TIBDN
TORONTO INVASIVE BACTERIAL DISEASES NETWORK

PANDEMIC H1N1 2009 INFLUENZA ACTIVITY UPDATE – 04.JANUARY.10

Worldwide, more than 208 countries have reported laboratory confirmed cases of Pandemic (H1N1) 2009, including at least 10,582 deaths. Activity has peaked in North America and in most parts of Europe; however activity continued to increase in parts of central and south-eastern Europe, as well as in central and south Asia. Influenza transmission remained active in much of western and central Asia and while declining in east Asia and Japan. There was evidence of Pandemic (H1N1) 2009 circulation in most regions of Africa.

In the United states, influenza activity continued to decline for the 6th consecutive week. Widespread activity was reported by seven states; Guam and one state reported no activity, while the remaining states reported regional, local or sporadic activity. Mortality due to pneumonia and influenza continued to decrease to levels below the epidemiologic threshold and lab-confirmed hospitalizations/deaths continued to decline.

In Canada, overall influenza activity continues to decrease. In week 50 (the week ending Dec. 19th) only one region in NL reported localized activity and there were no reports of widespread activity. The national ILI consultation rate was 20/1000 consultations, well below the expected range for this time of year. From Dec 13th to 19th, 121 new specimens were positive for influenza, with 99.1% of these being pandemic 2009 H1N1. Only Quebec has reported seasonal influenza A with 43 H3N2 cases reported since Aug 30, 2009. Only 9 pandemic H1N1 virus isolates in Canada have been resistant to oseltamivir.

How do public health officials measure influenza activity?

There are four ways that influenza activity is measured in Canada (see Table below). Influenza surveillance also includes assessment of which strains are causing infection, measurement of the rate of antiviral resistance, and assessing rates of pediatric hospitalization through the IMPACT system.

Measure	How measured	Winter baseline	Influenza season is starting	High levels of activity
Percentage of GP consultations that are for ILI	Sentinel family physicians (one per census tract) count total visits, and visits for ILI one day per week	About 2-2.5% (varies with month)	Activity above baseline for 2 consecutive weeks	5% or more visits due to ILI
Percentage of specimens submitted for influenza testing that are positive for influenza	Voluntary reporting by most of virology laboratories across Canada	Less than 2%	More than 5% of specimens are positive for 2 consecutive weeks	More than 15% of specimens are positive
Overall assessment by local public health unit epidemiologists	Best assessment of overall activity in region by epidemiologists	No activity, or sporadic activity	Localized activity	Widespread activity

As of December 19, 2009, there have been 8,436 hospitalizations, 1,404 ICU admissions, and 401 deaths due to pandemic H1N1 2009 influenza virus. Although activity is present, a continued decline was experienced by all provinces as indicated by the decreasing number of reported hospitalized cases (79 vs. 159), ICU admissions (21 vs. 40) and deaths (11 vs. 21) reported this week compared to the previous week.

Patients with underlying medical conditions were almost 5 times more likely to be hospitalized, 7 times more likely to be admitted to ICU and more than 14 times more likely to die compared to those without underlying medical conditions.

Public health and office-based vaccination campaigns targeting 2009 H1N1 continue across the country, although, as demand decreases, hours of operation of some public health clinics are being reduced. At present, three 2009 H1N1 vaccines are available. The first is an AS03-adjuvanted vaccine called Arepanrix™, made by GSK. The other two are unadjuvanted vaccines – one made by GSK (a monovalent unadjuvanted vaccine with no brand name), and a one made in Australia by CSL Biotherapies, and called Panvax® (CSL Biotherapies Inc).

The Public Health Agency of Canada continues to recommend that all Canadians be vaccinated against pandemic H1N1. Unadjuvanted vaccine is primarily reserved for pregnant women, while the adjuvanted form is recommended for all others. Supplies of unadjuvanted vaccine are now sufficient and may be used for anyone; however, it appears to be less immunogenic in children than the adjuvanted vaccine, so that children should preferentially receive Arepanrix™ (the adjuvanted vaccine).

January 2010
Volume 4, Issue 2

For persons over the age of 10 years, the dose of all vaccines is 0.5ml, given intramuscularly. In children aged less than 10 years, the dose of adjuvanted vaccine is 0.25ml IM. A second 0.25 ml dose should be given 21 or more days later to children aged 6-35 months, and those aged 3-9 years with immunosuppressive illnesses. If children are receiving unadjuvanted vaccine (not recommended unless parents refuse adjuvanted vaccine), the dose is 0.5 ml for children aged 3-9 years, and 0.25 mls for children aged 6-35 months. A second dose is necessary, and should be given at least 21 days later.

The Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) monitors vaccine adverse events for all licensed vaccines. The Public Health Agency of Canada (http://www.phac-aspc.gc.ca/index-eng.php) reports that as of December 12th, 2009, 24,071 million doses of the 3 types of 2009 H1N1 vaccine have been distributed across the country. Of 4,995 reported adverse events since the start of the vaccination campaign, 155 were considered serious, including 94 cases of anaphylaxis. Thus, the reported rate of serious adverse events is 0.64 per 100,000 doses of vaccine distributed, with a rate of anaphylaxis of 0.32 per 100,000 doses distributed. These numbers are consistent with reported rates of adverse events following other immunizations, including seasonal influenza vaccine. The overwhelming majority of reported adverse events have been mild in nature. One particular adjuvanted vaccine lot (lot 7A) has been associated with a higher than expected rate of anaphylaxis – 3.5 per 100,000 doses distributed - which led to a recall of lot 7A vaccines. Among the 6 cases of anaphylaxis linked to lot 7A vaccines, no hospitalizations or deaths occurred. Further information on CAEFISS and vaccine adverse event monitoring in Canada can be found at: http://www.phac-aspc.gc.ca/im/vs-sv/caefiss-eng.php.

HOW ACCURATE IS THE CLINICAL DIAGNOSIS OF INFLUENZA IN CHILDREN IN THE AMBULATORY SETTING: CAN PHYSICIANS DISTINGUISH H1N1 FROM SEASONAL INFLUENZA?

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Physicians might think that the clinical diagnosis of influenza in children is straightforward. It is anything but clear-cut. When it comes to children, symptoms are mostly age dependent. The classic presentation of influenza in school-age children and adolescents as described in the textbooks is the sudden onset of fever, often with chills or rigors, headache, malaise, myalgia, and non-productive cough. Sore throat, nasal congestion, rhinitis and worsening cough follow. Other common findings, not always highlighted in the literature, are severe prostration, exhaustion, and excess sleeping seen mainly in older children and adolescents. Parents often complain that their children 'just sleep all the time' and it is not unusual to find an adolescent sleeping in a doctor's office, while waiting to be examined. Other infrequent influenza symptoms include conjunctivitis, abdominal pain, nausea, vomiting and diarrhoea. At best, the sensitivity for making a diagnosis of influenza based on clinical history and examination in ambulatory school-age children is approximately 50%. If one includes pre-schoolers and young infants, accuracy decreases to 38%. The diagnosis is least accurate in those less than 3 years of age where the sensitivity of clinical diagnosis plummets to 21%. In young infants, fever and suspected sepsis may be the only presenting symptoms. One explanation for the low sensitivity in infants and toddlers is that they are unable to complain of the cardinal subjective symptoms of headache, myalgias or sore throat. In these young infants, surrogate non-specific clinical markers are often used, such as irritability (headache or myalgia) and refusal to eat or drink (sore throat).

Difficulty in making an accurate clinical diagnosis of influenza occurs because many other viral illnesses have a similar presentation. Most of these viruses circulate almost exclusively in the winter. Thus, when influenza is the predominant circulating virus and it occurs in an unusual season like the summer months, as with the 2009 pandemic H1N1, the clinical diagnosis of influenza is much easier to make, as it is the only game in town. However, during the winter months, other viruses such as rhinovirus, respiratory syncytial virus, parainfluenza, adenovirus, bocavirus and human metapneumovirus cause symptoms that mimic influenza. The term 'influenza like illness' or ILI (fever plus cough or sore throat) has been coined to describe this clinical presentation.

The symptoms of the 2009 pandemic H1N1 infection are not clinically distinguishable from regular seasonal influenza except possibly in a few instances. Diarrhoea has been reported to be more common in the 2009 pandemic H1N1 influenza than in seasonal influenza and one report has indicated that a fever of at least 38°C may be absent in up to 20% of children with 2009 pandemic H1N1. In both pandemic and seasonal influenza, upper respiratory symptoms with systemic symptoms (e.g. fever, lethargy etc.) constitute the most common presentation since the course of the illness is mild. In most cases, establishing the specific diagnosis of influenza on a clinical basis alone is not that important, as no antiviral treatment is required. On the other hand, the diagnosis of influenza is more important for those children who are vulnerable (under age 2, chronic conditions, immunocompromised etc.) or in those who were previously healthy but are now sick enough to possibly require hospitalization. In these cases, treatment with antiviral medication (oseltamivir) may be beneficial in preventing hospitalization or reducing symptom severity, even if given after the recommended 48 hours following the onset of symptoms.

