

Managing Seasonal and Pandemic Influenza in Infants, Children and Youth

N MacDonald, H Onyett, R Bortolussi; Canadian Paediatric Society, Infectious Diseases and Immunization Committee

This document is current as of March 31, 2010 and will be updated as new information becomes available.

1. CLINICAL PRESENTATION

Typical influenza in children and youth begins with sudden onset of fever accompanied by chills, rigor, malaise, diffuse myalgias and nonproductive cough. However, in infants and children, especially those less than 10 years of age, the clinical presentation may be atypical.

In younger children, especially those less than 5 years of age, influenza may be indistinguishable from other respiratory viruses, including mild fever with coryza, or croup, bronchiolitis or pneumonia. In young infants respiratory distress may be an early sign. In pH1N1 influenza, unlike seasonal influenza, gastrointestinal symptoms (including one or more of nausea, vomiting and diarrhea) may occur commonly. Those younger than six months of age are more likely to present with rhinorrhea and dehydration rather than cough and pneumonia. In those less than 3 months of age, fever alone or fever with dehydration are common presentations (1).

Complications of influenza in infants, children and youth may include pulmonary complications such as severe hemorrhagic viral pneumonia, secondary bacterial pneumonia (due to *Streptococcus pneumoniae*, *Staphylococcus aureus*, and group A *Streptococcus*), mixed viral and bacterial pneumonia, localized viral pneumonia, severe laryngotracheobronchitis (croup) and exacerbation of chronic pulmonary disease. Non-pulmonary complications include acute myositis, myocarditis or pericarditis, toxic shock-like picture (due to invasive secondary bacterial sepsis, febrile seizures, encephalitis/encephalopathy, Reye's syndrome and Guillain-Barré syndrome (2).

A prospective pan-Canadian study of infants, children and adolescents hospitalized with influenza, carried out by the Immunization Monitoring Program, ACTive (IMPACT) in 2003-04 noted that for the 505 hospitalized children, fever and cough were the most common presenting complaints but seizures occurred in 9% (3). Serious complications included myocarditis in two (0.4%) children aged 3 and 7 years; encephalopathy in 6 (1.2%)—all but one in children 6 to 23 months of age—and meningitis in a 13-month-old and one case of necrotizing fasciitis in a 7-year-old. There were three influenza related deaths—pneumonia and cardiac arrest in an adolescent with severe congenital heart disease, acute myocarditis in a previously healthy 7-year-old and pneumonia followed by septic shock in a 1-year-old with mild cardiac malformation (2,4,5).

Warning signs indicating that an infant, child or youth needs urgent attention and possible admission are shown in Table 1.

Serious illness and/or death with influenza can be due to one of several mechanisms: (1) direct viral infection with severe respiratory illness, e.g. severe pneumonitis exacerbated by a cytokine storm leading to ARDS and hypoxia; (2) secondary bacterial infection, eg., empyema and necrotizing pneumonia; and (3) indirect effects of influenza in patients with underlying illness where the infection leads to exacerbation of heart, respiratory or other system failure. In seasonal influenza, serious illness in the elderly is often due to the third mechanism while, in infants and toddlers—the group with the highest rate of hospitalization—the first mechanism is most common with fever and respiratory disease such as bronchiolitis or pneumonitis (3). For older children and youth, underlying medical conditions can predispose to more serious illness in both seasonal as well as pandemic influenza. These are noted in Table 2. Overall, hospitalized children with pH1N1 tended to be older than with seasonal influenza (5). Asthma as a predisposing factor for serious illness with influenza was more commonly seen with pandemic rather than with seasonal influenza (5,6).

For those needing intensive care with pH1N1 infection, bacterial superinfection was more common than with seasonal influenza (7,8) and underlying predisposing factors especially asthma were far more prevalent (9).

2. EPIDEMIOLOGY OF INFLUENZA

Influenza is spread from person to person through droplets produced from coughing or sneezing. Indirect transmission also likely occurs through self-inoculation after contact with surfaces or objects contaminated with the virus from infected persons' (10).

