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This newsletter is a publication of the Toronto Invasive Bacterial Diseases Network (TIBDN), a collaboration of the microbiology laboratories (private, hospital and public health) and infection control practitioners who serve the population of Metropolitan Toronto and Peel Region.

Questions or comments about the newsletter, or other activities of the network, should be directed to the network office:

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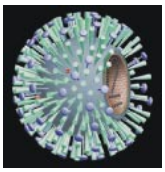
Toronto Invasive Bacterial Diseases Network

Flu Newsletter



Influenza in Canada, the 2000/2001 Season

The North American influenza season started in BC, Alberta and Saskatchewan just before Christmas. As often happens, influenza arrived in the west first, and eastern Canada was spared over the holidays and for most of January. However, in the last 10 days of January, both the number of influenza viruses isolated at the Ontario Public Health Laboratory and the frequency of influenza-like illness reported by the family physician surveillance networks began to increase, indicating that the flu season has now started in Ontario. In addition, in the week of January 22nd, the first Ontario nursing home influenza outbreak of the season was reported.

In most years, a single strain causes the great majority of influenza cases. This year, however, cases have been caused by three different strains. At the Ontario Public Health Laboratory, those isolates which have been subtyped so far include A/New Caledonia(H1N1), A/Panama (H3N2) and B/Yamanashi. It appears then, that this season will be a "mixed" season, with different strains and types causing disease. The good news is that all of the strains identified in Canada so far are included in this years vaccine.

Once again data about influenza will be published on the Canadian FluWatch website (www.hc-sc.gc.ca/hpb/lcdc/bid/respdis/fluwatch/), the Ontario Flu Bulletin website (www.gov.on.ca/health/english/program/pubhealth/flu_bul/flubul_mn.html), and by the Flu Report (www.flupill.com or www.theweathernetwork.com).

Websites with Information About Influenza

www.gov.on.ca/health/english/program/pubhealth/flu_bul/flubul_mn.html
The Ontario Influenza Bulletin - the most useful site for Ontario specific data on influenza. The Ontario Ministry of Health Web page for influenza bulletins. These are published weekly for the province and have region specific data for nursing home outbreaks, sentinel physician activity and laboratory testing. You can move to publications on immunization for public information on influenza and vaccine.

www.hc-sc.gc.ca/hpb/lcdc/bid/respdis/fluwatch/
Health Canada's web page in influenza surveillance. Updated every week during flu season, with data on laboratory results for respiratory virus identification, and influenza activity across Canada.

www.hc-sc.gc.ca/hpb/lcdc/new_e.html
Laboratory centre for disease control website; a search for influenza brings up Canadian Communicable Disease Report references for descriptions of influenza activity in previous years, and national recommendations for vaccination and control.

www.flupill.com; can be accessed by theweathernetwork.com
Funded by Hoffmann-La Roche Limited with basic information about influenza, along with cross-Canada data on influenza activity in different centres.

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More questions about influenza vaccine

I had the flu really badly in November – do I need to get the vaccine this year?

This November, several other viruses were circulating, but there was nearly no influenza activity. Thus, even severe respiratory illness was most likely due to another virus. Any respiratory virus (e.g. rhinovirus, respiratory syncytial virus, parainfluenza virus) can cause influenza-like illness on occasion. When influenza is not "in season", the chance that "the flu" (a.k.a. febrile respiratory illness) is due to influenza is less than 10%. Having had illness due to another virus does not protect you against influenza, and you should be vaccinated if you want to avoid influenza.

I got the flu shot one year, and that was the year I was really sick – every year since I haven't had the flu shot and I have been fine – why should I get vaccinated?

Adults get an average of just over one upper respiratory tract infection each year, with only 20% of them due to influenza. This means that some years when you get the flu shot, you will get sick from another virus. Similarly, some years when you don't get the flu shot, you might avoid influenza, and not get any other respiratory tract illness either. Because of this, it is impossible to measure the effect of influenza vaccine by considering any one person's experience. Overall, there is extensive evidence that influenza vaccine protects even healthy adults from illness, doctor visits, antibiotic use.

I heard that the government is investigating serious side effects from the influenza vaccine this year – why did they encourage everyone to get it?

One of the influenza vaccines used in Canada this year (not the one used in Ontario) caused an increased rate of an unusual allergic-type side effect. Some people (<1% of people getting vaccinated) got red eyes and airway irritation (causing cough and wheezing). In most cases, this lasted a few hours. A few people visited emergency departments because of the eye irritation and/or wheezing. For most people this was no worse that getting a sore arm, and, clearly, the benefits of vaccination still outweigh the risks. However, the government and vaccine manufacturer obviously want to understand what caused the reaction so that it will not occur again – numerous investigations are in progress (in BC and Quebec, where this particular vaccine was used) to identify the cause of the reaction.