OSELTAMIVIR DOSING INFORMATION

Oseltamivir has been approved for the treatment of influenza in children <1 year by the U.S. Food and Drug Administration (FDA) under an emergency use authorization. Prophylaxis is not recommended for children <1 year. The parents or guardian should be informed that this is exceptional use. Treatment dosing for these children is age and weight-based (see table below). For further information please consult the Public Health Agency of Canada[1].

Table 1. Recommended dosing for children <12 months.

Age	Recommended Dose (weight-based)[a,b]
1 month to < 12 months	3 mg/kg/dose twice daily for 5 days
< 1 month	2 mg/kg/dose twice daily for 5 days

[a] Not to exceed 30 mg twice daily, in accord with recommended dosing for patients > 1 year of age
[b] Weight-based dosing is preferred, however, if weight is not known, dosing by age for *full-term infants* may be necessary as follows: 0-<3 months = 12 mg twice daily; 3-<6 months = 20 mg twice daily; 6 -<12 months = 25 mg twice daily

For children >1 and adults, oseltamivir is licensed for both treatment and prophylaxis.

If Tamiflu suspension is ordered for children, the pharmacy can substitute the 30 and 45 mg capsules.

Table 2. Recommended dosing in children 1 to 12 years.

Body weight		Capsule Dose of Oseltamivir for Treatment* (duration 5 days)	Capsule Dose of Oseltamivir for Prevention** (duration 10 days)
Kg	Lbs		
≤15 kg	≤ 33 lbs	30 mg BID	30 mg OD
> 15 kg to 23 kg	> 33 lbs to 51 lbs	45 mg BID	45 mg OD
> 23 kg to 40 kg	> 51 lbs to 88 lbs	60 mg (2 x 30 mg) BID	60 mg OD
> 40 kg	> 88 lbs	75 mg BID	75 mg OD

Table 3. Recommended dosing in adults and adolescents (≥13 years).

Oseltamivir in Adults and Adolescents	
Treatment Dose* (duration 5 days)	Preventive Dose** (duration 10 days)
75 mg BID	75 mg OD

*Ideally, treatment should begin within 2 days after the onset of symptoms of influenza.

**Ideally, therapy should begin within 2 days of exposure after the onset of symptoms in the index case and continue for at least ten days.

For further information on oseltamivir dosing, please consult the TAMIFLU Product Monograph[2].

This dosing for infants under the age of 1 year is not intended for premature infants (those < 37 weeks gestational age at birth who have not reached their expected due date), and may result in high drug concentrations in this age group. Insufficient data is available at this time to make specific recommendations for premature infants.

Pediatric suspension should be used if available; if not, refer to "Emergency Compounding of an oral suspension from Tamiflu® capsules" on page 16 of the Tamiflu® product monograph.[2] Children under 1 year of age with influenza should be treated in hospital.

References:
[1]PHAC. Interim Guidance for emergency use of oseltamivir (Tamiflu®) in children under one year of age in the context of 2009 (H1N1) pandemic, available at: http://www.phac-aspc.gc.ca/alert-alerte/h1n1/guidance-orientation-07-20-eng.php
[2]Hoffmann-La Roche Limited. Tamiflu product monograph, available at: http://www.rochecanada.com/portal/eipf/ca/portal/roche/consumer_information

CLINICAL CASE SCENARIO

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A thirty five year old woman at 36 weeks gestation presents for her prenatal appointment and asks:

Should I get the H1N1 vaccine?

Yes. Pregnant women are just as likely as non-pregnant women to get H1N1 influenza, and they are more likely to suffer severe sequelae from influenza. The Public Health Agency of Canada, the Society of Obstetricians and Gynecologists of Canada, and the Centers for Disease Control all recommend that pregnant women receive both the H1N1 influenza vaccine and seasonal influenza vaccine. Women may be vaccinated at any time during pregnancy.

Immunization of pregnant women is key to minimizing the risks associated with influenza in pregnancy.