The incubation period for both seasonal and pandemic influenza is a median of 3 to 4 days with a range of 1 to 7 days. Virus shedding in nasopharyngeal secretions may precede symptoms, usually peaks during the first three days of illness and ceases by Day 7. However, in pH1N1 influenza, children may shed the virus up to 10 days and individuals who are severely ill or immunocompromised may shed the virus for weeks to months (4). Prolonged viral shedding, for both seasonal and pandemic influenza, can occur in immunocompromised children including neonates. Viral shedding in nasal secretions occurs for 24 hours before symptoms.

Influenza viruses can circulate year round in the tropics, but seasonal outbreaks are more common during the winter in Canada. Community outbreaks are reported to last 4 to 8 weeks in both seasonal and pandemic influenza. As was seen with the pH1N1 outbreak during the spring and fall of 2009 in Canada, when a pandemic strain first appears, major activity can occur outside of the usual winter influenza season and have a prolonged duration.

During a community outbreak of seasonal influenza, highest attack rates occur in school-age children. The attack rates for seasonal influenza in healthy children range from as low as 3% to 30% with usual seasonal influenza. Higher attack rates may occur in pandemics.

High rates of influenza immunization in the school aged population lead to a decrease in morbidity and mortality in the elderly as well as in preschool children (11,12).

Excess morbidity and mortality occurs during influenza outbreaks—both seasonal and pandemic. With seasonal influenza outbreaks, pediatric hospital admissions occur predominately in children under 2 years of age (57% of those admitted in the 2003-04 study noted above) and the majority occurring in previously healthy children (3). Of note, infants under 6 months of age have hospitalization rates that are higher than those for older infants and children and equivalent to persons 65 to 80 years of age (1). Pandemic influenza is associated with higher hospitalization rates in children and youth than for seasonal influenza. In Argentina, hospitalization rates with pH1N1 were double the rates seen in children with seasonal influenza (20.9/100,000 vs. 10.3/100,000) (9). During the recent pH1N1 outbreak in Canada, serious illness leading to hospitalization occurred more frequently in older children and less so in infants. Many (over two-thirds) of these older children and youth had underlying medical conditions. Secondary serious bacterial infections also appeared to be more common during the pH1N1 pandemic in Canada (5).

Deaths from seasonal influenza occurred more commonly among children who were previously healthy. During the 2009 pH1N1 outbreak in Argentina, fatalities occurred more commonly among children with significant underlying conditions (fatality rate 1.1/100,000) compared with the fatality rate during the 2007 seasonal influenza outbreak (rate 0.1/100,000) in 2007, with the majority of deaths due to refractory hypoxemia (9).

3. DIAGNOSIS

Laboratory verification that a respiratory illness is due to influenza requires isolating the virus in tissue culture, or detecting the virus by rapid antigen tests or RT-PCR. However, a new pandemic influenza strain may be missed by rapid respiratory virus antigen techniques since the test kits available initially may not be sufficiently sensitive to detect for the new strain. The most appropriate specimens for testing are nasal-pharyngeal aspirates or swabs (see video for specimen collection technique: www.youtube.com/watch?v=TFwSefezIHU). Serological testing is not helpful to diagnose acute illness in both seasonal and pandemic influenza as it does not provide timely information.

Health care providers should use their judgment in testing. Not all children and youth with respiratory symptoms suggestive of influenza need to be tested. Testing is indicated only for those with serious illness in an outbreak, or to confirm appropriateness of empiric antiviral therapy in time of low influenza activity, or multiple circulating strains, or to test for resistance if not responding to antiviral therapy

4. MANAGEMENT

4.1. Home care

Infants, children and youth who are ill with influenza, whether seasonal or pandemic, should stay home and away from daycare, school or work, and avoid non-household contacts until their symptoms have resolved. If the illness is mild, patients should avoid visiting their

physician's office, walk-in clinic or emergency room unnecessarily, as it may put others at risk. This recommendation is appropriate for both seasonal and pandemic influenza. Symptomatic treatment should be offered for mild illness. Fever may be controlled with acetaminophen or ibuprofen. Aspirin and medications containing salicylates should be avoided because of the potential risk of developing Reye's syndrome. Fluids should be encouraged, including ongoing breastfeeding, in order to avoid dehydration. For both seasonal and pandemic influenza, parents are advised to seek medical care for their child or youth if symptoms progress (Table 1). Clinicians should pay particular attention to clinical deterioration during the course of illness, or after initial recovery as evidenced by new onset of fever, shortness of breath, unexplained chest or abdominal pain, lethargy or change in the level of consciousness. Deterioration after initial signs of recovery may be an indication of secondary bacterial infection.