Diagnosing Influenza

To be effective against influenza, antiviral therapy must be initiated as soon as possible after symptom onset. This means that decisions about therapy must be made before traditional laboratory test results are available. Several point-of-care tests for influenza are now available: unfortunately they are neither very sensitive nor very specific. Although they are useful for identifying when influenza is present in a community or practice, they are not useful for individual diagnosis of disease. Rapid antigen testing for influenza is available from some hospital and all public health laboratories – however, results take several hours at a minimum (next day, unless taxi or same day courier is used) – this testing is essential for the detection of institutional outbreaks, but is rarely useful in individual cases.

When influenza is not "in season" – that is, outside the 6-12 week time period each year when influenza is common in a community – the best combination of symptoms has a positive predictive value for influenza of 20-30%. That is, few people with respiratory tract illness, even those with fever, prostration and cough, have influenza, and anti-influenza medications are not of value.

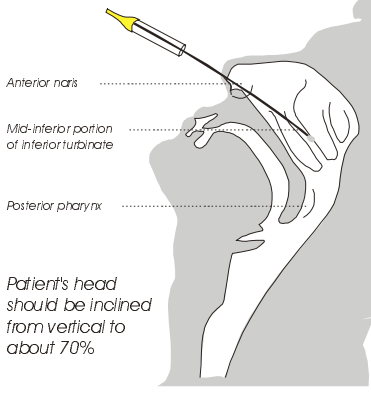
During the influenza season, the probability that anyone with a respiratory tract illness has influenza increases. Several studies have now shown that the symptoms which best predict influenza are sudden onset, fever and cough, and that, the higher the fever, the greater the probability of influenza (see Figure 1). During influenza season, healthy adults who have acute upper respiratory symptoms with fever (measured in the office) and cough have a 60-80% chance of having influenza. If they have been ill for less than 48 hours when you see them, prescribing antiviral medications will reduce the duration and severity of their symptoms, and the likelihood of complications. Signs and symptoms which predict influenza in the frail elderly, or in children have not been assessed.

There is one important consideration in the diagnosis of influenza: serious bacterial illness sometimes starts with non-specific symptoms such as fever and myalgias. What initially appears to be a viral illness may in fact be the early stages of meningococcemia, streptococccal toxic shock syndrome, or other bacterial sepsis (REF CCDR). Viral illness is common, and these diseases are rare: it is not often not possible to make the diagnosis of bacterial infection at the initial visit. However, it is important that we do not become overconfident in diagnosing influenza. It is also important that, by prescribing anti-influenza medications, we do not provide the patient with such reassurance of certainty about the diagnosis, that the patient fails to seek help if their illness worsens significantly.

NASOPHARYNGEAL SPECIMEN COLLECTION

Ontario

Nasopharyngeal swab method for pertussis culture or respiratory virus detection



The laboratory needs high levels of organism to culture successfully for Bordetella pertussis or respiratory viruses such as RSV, influenzavirus A & B or parainfluenzavirus. A properly taken nasopharyngeal swab will yield high levels of organism.

1. Insert flexible wire nasopharyngeal swab into one nostril.
2. Press the swab tip on the mucosal surface of the mid-inferior turbinate.
3. Rub swab back and forth about 5 times.
4. Leave swab in place for a few seconds to absorb material.
5. Withdraw swab and insert into transport medium.
6. Cut excess wire with scissors.

N. B. Rule of thumb to determine when swab is placed properly: insert swab to one-half the distance from the tip of the nose to the tip of the earlobe.

Antiviral Medications

There are now three medications licensed in Canada for treating influenza. Their characteristics are summarized in the Table. It is important to realize that they have no effect in treating either bacterial infections, or in treating infections due to viruses other than influenza. In addition, they are not effective if started more than 48 hours after the onset of illness. However, when they are prescribed early in the course of an infection due to influenza, they have a clinically important effect in reducing the severity and duration of symptoms, the rate of complications, and the need for antibiotics. Patients who have more severe symptoms, and those who are at higher risk of complications will derive a greater absolute benefit.

The most important question that remains unanswered about treatment is that of whether treatment of influenza with these medications reduces the rate of serious complications resulting in hospitalization and death. Some reviewers have made the assumption that if complications in general are reduced, then those that result in hospitalization are likely also to be reduced. Others believe that specific evidence relating to these more severe complications is needed. Part of the reason that the answer to this question is important is that it may determine whether provincial pharmacies are willing to add neuraminidase inhibitors to their formularies. If these drugs reduce hospitalization to any significant degree, then their cost per quality adjusted life year gained is in the generally-accepted range for medications. If, however, these medications reduce minor complications (e.g., bronchitis) more than they reduce the risk of hospitalization or death, then their high cost per quality adjusted life year is high enough that they may not be approved for provincial formularies.

