. Measurement of peripheral oxygen saturation by pulse oximetry is essential to exclude hypoxaemia. Absence of cyanosis does not exclude hypoxaemia.
4. All adults who have a peripheral oxygen saturation measured by pulse oximetry ( $SpO_2$ ) less than 94% should be considered for hospital referral and oxygen supplementation.<sup>17</sup>
5. Children who have a  $SpO_2$  less than or equal to 94% should be considered for hospital referral and oxygen supplementation.<sup>18</sup>
6. Guidance should not supersede the decision of an experienced clinician to refer a sick patient to hospital for further assessment and management.

7. Patients with worsening of pre-existing co-morbid medical conditions should be managed according to best practice for that condition with reference to published disease-specific guidelines, where available. This may include referral to hospital.

## 3. Recommendations for secondary care

### 3.1 Assessment and management of children and adults in secondary care

1. Consideration and exclusion of other pathologies (e.g. meningococcal sepsis, herpes encephalitis, group A streptococcal infections) must be part of the assessment of all patients, since these will continue to present during an influenza pandemic.
2. In patients admitted to hospital, age appropriate early warning tools should be used to facilitate identification of deteriorating patients.
3. Patients with worsening of pre-existing co-morbid medical conditions should be managed according to best practice for that condition with reference to published disease-specific guidelines.
4. For patients who have low blood pressure and compromised urine output / renal function, intravenous fluid boluses are a routine and appropriate initial therapy. However, there are some early indications that excessive fluid volumes may lead to serious pulmonary compromise. For patients whose condition seems refractory to fluid resuscitation it may be advisable to consider central venous cannulation and early initiation of inotrope / vasopressor support.

### 3.2 Antiviral therapy in children and adults admitted to hospital

1. Treatment with oseltamivir should be started on clinical grounds whilst awaiting test results.

2. Oseltamivir dosing should follow current national guidelines.
3. Doses and indications for antiviral therapy in children are subject to change as knowledge of pharmacodynamics and efficacy advances.
4. Some clinicians have doubled the dose in older critically ill children and adults; however the risks and benefits of this are yet to be fully evaluated.
5. Oseltamivir dose should not be doubled in children under the age of one year.
6. Consideration should be given to extending the duration of antiviral treatment in critically ill children and adults.
7. Liaise with local experts for most up to date antiviral guidance or when considering deviating from national guidance.

### **3.3 Empiric antibiotics for children and adults in secondary care**

These guidelines offer recommendations for the empiric antibiotic regimen in patients with influenza-related pneumonia and other respiratory tract infections.

1. Adults and children with features of influenza complicated by lower respiratory tract signs, severe painful pustular tonsillitis/sore throat, severe painful cervical lymphadenopathy and significant acute suppurative otitis media should be offered empiric antibiotic therapy, whether or not they are admitted to hospital.
2. A patient with uncomplicated influenza admitted to hospital for other reasons and who has no risk factors for severe disease does not routinely require antibiotic therapy.
3. Patients with pre-existing co-morbidities (such as chronic lung, heart, renal, liver or neuromuscular disease and immunosuppression) who are therefore at high risk of severe disease and complications, and who present with an influenza-like illness, should be strongly considered for antibiotics in addition to antiviral treatment.

4. Most patients with non-severe influenza-related pneumonia can be treated with oral antibiotics. When antibiotics are indicated, children should receive co-amoxiclav (or clarithromycin if penicillin allergic). Adults should receive doxycycline or co-amoxiclav (or clarithromycin if penicillin allergic). A total of five days of antibiotics is recommended.
5. Antibiotics should ideally be administered within four hours of admission.
6. Patients with severe influenza-related pneumonia should be treated promptly with parenteral antibiotics. An intravenous combination of co-amoxiclav together with a macrolide such as clarithromycin is preferred. In patients who are penicillin allergic, a second generation cephalosporin, such as cefuroxime, may be an alternative to co-amoxiclav.
7. In adults with severe, microbiologically undefined pneumonia, a 10 day course of treatment is proposed. This should be extended to 14–21 days where *S. aureus* or Gram negative enteric bacilli pneumonia is suspected or confirmed.<sup>19</sup>
8. Adult patients presenting with an exacerbation of COPD should be considered for antibiotics in accordance with existing guidelines for the management of COPD.<sup>15,16</sup>
9. The use of antibiotics should be reviewed daily. Prophylactic or prolonged use of antibiotics for pneumonia may increase the risk of late superinfection with resistant organisms particularly in those requiring prolonged ventilatory support. Such infections are often associated with rapid deterioration.
10. Empirical antibiotic therapy should be switched to narrow spectrum antibiotics if there is laboratory confirmation of infection with sensitive organisms.
11. Intravenous antibiotics should be switched to orally administered antibiotics as soon as the physician judges this to be appropriate.