Antiviral therapy may be considered for some children managed at home—see Antivirals.

When influenza is in the community, especially if a pandemic strain, if possible, only family members who are not sick should care for infants. Attention needs to be paid to usual precautions, especially ensuring good hand hygiene before touching the infant to decrease the risk of transmission. If the mother develops symptoms suggestive of influenza it is preferable for the infant to be cared for by another household member if possible. If the baby is being breastfed, another caregiver can give the baby expressed milk until the mother is better, especially during the first few days of the influenza. Even if the mother is on oseltamivir, this is not a contraindication for giving the baby the breast milk. If there is no other caregiver able to help the mother with the breastfeeding, the mother should be encouraged to wear a mask if available while breastfeeding and to be especially diligent with hand hygiene. If a mask is not available and/or tolerable, the mouth and nose need to be covered with a tissue when coughing or sneezing (2,13).

4.2. Hospital care

Infants, children and youth who are ill with influenza, including those with pandemic influenza, require aggressive supportive care which may include oxygen, intravenous fluids, antivirals (see below) and in some instances antibiotic therapy when a secondary bacterial infection is suspected. Underlying medical conditions need to be aggressively managed. Children with evidence of progressive respiratory failure, shock or obtundation require intensive care. In some patients, respiratory failure may be so severe as to require advanced ventilatory techniques such as high frequency oscillation or ECMO (7,8). Children with large empyemas may need repeated chest tube placement and drainage procedures as well as very prolonged courses of antibiotics. All of these more significant complications have occurred in older children with pH1N1 compared with seasonal influenza.

5. DRUGS FOR THE TREATMENT AND PREVENTION OF INFLUENZA

5.1. Antivirals for the treatment of influenza illness

The recommendations for use of antiviral drugs for the treatment or prevention of influenza infection including pandemic influenza, is available in the Canadian Paediatric Society document at www.cps.ca/english/statements/ID/ID06-04.htm.

Three antivirals are available in Canada: amantadine, only for influenza A; oseltamivir for both influenza A and B; and zanamivir, also for influenza A and B. Antiviral resistance is an emerging concern.

Several factors are key in determining whether to use an antiviral and which one to use:

- Is the strain known?
- Is it sensitive to antivirals and if so to which ones?
- What is the age of the child (some antivirals are not recommended for young infants or children)?
- What are the potential risks and benefits of the antiviral in the clinical setting?

For example, the recent pH1N1 was always sensitive to zanamivir and almost always sensitive to oseltamivir. Zanamivir is not recommended for those under 7 years of age as younger children cannot easily use the aerosolization delivery device. An intravenous form of zanamivir may be available through the Special Access Program of Health Canada (www.hc-sc.gc.ca/dhp-mps/acces/drugs-drogues/index-eng.php) (14). Although the data for use of antivirals such as oseltamivir in infants and young children was limited, oseltamivir was used in infants under 1 year of age during the pH1N1 pandemic because of the severity of illness and risk benefit ratio. A third agent, peramivir-intravenous, also had emergency use authorization in the USA through their “special access” programs, but was not available in Canada.

In general antiviral therapy is recommended for individuals with severe illness and those outpatients most likely to develop complications of influenza or to die prematurely as a result (Table 2). The duration of recommended therapy is five days. Ten days may be indicated in patients with severe immunodeficiency who remain symptomatic and virus-positive and for those with severe disease requiring intensive care. There are differences in treatment recommendations when pH1N1 is circulating in the community vs. seasonal influenza. In part this may be due to the sensitivity of the circulating strain of influenza to the antiviral drug and the approved anti-viral drugs available for children. Therefore, even though noted in Table 2 as being at higher risk for severe illness with influenza, children under 2 years of age who are otherwise healthy and have mild disease and do not require hospitalization do not routinely need antiviral treatment. Antiviral therapy would be considered based on clinical judgment of these children under 2 years of age who are otherwise healthy, have mild disease and do not require hospitalization.

Because there have been no studies directly comparing the relative efficacies and safety of zanamivir, the selection of one or the other of these agents needs to be based on several factors including the age of the child, the ability to inhale zanamivir or tolerate its uncommon irritant effect on the tracheobronchial tree with resulting bronchospasm. When indicated, antivirals should be started as soon as possible after the onset of symptoms—within 48 hours—for best effect. However they may be helpful even if started later if severe, progressive illness occurs. In the recent pH1N1 pandemic late onset of antiviral treatment for severe illness had a higher probability of need for intensive care (8).