Two different H1N1 vaccines are available for pregnant women. One is a "regular" influenza vaccine – made in the usual way we make influenza vaccines in North America, with 15µg of influenza antigen in each dose. These types of influenza vaccines have been used for many years in North America. The second type of vaccine is called an adjuvanted vaccine. In addition to influenza antigen (in a smaller concentration), this vaccine contains squalene (a natural cholesterol precursor) and a form of vitamin E (alpha-tocopherol) – chemicals which stimulate the immune system to create a better response to the antigen. Influenza vaccines containing squalene as an adjuvant have been used for more than 10 years in Europe; however, they have not been used for pregnant women. They have the advantage of creating a more robust antibody response than usual influenza vaccines, and there are no data to suggest that they might be a risk in pregnancy. However, because adjuvanted vaccines have not been used in pregnant women before, it is recommended that they not be given to pregnant women who are less than 20 week gestation.

Is the H1N1 vaccine safe for me and my fetus?

Following vaccination, approximately 70% of people experience a sore arm. These symptoms are usually mild and last a day or two. Very rarely, people can develop allergic reactions to influenza vaccine. The vaccine may contain traces of egg protein and thus people who are allergic to eggs should not be vaccinated. Very rarely the influenza vaccine may be associated with Guillian Barre Syndrome (less than 1 in a million chance.) However, influenza itself can also cause this syndrome.

There are no concerns in regards to the safety of the influenza vaccine for the fetus. More importantly, for infants whose mothers were vaccinated while pregnant, research trials have demonstrated a significant reduction in the risk of influenza for infants between 0 to 6 months of age.

She gets vaccinated against the H1N1 virus. Five days later, her husband comes home with fever (39° C), sore throat and muscle aches. His family physician suspects that he has the H1N1 flu and as his wife is pregnant, initiates treatment of H1N1 with oseltamivir (Tamiflu®) 75mg po BID x 5 days. His pregnant wife has several questions.

What are the chances that she will get the flu?

When a household contact has H1N1, the chance of acquiring H1N1 is approximately 25%.

How long will it take for the H1N1 vaccine to be effective?

Following vaccination, antibodies against the H1N1 virus develop within 10 to 21 days. She does not yet have sufficient antibodies to be protected.

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Should I take prophylaxis with oseltamivir, just in case?

Because the risk of getting influenza is only about 25%, and because it can be reduced by at least 50% by adherence to preventive measures, it is generally not recommended that pregnant women take oseltamivir preventatively. However, if she develops any symptoms of influenza, she should begin on treatment immediately.

What can she do to protect herself from H1N1 influenza?

There are several preventative measures she can take to help avoid contracting H1N1.

1. Wash hands at least 5 times a day with soap and water or alcohol-based hand rub. Because her husband is ill, she should be careful to wash her hands after any contact with him, or with objects that he has recently touched.
2. Avoid the spread of germs by avoiding touching her eyes, nose or mouth.
3. Avoid close contact with (that is, stay at least 6 feet away from) her husband, and with any other people who have symptoms of influenza.
4. If possible, have another family member take care of her husband.
5. Do not share items that may have come into contact with his saliva (cups, tooth brushes).
6. If possible, have her husband stay in a room by himself.

Three days later, she develops a fever of 38.5°, a cough, sore throat and myalgias.

What should she do now?

She should be started on treatment for H1N1 influenza with oseltamivir (75mg po BID for 5 days) or zavamivir (two 5-mg inhalations (total 10mg) twice daily for 5 days). She should also be counseled to take acetaminophen (Tylenol) for temperatures greater than 38.0° C and that she should call her physician or come to hospital with worsening symptoms (difficulty breathing, chest pain, dizziness, persistent vomiting, decreased fetal movement or fever not responding to acetaminophen).

She is started on oseltamivir (75mg po BID for 5 days). Later that evening, she goes into spontaneous labour and gives birth to her infant.

What precautions should be taken?

1. Isolate the sick mother from other healthy mothers.
2. If possible, place a mask on mother during labour to protect staff and the newborn from H1N1.
3. Mother should consider avoiding contact with the infant, until she has been on oseltamivir for 48 hours, is no longer febrile and can control her cough and secretions.
4. Following this, mother should be encouraged to wear a mask and clean clothing when with the infant and also to ensure that she washes her hands carefully before touching or feeding her infant. She should adhere to these precautions for 7 days after the onset of symptoms

References:
1. Centers for Disease Control http://www.cdc.gov/H1N1flu/clinician_pregnant.htm
2. Public Health Agency of Canada http://www.phac-aspc.gc.ca/alert-alerte/h1n1/guidance-orientation-07-09-eng.php
3. Society of Obstetricians and Gynecologists of Canada http://www.sogc.org

For additional information and answers to previously asked questions, please see our online version of this newsletter at http://microbiology.mtsinai.on.ca/avian/tibdn_newsletters.asp

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PM40064463

Roche This newsletter has been generously sponsored by Hoffmann-La Roche Limited.