### 3.4 Respiratory disease

1. Children who have a SpO<sub>2</sub> less than or equal to 92% should be given oxygen and admitted to hospital.
2. The decision to admit a child with a SpO<sub>2</sub> between 92% and 94% should be informed by expert clinical assessment, consideration of the phase of illness, and social and geographical factors.<sup>18</sup>
3. In adult patients not at risk of hypercapnic respiratory failure, the recommended target oxygen saturation range is 94 to 98%.<sup>17</sup>
4. For most adult patients with known chronic obstructive pulmonary disease (COPD) or other known risk factors for hypercapnic respiratory failure (e.g. morbid obesity, chest wall deformities or neuromuscular disorders), a target oxygen saturation range of 88 to 92% is suggested pending the availability of blood gas results.
5. Hypoxaemic patients should receive appropriate oxygen therapy with monitoring of oxygen saturations and inspired oxygen concentration.
6. Hypoxaemia is a common cause for escalation to critical care, so oxygen saturation monitoring on the ward is an important observation, along with clinical signs of respiratory distress and exhaustion.
7. The majority of patients with diffuse pneumonitis are likely to need intubation within 24 hours of presentation.
8. Non-invasive ventilation (NIV) has been used in hypoxaemic children with H1N1 lower respiratory tract infection where there is a bronchiolitic or pneumonic process but appears to confer no advantage in those with acute respiratory distress syndrome (ARDS) or severe hypoxaemia.
9. Routine use of corticosteroids in influenza-associated pneumonitis/pneumonia is not recommended.

10. NIV may be helpful in the management of adult patients presenting with acute exacerbations of COPD and who are in respiratory failure.
11. NIV has had a role in weaning and the convalescent phase in the adult and paediatric critically ill H1N1 population.
12. Note well that NIV is a potential aerosol-generating procedure (see Infection control below).

### **3.5 Influenza-related pneumonia in adults and pneumonia severity assessment**

1. In patients presenting with an influenza-like illness and features of pneumonia, the local epidemiology of H1N1 2009 influenza should be taken into account when making a diagnosis of either H1N1 influenza-related pneumonia or non-H1N1 related community acquired pneumonia.
2. When assessing disease severity, clinical judgement must be applied in all instances, and may be supported by severity assessment tools commonly applied to patients with community acquired pneumonia, such as the CURB65 score.
3. Patients with bilateral lung infiltrates consistent with primary viral pneumonia on chest radiography should be managed as having severe pneumonia regardless of their CURB65 score.

### **3.6 Cardiovascular disease and shock**

1. Cardiac enzymes can be raised (troponin and CK-MB) and this must be differentiated from the raised CK due to myositis or rhabdomyolysis that may also be seen in influenza.
2. Patients should be assessed for cardiac complications and their need for additional intravenous fluids. However, the risk of excessive fluid volumes leading to serious

pulmonary or cardiac compromise requires consideration. For patients whose condition seems refractory to fluid resuscitation it may be advisable to consider central venous cannulation and early initiation of inotrope / vasopressor support.

3. Early echocardiography in shocked children is recommended to exclude viral cardiomyopathy as a cause of circulatory failure.