Because of the high probability of the emergence of resistance, amantadine should not be prescribed for treatment of influenza A strains that are sensitive to neuraminidase inhibitors. Resistance may spread to other strains. The seasonal influenza A H1N1 strain in circulation in recent years is resistant to oseltamivir and requires zanamivir or amantadine for treatment. If this strain remains in circulation, zanamivir or combination therapy needs to be considered for empiric treatment of severe influenza.

See Table 3 for dosing of oseltamivir, Table 4 for zanamivir and Table 5 for amantadine. No firm recommendations can be made for use of antivirals in premature infants. Consultation with a pediatric infectious disease specialist and pediatric clinical pharmacist is advised.

5.2. Antivirals for the prevention of influenza illness

Antiviral drugs are no substitute for other measures such as influenza vaccine or use of infection control measures including hand hygiene. Most experts recommend early therapy rather than prophylaxis because of the risk of precipitating viral resistance. Prophylaxis might be considered if immediate protection is required for individuals at very high risk during an influenza outbreak: (a) in a closed institutional setting; or (b) in the family setting. For more details go to www.cps.ca/english/statements/ID/ID06-04.htm. When antiviral agents are used to prevent influenza, effectiveness is 70% to 90% for viral strains that are sensitive to the antiviral medication.

5.3. Vaccines for the prevention of influenza

The National Advisory Committee on Immunization (NACI) produces an annual *Statement on Influenza Vaccination* that contains specific information and recommendations regarding the vaccine to be used in the upcoming influenza season (15). In Canada, a trivalent inactivated influenza vaccine grown in hens eggs is made available each year usually by late September or early October. The vaccine components are adjusted each year to take into account changes in the seasonal influenza A and B strains that are expected to circulate. Intramuscular administration of the vaccine results in the production of both circulating IgG antibody to the viral hemagglutinin as well as a cytotoxic T lymphocyte response. Both are thought to be important for immunity to influenza (16). The production and persistence of antibody after vaccination depends on several factors, including the age and immunocompetence of the recipient and prior and subsequent exposure to influenza antigens.

Infants under 6 months of age do not respond well to vaccine and children 6 months to 9 years need two doses at least one month apart to achieve good protective titers the first time they receive seasonal influenza immunization. Immunity starts to appear about two weeks after immunization and usually lasts less than one year. Given that the seasonal strain of influenza may change, yearly immunization is recommended.

In Canada, yearly immunization of those listed in Table 2, i.e. those with underlying conditions that increase the risk of more serious illness with influenza as well as all children under 6 to 23 months is strongly recommended. Given the role that school age children play in community outbreaks of influenza (11), routinely offering influenza immunization to all children and youth up to age 18 years of age is recommended.

The effectiveness of influenza vaccine varies with age and immunocompetence of the vaccine recipient, the endpoint studied, the incidence of infection and the degree of similarity (“match”) between the vaccine strains and the viral strain(s) circulating during the influenza season. With a good match, vaccine efficacy is approximately 70% to 90% in healthy children. If the match of the vaccine types with the circulating strains is not good then vaccine efficacy may only be 30% to 60% (16).

When a new pandemic influenza virus arrives, a new vaccine must be made. For pH1N1 in 2009, Canada used three types of vaccine: Arepanrix (adjuvanted H1N1 flu vaccine from GlaxoSmithKline), Influenza A (H1N1) 2009 Pandemic Monovalent Vaccine (without adjuvant from GlaxoSmithKline) and Panvax (unadjuvanted H1N1 flu vaccine from CSL Australia). Preliminary reports noted that the vaccine was highly effective and that the side effects were similar to those seen with seasonal influenza with the exception of noting in one study increased rates of fever in children, especially young children 6 months to 3 years of age who received adjuvanted vaccine. (17).

A live attenuated nasal spray influenza vaccine has been available for a number of years for use in children over the age of 2 years in the United States (18).

Canada has a strong vaccine safety system (19). This eight-component system ensures that all vaccines used in Canada, including both seasonal influenza vaccine and any pandemic vaccine, are well manufactured, potent, and as safe as possible.