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FREQUENTLY ASKED QUESTIONS (Appendix to TIBDN newsletter January 2010, volume 4, Issue 2)

As with any novel or emerging pathogen, the management of pandemic H1N1 2009 Influenza can sometimes be confusing, especially when new information about the virus results in changes to guidelines. Answers to questions from physicians in Ontario can be found in the on-line version of this newsletter at www.pandemicwatch.ca/. In addition, we encourage health care providers to consult publicly available resources on pandemic H1N1 2009 influenza, such as the Public Health Agency of Canada (www.phac-aspc.gc.ca/alert-alerte/h1n1/index-eng.php), the Centers for Disease Control and Prevention (CDC) (www.cdc.gov/h1n1flu/), and their provincial health ministry websites), for further information and direction.

1. A patient comes to the clinic with relatively mild influenza. The physician on duty decides not to treat because the patient has no risk factors for complicated infection. Two to three days later, their symptoms have worsened and now they present quite ill, possibly requiring hospitalization. Should the physician have started treatment when the patient first presented? If a patient presents on day 5 with worsening disease is an antiviral effective?

As always, clinical judgment is needed to guide treatment decisions. Most patients with pandemic H1N1 2009 influenza have a self-limited respiratory illness similar to typical seasonal influenza. For these patients, the benefits of using antivirals are modest. There are two recently published meta-analyses on neuraminidase inhibitors and influenza: 1 in adults published in *Lancet Infectious Diseases*[1], and 1 in children published in *BMJ*[2]. For healthy adults with influenza like illness, duration of symptoms was reduced by 0.55 days for oseltamivir, and for "at-risk" adults, symptom duration was reduced by 0.98 days. There were insufficient data to give a reliable number for averted complications, but antibiotic use was reduced when either zanamivir or oseltamivir were prescibed. For children, symptom duration was reduced by 0.5-1.5 days, but there was little effect on the rate of asthma exacerbation or antibiotic use. Therefore, healthy adults with mild disease will not benefit substantially from treatment. During a week with high influenza activity (whether seasonal or pandemic), treatment should be considered for persons who are at risk for complications. Treatment is recommended for anyone ill enough to require hospitalization. As the CDC notes, "persons presenting with suspected influenza and more severe symptoms such as evidence of lower respiratory tract infection or clinical deterioration should receive prompt empiric antiviral therapy, regardless of previous health or age".

Treatment, if offered, should be initiated as soon as possible after the onset of symptoms. Evidence for benefit is strongest when treatment is started within 48 hours of illness onset. However, studies on treatment of hospitalized patients with seasonal influenza and pandemic H1N1 influenza have indicated benefit, including reductions in mortality or duration of hospitalization, in patients whose treatment was started more than 48 hours after illness onset. Thus, if a patient presents with worsening symptoms of influenza, it is reasonable to start antivirals even if symptoms have been present for more than 48 hours.During influenza seasons, patients who require hospital admission for influenza-like illness or pneumonia should receive empiric antivirals.

2. An otherwise healthy patient comes into the walk in clinic with an influenza-like illness (ILI). Physicians are often not asking about others in the household (eg, children < 1-2 years of age, immunocompromised family members, etc). Should the physician treat the patient if there are "at risk" family members (ie, will this reduce transmission)? Should the physician be considering a preventative treatment for the 'at risk' household member? What is the best/ideal way to handle this situation?

The highest risk of influenza transmission occurs in households: with pandemic H1N1 2009 influenza, the risk that a second household member will become infected is 15-35%. We also know from laboratory studies that viral shedding is greatest on the first and second day of illness, and declines significantly thereafter. Practically speaking, then, it is unclear exactly how much of a reduction in household transmission would be achieved by starting treatment in such a scenario, especially since most patients don't seek or receive care within 48 hours of symptom onset. If the household includes a child <2 years of age, a pregnant woman, or another person at high risk of complications, such as a person with immune suppression, prophylaxis for household contacts may be considered. However, in general, the benefits of prophylaxis are relatively small, and most physicians would recommend non-pharmaceutical prevention measures combined with early therapy if symptoms develop. Non-pharmaceutical measures include frequent hand washing/use of handrub, good respiratory etiquette, maintaining distance (>6 feet) between ill and well family members, and surface cleaning. A recently published randomized controlled trial in the *Annals of Internal Medicine*[3] demonstrated a significant reduction in household influenza transmission when enhanced hand hygiene and face masks were implemented within 36 hours of symptom onset in the index patient. Most of the effect appeared to be associated with increased hand hygiene, but face masks may also be appropriate in households where an "at-risk" person resides.