### 3.7 Neurological disease

1. Seizure control and airway management should follow standard guidelines.
2. CT scans should be considered as per usual practice to exclude other pathology. CT scans in children with pandemic H1N1 2009 influenza and neurological features have revealed significant pathology including cerebral oedema and infarction. If patients have a significant degree of conscious level impairment (GCS<10; 'P' on the AVPU scale) they may need to be intubated and ventilated for safety reasons prior to a scan being performed.
3. Lumbar puncture, after exclusion of contraindications to the procedure, continues to have an important role in excluding other causes of meningoencephalitis (e.g. herpes simplex virus types I & II). Pandemic H1 RNA PCR may be positive on CSF but the relevance is unknown.
4. The empirical use of acyclovir should be considered for all infants with a neurological presentation pending an HSV PCR result on CSF.
5. Acute neurological symptoms should not limit other therapy except where clear evidence of an irreversible deficit exists.
6. It has been suggested that diclofenac and mefenamic acid are associated with a worse prognosis in influenza related encephalopathy.<sup>20</sup> Neither of these drugs should be used in children with influenza and should be avoided in adults with influenza-related encephalopathy.

### 3.8 Microbiology investigations

The range, availability and turnaround times of microbiological investigations will vary depending on local factors and the degree of pressure on clinical and laboratory services. Further advice/information should be sought from local microbiologists.

1. PCR is more sensitive than immuno-fluorescence for H1N1 detection and hence should be used in preference.
2. Antiviral and antimicrobial treatment, where clinically indicated, should not be delayed pending the results of investigations.
3. Ideally, all patients admitted to hospital with influenza-like illness should be tested as a minimum for H1N1 in order to facilitate appropriate treatment and infection control precautions.
4. Where virological testing cannot be offered to all cases, high priority should be accorded to virological confirmation of H1N1 (as a minimum) in patients admitted with influenza-like illness who are in high risk groups, including pregnant women, those admitted to critical or high dependency care or who have influenza-related pneumonia.
5. When deterioration occurs viral and bacterial screening should be repeated to screen for other pathogens.
6. Bacteriological investigations should be undertaken in critically ill patients and those with evidence of influenza-related pneumonia, and should follow locally agreed protocols and/or BTS Community Acquired Pneumonia Guidelines 2009.
7. The following bacteriology investigations are recommended as a minimum: blood cultures, pneumococcal and legionella urine antigen (where offered locally), and culture of purulent sputum or other lower respiratory tract samples.

8. If patients continue to deteriorate whilst on antiviral treatment, consideration should be given to testing for antiviral resistance and advice should be sought from a microbiologist.

### 3.9 Infection control

1. Management of patients with ongoing respiratory symptoms should be in accordance with local guidelines for infection control.
2. It is appropriate to observe full infection control measures for all suspected cases pending laboratory results. Isolation is preferred to cohorting, if feasible. Diligence in hand hygiene must be maintained at all times and in particular between patients.
3. Correct protective equipment is required during potential infectious aerosol generating procedures (AGPs) such as tracheostomy toilet, intubation and bronchoscopy. Such AGPs are listed in current DH & HPA infection control guidelines.
4. Non-invasive ventilation (NIV) is potentially an infectious aerosol generating procedure and correct personal protective equipment (PPE) should be worn when caring for patients. Nosocomial spread has been reported in this context associated with sub-optimal PPE usage. Respiratory and/or critical care units experienced in the use of NIV are best placed to ensure the appropriate infection control measures are adopted at all times.

### 3.10 Escalation and referral to critical care in children

Criteria for identifying children who may benefit from critical care and which should trigger discussion with intensivists would include:

1. Hypoxaemia ( $SpO_2 < 92\%$ ) resistant to high flow oxygen therapy.
2. Worsening respiratory failure characterised by: severe, recurrent, prolonged apnoea requiring resuscitation; worsening tachypnoea with gasping or grunting; or a rising  $PaCO_2$  on sequential blood gas analysis.

3. Cardiovascular collapse/shock that does not respond to a fluid resuscitation (equal to or greater than a total of 40 ml/kg of 0.9% saline or Hartmann's).
4. Encephalitis with coma (GCS < 9) or seizures requiring intubation for airway control.

### **3.11 Escalation and referral to critical care in adults**

Criteria for identifying adults who may benefit from critical care and which should trigger discussion with intensivists would include:

1. Severe dyspnoea
2. Patients with influenza-related pneumonia and a CURB65 score  $\geq 4$ , or who have bilateral primary viral pneumonia
3. Hypoxaemia with  $\text{PaO}_2 < 8$  Kpa despite maximal oxygen administration
4. Progressive hypercapnia
5. Refractory hypotension (some emerging evidence suggests that excessive fluid resuscitation may contribute to the severity of respiratory compromise)
6. Septic shock
7. Severe acidosis (pH <7.26)
8. GCS<10 or deteriorating conscious level

### **3.12 Post-mortem examination**

1. Clinicians are encouraged to seek post-mortem examination of fatal cases of influenza-like illness and influenza-related pneumonia.