6. INFECTION CONTROL

Recommendations for infection control precautions for infants, children and youth for the office, hospital and home are outlined in the CPS statement at www.cps.ca/english/statements/ID/PandemicInfluenza.htm.

Personal measures (respiratory hygiene) to minimize transmission include: covering a cough or sneeze using a sleeve or a tissue (see video: www.coughsafe.com/media.html). In ambulatory settings such as a doctor’s office or clinic, standard respiratory hygiene procedures must be followed. Signs should be posted at entrances with instructions to tell the receptionist promptly if

symptoms of a respiratory infection are present, and to practice proper respiratory hygiene. Ideally, patients with a respiratory illness should be separated from other patients and wear a surgical mask in the waiting room. If masks are not available, or not feasible because of a child's inability to comply, the child's nose and mouth should be covered with tissues when coughing or sneezing. Waiting areas should be equipped with conveniently located hand sanitizer dispensers. Where sinks are available, ensure supplies for hand washing (ie., soap, disposable towels) are frequently replenished. After a patient with suspected influenza leaves, surfaces and equipment that the child may have come in contact with need to be cleaned using a germicidal disinfectant (4,20).

In hospitals, institutional or local guidelines should be consulted.

7. SPECIAL CONSIDERATIONS

7.1. Immunocompromised children

Due to the heterogenous nature of this group of patients, a single uniform approach is not possible. Children who are immunocompromised (eg., immune deficiency, either congenital or acquired) or who have underlying conditions that put them at risk for serious illness (Table 2) but who cannot be immunized may be considered for prophylaxis with antivirals (see above) for six to eight weeks during a serious outbreak (21). This is especially relevant when only a poorly matched vaccine is available. The foregoing notwithstanding, chemoprophylaxis should generally be discouraged because of the risk of development of resistance and should only be employed with guidance from local experts and public health authorities. Early treatment instead of prophylaxis is the more preferred strategy. Immunocompromised children are also more likely to have prolonged symptoms and hence remain infectious and require infection control measures for a more prolonged period than the typical seven days.

7.2. Newborns, infants under 6 months of age and their mothers

Infants under 6 months, including newborns are at high risk for hospitalization with seasonal influenza or pandemic influenza (1). In the United States, influenza hospital admission rates for infants younger than 6 months of age range between 1.8 and 7.2 per 1000 young infants; many-fold higher than the rates of influenza hospitalization for older infants and children, and for older adults. These may well be underestimates of hospitalization rates because many infants and children with influenza are not accurately diagnosed by physicians as influenza cases.

Although infants younger than 6 months of age are known to be at high risk for serious influenza illness, prevention is problematic. In contrast to infants older than 6 months of age, the influenza vaccine has limited immunogenicity in these very young infants. There are now two recommended strategies for decreasing seasonal influenza risk in this vulnerable young infant age group: (1) influenza immunization of the caregivers and family of the young

infant; and (2) influenza immunization of the pregnant woman. These strategies are more fully outlined in www.cps.ca/english/H1N1_IllnessAntiviral.htm as well as <http://www.phac-aspc.gc.ca/alert-alerte/h1n1/postpart-eng.php> and <http://www.phac-aspc.gc.ca/alert-alerte/h1n1/guidance-orientation-07-09-eng.php> (22).

TABLE 1
Warning signs requiring urgent medical attention

Children and youth

- Difficulty breathing or shortness of breath
- Flu-like symptoms improve but then return with fever and worse cough
- Confusion, listlessness, altered consciousness
- Severe or persistent vomiting
- Fever with rash
- Severe chest pain or abdominal pain
- Seizure

Infants and toddlers

- Fast breathing or trouble breathing
- Bluish skin colour
- Not drinking enough fluids
- Not waking up or not interacting
- Being so irritable that the child does not want to be held
- Flu-like symptoms improve but then return with fever and worse cough
- Fever with a rash
- Seizures

Table adapted from Reference 23.