Ideally, this situation should be avoided by strongly and repeatedly recommending influenza vaccination for all persons who live in households where an at-risk person is present.

3. Some people are not feeling better after 5 days of therapy. Should a physician consider extending the treatment days from 5 to 7-10? What are the thoughts on duration of therapy?

The standard duration of antivirals for the treatment of pandemic H1N1 2009 influenza is 5 days, although longer durations have been used for severely ill, hospitalized patients. There are no data on the potential benefits of prolonged antiviral therapy in outpatients with influenza.

Fatigue, cough, and green nasal discharge/post-nasal drip commonly persist for longer than 5 days, but will not benefit from further treatment with antivirals or from antibacterial therapy.

In patients with persisting fever, or increasingly productive cough, consideration must be given to the possibility of complicating bacterial infections. If bacterial infection is thought not to be present, teaching about warning signs that may indicate a worsening infection and require appropriate referral to an escalated level of care is likely a superior approach to extension of antiviral treatment. Warning signs and symptoms that should prompt urgent medical attention in adults include persistently high fever after day 5, increasing fever/chills, tachypnea, dyspnea, pain or pressure in the chest or abdomen, confusion, sudden dizziness, and severe or persistent vomiting. In children, additional warning signs include laboured breathing, cyanosis, severe somnolence and difficulty rousing, dehydration, and severe irritability.

4. Why are women more likely to get sick longer and/or need hospitalization more often then men? Does it have to do with body fat composition and the virus' ability to build up toxins in females?

In a study of 168 Canadian patients with pandemic H1N1 2009 influenza admitted to the ICU and reported in *JAMA*[4], 67.3% were female. Thus, there appeared to be an association between female gender and severe influenza. This excess has not been seen in other studies,and, during the second wave of the pandemic in Canada, 49% of 4,843 patients hospitalized with H1N1, 47.6% of cases admitted to the ICU,and 47.9% of the deaths due to H1N1 have been female. It seems likely that the overrepresentation of women during the first wave was a result of a large number of cases from aboriginal communities in Manitoba, which have relatively high rates of both pregnancy and underlying chronic illnesses such a diabetes. There is no evidence that body fat composition increases the risk of severe influenza, due to this pandemic virus, or other influenza strains.

5.Can you provide information on prescribing antivirals in pregnancy?

Pregnant women, particularly in their second and third trimester of pregnancy and up to 6 weeks post-partum, are at elevated risk of complicated influenza infection. For this reason, the **Society of Obstetricians and Gynecologists of Canada** (www.sogc.org) recommends that pregnant women speak to their doctors about a plan for prompt treatment with antivirals should they develop an influenza-like illness during peaks of influenza activity. It is not recommended that the drug be taken in the absence of symptoms, but it is recommended to start treatment as early as possible after development of symptoms (preferably within 48-hours of symptom onset). Early treatment of influenza in pregnant women can help reduce the risk of severe or complicated infection.

Both oseltamivir (Tamiflu) and zanamivir (Relenza) are active against the pandemic H1N1 2009 influenza virus, however, zanamivir is not reliably available in pharmacies. Tamiflu is usually well tolerated, but can cause nausea and vomiting, both of which may be reduced by taking the medicine with food. Zanamivir comes as an inhaled formulation and can induce bronchospasm; thus, it is not recommended for treatment of patients with underlying lung disease. Oseltamivir and zanamivir are class C drugs, with limited safety data on their use during pregnancy. The US Centers for Disease Control and Prevention and the Public Health Agency of Canada recommend oseltamivir treatment of all pregnant women with laboratory confirmed or suspected pandemic H1N1 2009 influenza. The few studies that are available suggest that Tamiflu is safe to use during pregnancy. This was reiterated in a recently published study in the *Canadian Medical Association Journal*[5]. Treatment dosing in pregnant women is the same as for other adults: oseltamivir (Tamiflu) 75 mg twice daily for 5 days or zanamivir (Relenza) two 5-mg inhalations (10 mg total) twice daily for 5 days.

During periods of high influenza activity, empiric therapy of influenza-like illness in pregnant women may be warranted. When little influenza activity is occurring, treatment should not be offered to those without laboratory confirmation of disease.

References:
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[3]Cowling B et al. Ann Intern Med 2009;151:437-446, available at: http://www.annals.org/content/151/7/437.full
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