2. Post-mortem examination should include comprehensive virological and bacteriological investigation.

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## References

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<sup>1</sup> Pandemic flu: clinical management of patients with an influenza-like illness during an influenza pandemic. Provisional guidelines from the British Infection Society, British Thoracic Society, and Health Protection Agency in collaboration with the Department of Health. *Thorax*. 2007 Jan;62 Suppl 1:1-46. No abstract available. Erratum in: *Thorax*. 2007 Jun;62(6):474.

<sup>2</sup> <http://www.rcpch.ac.uk/Policy/Swine-Flu>

<sup>3</sup> <http://www.rcoa.ac.uk>

- <sup>4</sup> HPA Clinical notes. <http://www.hpa.org.uk/HPA/Topics/InfectiousDiseases/InfectionsAZ/1242949541960/>
- <sup>5</sup> S Hackett, L Hill, J Patel et al. Clinical characteristics of paediatric H1N1 admissions in Birmingham, UK. *Lancet* 2009 374:605.
- <sup>6</sup> Centers for Disease Control and Prevention (CDC) Neurologic complications associated with novel influenza A (H1N1) virus infection in children - Dallas, Texas, May 2009. *MMWR Morb Mortal Wkly Rep.* 2009 Jul 24;58(28):773-8.
- <sup>7</sup> Centers for Disease Control and Prevention (CDC). Surveillance for pediatric deaths associated with 2009 pandemic influenza A (H1N1) virus infection - United States, April-August 2009. *MMWR Morb Mortal Wkly Rep.* 2009 Sep 4;58(34):941-7.
- <sup>8</sup> Jain S, Kamimoto L, Bramley AM, Schmitz AM, Benoit SR, Louie J, et al. Hospitalized Patients with 2009 H1N1 Influenza in the United States, April-June 2009. *N Engl J Med* 2009; 361 (10.1056/NEJMoa0906695).
- <sup>9</sup> The ANZIC Influenza Investigators. Critical Care Services and 2009 H1N1 Influenza in Australia and New Zealand. *N Engl J Med* 2009; 361 (10.1056/NEJMoa0908481)
- <sup>10</sup> Bacterial coinfections in lung tissue specimens from fatal cases of 2009 pandemic influenza A (H1N1) - United States, May-August 2009. *MMWR Morb Mortal Wkly Rep* 2009; 58(38):1071-4.
- <sup>11</sup> [http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_106495](http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_106495)
- <sup>12</sup> Over-the-counter cough and cold medicines for children. MHRA Dear Colleague letter dated 28 February 2009
- <sup>13</sup> British Guideline on the Management of Asthma. *Thorax* 2008;63 Suppl 4:iv1-121.
- <sup>14</sup> NICE Clinical Guideline 69. July 2008. Respiratory tract infections – antibiotic prescribing. Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care.
- <sup>15</sup> NICE Clinical Guideline 12. Feb 2004. COPD. Management of chronic obstructive pulmonary disease in adults in primary and secondary care.
- <sup>16</sup> Global Initiative for Chronic Obstructive Lung Disease. Global strategy for diagnosis, management, and prevention of COPD [Internet] [updated Nov 2008]. Available from: <http://www.goldcopd.org>
- <sup>17</sup> O'Driscoll BR, Howard LS, Davison AG. British Thoracic Society guideline for emergency oxygen use in adult patients. *Thorax* 2008;63 Suppl 6:vi1-68.
- <sup>18</sup> Bronchiolitis in children, a national clinical guideline. Scottish Intercollegiate Guideline Network. Guideline 61, November 2006
- <sup>19</sup> British Thoracic Society Guidelines for the management of community acquired pneumonia in adults: update 2009 *Thorax*, 2009, Vol 64, Supplement III, iii1-55
- <sup>20</sup> Prognosis in influenza associated encephalopathy. Nagao T et al. *Pediatr Infect Dis J.* 2008; 27: 384-389