Table 2 – Underlying conditions that place children and youth at higher risk of a serious outcome from influenza including pandemic H1N1

<ul style="list-style-type: none">• Neurological disorders, such as:<ul style="list-style-type: none">○ Epilepsy or cerebral palsy, especially when accompanied by neurodevelopmental disabilities (eg., moderate to profound intellectual disability or developmental delay).○ Neuromuscular disorders (eg., muscular dystrophy), when associated with impairment in respiratory functioning.• Chronic respiratory diseases associated with impaired pulmonary function and/or difficulty handling lung secretions; moderate and especially severe persistent asthma; technology-dependent children (eg., those requiring oxygen, tracheostomy, or a ventilator).• Moderate to profound intellectual disability (mental retardation) or developmental delay, especially when associated with other specific conditions (see above).• Morbid obesity with BMI > 35• Deficiencies in immune function or conditions that require medications or treatments (eg., certain cancer treatments) that result in significant immune deficiencies.• Congenital heart disease or significant metabolic or endocrine disorders, especially if a child has specific respiratory conditions (see above).• Renal, hepatic, hematological (including sickle cell disease) disorders.• Receiving chronic aspirin therapy.• Pregnancy or up to 2 weeks post-partum regardless of how the pregnancy ended.• Infants and children under 23 months of age are also at high risk
--

(Adapted from the AAP website ‘Novel Influenza A (H1N1) Virus and Children with Underlying Medical Conditions - AAP Work Group Clarifies Children at Highest Risk – October 1, 2009)

Table 3 – Dosage guidelines for oseltamivir (Tamiflu®) in infants, children and youth

Age or Body Weight	Treatment Dosage*
≥ 13 years (or 40 kg)	75 mg capsule Twice daily X 5 days
1 year to 13 years	
≤ 15 kg	30 mg capsule or oral solution# twice daily X 5 days
> 15 to 23 kg	45 mg capsule or oral solution# Twice daily X 5 days
24 to 40 kg	60 mg capsule or oral solution# Twice daily X 5 days
Birth to 12 months	
Birth to 1 month	2 - 3 mg/kg oral solution# Twice daily X 5 days
> 1 to 3 months	2.5 - 3 mg/kg oral solution# Twice daily X 5 days
> 3 to 12 months	3 mg/ kg oral solution# Twice daily X 5 days

References:

1. United States (FDA), <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafety/InformationforPatientsandProviders/ucm183870.htm>
2. Europe (EMA), http://www.emea.europa.eu/humandocs/PDFs/EPAR/tamiflu/Tamiflu_PI_clean_en.pdf
3. United States (CDC), http://www.cdc.gov/h1n1flu/recommendations_pediatric_supplement.htm
4. Canada (PHAC), www.phac-aspc.gc.ca/alert-alerte/h1n1/guidance-orientation-07-20-eng.php

Footnotes:

* **CAUTION:** Dosage adjustment required in renal failure if creatinine clearance < 30 mL/min

CAUTION: oral solution is prescribed in milligrams (mg) of solution (not milliliters, mL). Errors have been made when parents interpreted mg as mL. The dosing dispenser packaged with oseltamivir (Tamiflu®) has markings only in 30, 45 and 60 mg. This works well for those over 15 kg and over 1 year. If under 1 year or less than 15 kg, a ml dropper or ml oral syringe needs to replace the prepackaged dosing dispenser with clear instructions to the parent on mls prescribed. Oseltamivir suspension dosage (either manufacturer prepared or pharmacy prepared suspensions) depends on the weight/age of the infant/child.

Note: Dosage recommendations may be changed as new information becomes available. Please refer to reference sources for updates on dose recommendations. Current weight-based dosing recommendations are not intended for premature infants. Please seek consultation from an infectious disease clinician if treatment is being considered for such infants. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2009/2009_158-eng.php

Table 4 – Dosage Recommendations for Zanamivir for Children and Youth

Age	Treatment* (5 Days)
≥ 7 years of age and adults	10 mg – in 2 inhalations Twice daily x 5 days
Administered by inhalation using one 5mg package for each inhalation.	

Table adapted from References 24 and 25.

Table 5 – Dosage Recommendations of Amantadine for Children and Youth

Age	Dosing
1 to 9 yrs	5 mg/kg/day not to exceed 150mg/day in two divided doses
10 yrs and over	<40kg – 5mg/kg/day in two divided doses maximum 200mg/day >40 kg – 200mg/day in two divided doses

*Use of amantadine among children aged 1 year and younger has not been adequately evaluated.

Table adapted from Reference 26.

