DRAFT **Last revised: April 2006**

Fraser Health Clinical Features Guide – Pandemic Influenza

1. CLINICAL FEATURES FOR ALL HEALTH CARE WORKERS

1.1. Overview

Many experts have noted that the clinical features of the anticipated pandemic influenza virus will be similar to those found in interpandemic influenza A infections. Although the spectrum of clinical diseases associated with a novel influenza A subtype cannot currently be determined, Fraser Health has provided specific information on the most likely cause of the next pandemic strain (as of March 2006), which will be a variant of the current avian influenza A/H5N1 virus. As a result, this Clinical Features Guide will outline a number of key clinical descriptors in terms of interpandemic influenza A, as well as avian influenza A/H5N1.

1.2. Case definition (ADULTS AND CHILDREN)

	INTERPANDEMIC INFLUENZA A	AVIAN INFLUENZA A/H5N1

Case Definition* (Oct. 2005)	• The presence of fever and new (or, in those with chronic lung disease, worsening) cough of acute onset in the context of influenza circulating in the community.
	
	NOTE: In children under 5, gastrointestinal symptoms may also be present.
		• The presence of all of the following in a patient:
		  • Documented fever of over 38°C (100.4°F)
		  • Cough, sore throat, or shortness of breath; and
		  • History of contact with poultry or domestic birds (e.g., visited a poultry farm, a household raising poultry, or a bird market), or a known or suspected patient with avian influenza H5N1 in an H5N1-affected country within 10 days of symptom onset.**

It is important to note that the case definition will need to be updated regularly as outbreaks of pandemic influenza are identified.

****It is likely that the contact history of patients with poultry, or infected birds, or a known or suspected patient with avian influenza H5N1, will be removed from the case definition during a pandemic.***

During a global influenza pandemic, when a pandemic strain is known to be circulating locally in an immunologically-susceptible population, the presence of a fever and new cough of acute onset would be expected to be highly predictive for influenza infection.

The probability of influenza infection also increases with an increasing level of fever.

1.3. Incubation (ADULTS AND CHILDREN)

	INTERPANDEMIC INFLUENZA A	AVIAN INFLUENZA A/H5N1
Incubation	• 2-4 days (range 1-7)	• 2 to 8 days, and possibly as long as 17 days. • WHO currently recommends that an incubation period of 7 days be used for field investigations and the monitoring of patient contacts.

1.4. Clinical presentation

NOTE: This overview of the clinical presentation for avian influenza A/H5N1 is for both adults and children, as the majority of cases presenting have been young adults and children (≤ 20).

	INTERPANDEMIC INFLUENZA A	AVIAN INFLUENZA A/H5N1
Clinical Presentation	• Abrupt onset of fever, accompanied by a range of symptoms (see below for range of symptoms). • • Fever usually ranges between 38°C – 40°C. • • The peak occurs within 24 hours of onset and lasts typically for 3 days (range 1 – 5 days).	• Abrupt onset of fever, accompanied by a range of symptoms (see below for range of symptoms).
Range of Symptoms	• cough (85%) • malaise (80%) • chills (70%) • headache (65%) • anorexia (60%) • coryzal symptoms (60%) • myalgia (53%) • sore throat (50%)	• cough • malaise • chills • headache • myalgia • sore throat • coryzal symptoms • chest pain • shortness of breath • abdominal pain* • vomiting* • diarrhea* • encephalitis* **Patients may present with GI or CNS and NO associated respiratory symptoms.*

1.5. Clinical course (ADULTS AND CHILDREN)

	INTERPANDEMIC INFLUENZA A	AVIAN INFLUENZA
Clinical Course	• Uncomplicated influenza illness is characterized by the abrupt onset of constitutional and respiratory signs and symptoms (e.g., fever, myalgia, headache, malaise, nonproductive cough, sore throat, and rhinitis). • Among children, otitis media, nausea, and vomiting are also commonly reported with influenza illness. • Influenza illness typically resolves after 3–7 days for the majority of persons, although cough and malaise can persist for >2 weeks. • Among certain high risk individuals (see table below), influenza can exacerbate underlying medical conditions and lead to secondary bacterial pneumonia or primary influenza viral pneumonia, or occur as part of a co-infection with other viral or bacterial pathogens. • Young children with influenza infection can have initial symptoms mimicking bacterial sepsis with high fevers, and < 20% of children hospitalized with influenza can have febrile seizures.	• Lower respiratory tract manifestations are found at presentation. • Almost all patients have clinically apparent pneumonia. • Dyspnea developed a median of five days after onset of illness. • Radiographic changes include diffuse, multifocal, or patchy infiltrates. • Pleural effusions are uncommon. • Limited microbe data indicated that this process is a primary viral pneumonia. • Progression to respiratory failure has been associated with diffuse, bilateral, ground-glass infiltrates manifestations of the acute respiratory distress syndrome (ARDS).

1.6. Complications (ADULTS AND CHILDREN)

COMPLICATIONS	INTERPANDEMIC INFLUENZA A	AVIAN INFLUENZA A/H5N1
Respiratory	• Upper respiratory: Otitis media, sinusitis, conjunctivitis • Acute laryngo-tracheo-bronchitis (croup) • Bronchitis • Bronchiolitis • Pneumonia: Primary viral, secondary bacterial or combined • Complication of pre-existing disease	• Upper respiratory • Pneumonia: Primary viral, secondary bacterial or combined • Pulmonary hemorrhage • pnuemothorax
Cardiovascular	• Pericarditis • Myocarditis • Complication of pre-existing disease	• Myocarditis • Supraventricular tachyarrhythmias
Muscular	• Rhabdomyositis • Rhabdomyolisis with myoglobinuria and renal failure	• N/A
Neurologic	• Encephalitis • Reye's syndrome • Guillain-Barre • Transverse myelitis	• Encephalitis • Reye's syndrome
Systemic	• Toxic shock syndrome • Sudden death	• pancytopenia • Sepsis

1.7. Patient factors: High-risk groups to interpandemic influenza A and avian influenza A/H5N1

INTERPANDEMIC INFLUENZA A	AVIAN INFLUENZA A/H5N1
• Age: < 2 or >65 years • Pregnancy (2nd and 3rd trimesters) • Cardiovascular diseases (congenital, rheumatic, ischemic heart disease, congestive heart failure) • Asthma, bronchitis, bronchiectasis, emphysema, cystic fibrosis • Metabolic diseases (diabetes) • Significant renal or hepatic diseases • Malignancies • Immunodeficiency, AIDS, immunosuppression, transplant recipients • Anemia and hemoglobinopathies • Long-term salicylate therapy and younger than 18 years of age (Kawasaki disease, rheumatoid arthritis, acute rheumatic fever, others)	• Infants, young children, and young adults *(NOTE: In contrast to 1997, when most deaths occurred among patients older than 13 years of age, recent avian influenza A (H5N1) infections have caused high rates of death among infants and young children.* Additional high risk groups are those with the following conditions: • Chronic respiratory disease (including asthma, cystic fibrosis, chronic lung disease of prematurity, bronchiectasis) • Congenital heart disease • Chronic renal disease eg nephrotic syndrome, renal failure • Chronic liver or Gastrointestinal disease, including inflammatory bowel disease • Immunodeficiency • Malignancy • Diabetes and other metabolic conditions • Haemoglobinopathies • Neurological disease (e.g., diseases with muscle weakness and cerebral palsy)

1.8. Mortality

	INTERPANDEMIC INFLUENZA A	AVIAN INFLUENZA A/H5N1
Overview of Mortality	• Yearly average mortality is about 0.02%, or about 7,000 annually in Canada.	• Overall, the case-fatality rate for H5N1 influenza is approximately 50%. Unlikely to remain this high if it becomes sustained human to human.
		• In Thailand, the case fatality rate was 89 percent among those younger than 15 years of age.
		• Death has occurred an average of 9 or 10 days after the onset of illness, and most patients have died of progressive respiratory failure.

1.8.1. ISSUE OF NOTE: CYTOKINE STORM

The high case-fatality rate suggests that the pathogenicity of avian influenza A/H5N1 may be similar to the 1918 H1N1 pandemic strain. Researchers have hypothesized that cytokine storm (i.e., overproduction of cytokines) may have played an important role in the pathogenesis of the 1918 pandemic strain. A laboratory-based study involving H5N1 strains taken from ill humans in Asia (during 1997 and 2004), and an ordinary current H1N1 strain (circulating in Asia in 1998), found that all the H5N1 viruses caused human alveolar cells and bronchial epithelial cells to secrete significantly higher levels of various cytokines and chemokines than did the ordinary virus. These findings support the role of cytokine storm in the pathogenesis of H5N1, although further work is needed to clarify the clinical implications of these findings.

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