REFERENCES

1. Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Protecting your babies from influenza. *Paediatr Child Health* 2009;14:612-4.
<http://www.cps.ca/english/statements/ID/ProtectingBabies.htm> (Version current at April 7, 2010).
2. Canadian Paediatric Society. Questions and Answers on Pandemic (H1N1) 2009 Influenza: The Illness and Antiviral Drugs. http://www.cps.ca/english/H1N1_IllnessAntiviral.htm (Version current at April 7, 2010).
3. Moore DL, Vaudry W, Scheifele DW, et al. Surveillance for influenza admissions among children hospitalized in Canadian immunization monitoring program active centers, 2003-2004. *Pediatrics* 2006;118:e610-9. <http://pediatrics.aappublications.org/cgi/content/full/118/3/e610> (Version current at April 7, 2010).
4. Canadian Paediatric Society, Infectious Diseases and Immunization Committee. The new influenza A virus: A/Mexico/2009 (H1N1) practice point for caregivers of children and youth. *Paediatr Child Health* 2009;14:337.
<http://www.cps.ca/english/statements/ID/H1N1Mexico2009.htm> (Version current at April 7, 2010).
5. O'Riordan S, Barton M, Yau Y, Read S, Allen U, Tran D. Risk factors and outcomes among children admitted to hospital with pandemic H1N1 influenza. *CMAJ* 2010;182:39-44.
<http://www.cmaj.ca/cgi/content/full/182/1/39> (Version current at April 7, 2010).
6. 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;58:941-7.
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5834a1.htm> (Version current at April 7, 2010).
7. Lockman JL, Fischer WA, Perl TM, Valsamakis A, Nichols DG. The critically ill child with novel H1N1 influenza A: a case series. *Pediatr Crit Care Med* 2010;11:173-8.
8. Zarychanski R, Tuart TL, Kumar A, et al. Correlates of severe disease in patients with 2009 pandemic influenza (H1N1) virus infection. *CMAJ* 2010;182:257-64.
<http://www.cmaj.ca/cgi/rapidpdf/cmaj.091884v1> (Version current at April 7, 2010).
9. Libster R, Bugna J, Coviello S, et al. Pediatric hospitalizations associated with 2009 pandemic influenza A (H1N1) in Argentina. *N Engl J Med* 2010;362:45-55.
<http://content.nejm.org/cgi/reprint/362/1/45.pdf> (Version current at April 7, 2010).
10. Public Health Agency of Canada. Individual and Community Based Measures to Help Prevent Transmission of Influenza-Like-Illness (ILI) in the Community, Including the Pandemic Influenza (H1N1) 2009 Virus. http://www.phac-aspc.gc.ca/alert-alerte/h1n1/hp-ps-info_health-sante-eng.php (Version current at April 7, 2010).
11. Reichert TA, Sugaya N, Fedson DS, Glezen WP, Simonsen L, Tashiro M. The Japanese experience with vaccinating schoolchildren against influenza. *N Engl J Med* 2001;344:889-96.
<http://content.nejm.org/cgi/reprint/344/12/889.pdf> (Version current at April 7, 2010).
12. Sugara N, Takeuchi Y. Mass vaccination of schoolchildren against influenza and its impact on the influenza-associated mortality rate among children in Japan. *Clin Infect Dis* 2005;41:939-47.
<http://www.journals.uchicago.edu/doi/pdf/10.1086/432938> (Version current at April 7, 2010).
13. Centers for Disease Control and Prevention (CDC). 2009 H1N1 Flu (Swine Flu) and Feeding your Baby: What Parents Should Know. <http://www.cdc.gov/h1n1flu/infantfeeding.htm> (Version current at April 7, 2010).
14. Public Health Agency of Canada. Guidance for expanded use of oseltamivir (Tamiflu®) in children under one year of age in the context of Pandemic (H1N1) 2009. http://www.phac-aspc.gc.ca/alert-alerte/h1n1/guidance_lignesdirectrices/guidance-tamiflu-eng.php (Version current at April 7, 2010).

15. Public Health Agency of Canada. National Advisory Committee on Immunization (NACI) <http://www.phac-aspc.gc.ca/naci-ccni/index-eng.php> (Version current at April 7, 2010).
16. Public Health Agency of Canada. Canadian Immunization Guide Seventh Edition – 2006. Influenza Vaccine. Efficacy and immunogenicity. <http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-inf-eng.php#effimm> (Version current at April 7, 2010).
17. European Medicines Agency pandemic influenza (H1N1) website. Pandemrix. Annex 1- Summary of Product Characteristics. <http://www.ema.europa.eu/humandocs/PDFs/EPAR/pandemrix/D-H1N1%20single%20PDFs/SPC/emea-spc-h832pu17en.pdf> (Version current at April 7, 2010).
18. Centers for Disease Control and Prevention (CDC). Advisory Committee on Immunization Practices (ACIP). <http://www.cdc.gov/vaccines/recs/acip/default.htm> (Version current at April 7, 2010).
19. Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Canada's eight-step vaccine safety program: Vaccine literacy. *Paediatr Child Health* 2009;14:605-8. <http://www.cps.ca/english/statements/ID/VaccineLiteracy.htm> (Version current at April 7, 2010).
20. http://www.phac-aspc.gc.ca/alert-alerte/h1n1/guidance_lignesdirectrices-eng.php#3
21. Canadian Paediatric Society, Infectious Diseases and Immunization Committee. The use of antiviral drugs for influenza: Recommended guidelines for practitioners. *Paediatr Child Health* 2006;11:520-522. <http://www.cps.ca/english/statements/ID/ID06-04.htm> (Version current at April 7, 2010).
22. Public Health Agency of Canada. Additional Infection Prevention and Control Guidance for Pregnant Women, Newborns and the Postpartum Period. <http://www.phac-aspc.gc.ca/alert-alerte/h1n1/postpart-eng.php> (Version current at April 7, 2010) and Clinical Guidance for Pregnant and Breastfeeding Women with Influenza-Like Illness in the context of the Pandemic H1N1 2009 Virus. <http://www.phac-aspc.gc.ca/alert-alerte/h1n1/guidance-orientation-07-09-eng.php> (Version current at April 7, 2010).
23. Centers for Disease Control and Prevention (CDC). H1N1 Flu (Swine Flu) and You. May 5, 2009. www.cdc.gov/h1n1flu/swineflu_you.htm (Version current at April 7, 2010).
24. Canadian Pharmacists Association. Compendium of pharmaceuticals and specialties (CPS) 2009. www.e-cps.ca (by subscription only) (Version current at April 7, 2010).
25. Centers for Disease Control and Prevention. Recommendations for Use of Antiviral Medications for the Management of Influenza in Children and Adolescent for the 2009-2010 Season -- Pediatric Supplement for Health Care Providers. http://www.cdc.gov/h1n1flu/recommendations_pediatic_supplement.htm (Version current at April 7, 2010).
26. Centers for Disease Control and Prevention (CDC) Antiviral Agents for Seasonal Influenza: Dosage. <http://www.cdc.gov/flu/PROFESSIONALS/ANTIVIRALS/dosage.htm> (Version current at April 7, 2010).

INFECTIOUS DISEASES AND IMMUNIZATION COMMITTEE

Members: *Drs Robert Bortolussi, IWK Health Centre, Halifax, Nova Scotia (Chair); Jane Finlay, Richmond, British Columbia; Jane C McDonald, The Montreal Children's Hospital, Montreal, Quebec; Heather Onyett, Queen's University, Kingston, Ontario; Joan L Robinson, Edmonton, Alberta; Élisabeth Rousseau-Harsany, Sainte-Justine UHC, Montreal, Quebec (Board Representative)*

Liaisons: *Drs Upton D Allen, The Hospital for Sick Children, Toronto, Ontario (Canadian Pediatric AIDS Research Group); Charles PS Hui, Children's Hospital of Eastern Ontario, Ottawa, Ontario (CPS Liaison to Health Canada, Committee to Advise on Tropical Medicine and Travel); Nicole Le Saux, Children's Hospital of Eastern Ontario, Ottawa, Ontario (Immunization Program, ACTive); Larry Pickering, Elk Grove, Illinois, USA (American Academy of Pediatrics); Marina I Salvadori, Children's Hospital of Western Ontario, Ottawa, Ontario (CPS Liaison to Health Canada, National Advisory Committee on Immunization)*

Consultants: *Drs James Kellner, Calgary, Alberta; Noni E MacDonald, IWK Health Centre, Halifax, Nova Scotia; Dorothy L Moore, The Montreal Children's Hospital, Montreal, Quebec*