Comparison of medications which can be used to treat influenza

Characteristic	Amantadine (Symmetrel®)	Zanamivir (Relenza®)	Oseltamivir (Tamiflu®)
Viruses	Effective against influenza A only	Effective against influenza A and B	Effective against influenza A and B
Treatment effect[1]: Symptom severity Duration of illness Complications Antibiotic use	 30% reduction decreased by 1 day (no data) (no data)	 30% reduction decreased by 1 day 25-30% reduction 25% reduction	 30% reduction decreased by 1 day 25-30% reduction 25% reduction
Prophylactic efficacy[2]	70-80%	70-80%	70-80%
Route of administration	Oral (capsule, syrup)	Oral (inhalation)	Oral (capsule)
Dose Treatment Prophylaxis[3]	 100mg bid[4] x 5days 100mg daily[4]	 10mg (2 puffs) bid x 5days 10mg (2 puffs) daily	 75mg[5] bid x 5days 75 mg daily
Metabolism and elimination	Renal clearance by filtration and tubular secretion	<10% absorbed, renally excreted as unchanged drug	Converted to oseltamivir carboxylate in liver, then renally excreted
Limitations	Not effective for treatment if started >48 hours after symptom onset Household contact prophylaxis not effective if index patient treated, due to rapid development of resistance	Not effective for treatment if started >48 hours after symptom onset	Not effective for treatment if started >48 hours after symptom onset
Precautions and warnings	Serious side effects may occur in elderly if dosage not adjusted for creatinine clearance Avoid in patients with seizure disorders	May (rarely) cause bronchospasm in patients with asthma or COPD	
Drug interactions	CNS stimulants, antihistamines, anticholinergic agents	None known[6]	None known[6]
Side effects	CNS (insomnia, irritability, dizziness), dry mouth, gastrointestinal	Rarely, bronchospasm in patients with asthma, COPD	Nausea & vomiting (reduced by administration with food); diarrhea, headache
Cost for 5 day treatment course[7]	$16	$45-56	$54-69

[1] The effects described are from trials involving healthy adults, at risk adults (those over 65 or with chronic illness), and children. Results of individual trials vary somewhat. There is no evidence that treatment effects are different in different age groups. No trials had adequate sample size to determine whether there is an effect of treatment on hospitalization or death.

[2] Although zanamivir and oseltamivir are not yet licensed for prophylaxis, there is good evidence from published randomized controlled trials that these medications are effective. The percentage given is the reduction in the risk of influenza-like illness when people exposed to influenza (eg. household, nursing homes) are given antiviral instead of placebo.

[3] The duration of prophylaxis varies depending on the circumstances. For household contacts, prophylaxis should be given for 7-10 days. Individualized decisions must be made in outbreaks – in general, in nursing home outbreaks, prophylaxis is required for a period between 7 and 14 days.

[4] Dosing for amantadine depends on age and renal function. Recommended dose for those aged 10-64 years with normal renal function is 200mg/day. For children aged 1-9 years, the recommended dose is 5mg/kd/day up to a maximum of 150 mg, given in two divided doses. For adults over the age of 65 years, and all those with reduced renal function, the maximum daily recommended dose is 100mg, and the dose should be adjusted based on estimated creatinine clearance as necessary (see CPS).

[5] Dosage reduction is recommended (to 75 mg daily) in patients with a creatinine clearance of <30ml/minute.

[6] These medications have only been on the market for one influenza season; very rare but serious side effects may not yet have been detected

[7] Costs were obtained by calling 5 pharmacies in Toronto. The markup on oseltamivir and zanamivir may vary.

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www.city.toronto.on.ca/health/flu.htm
City of Toronto Public Health web page for influenza. Good public information about influenza and vaccination

www.cdc.gov./ncidod/diseases/flu/fluvirus.htm

Centers for Disease Control and Prevention web page for influenza prevention and control. Patient information on influenza and current US influenza surveillance reports.

www.flu.lanl.gov/links.html
Links to other influenza websites including WHO influenza webpages fpr international influenza updates.

www.influenza.cpha.ca
Web page of the Canadian Coalition for Influenza Immunization. Good patient information, useful statistics, contact emails for vaccine manufacturers.

Infectious Diseases Notes

Pertussis (Whooping cough)

Over the last 20 years, vaccination against pertussis has dramatically reduced the rate of this highly contagious illness. However, increases in the rate of pertussis, particularly in adolescents and adults, have recently been seen in different areas across North America.

Pertussis infection starts like any other upper respiratory tract infection – with a runny, stuffy nose, scratchy throat, mild cough and sometimes fever. Over the first week, the dry cough becomes progressively worse, causing paroxysms of coughing which may end in whooping, vomiting, or loss of breath. The coughing may persist for 1-2 months, or even longer.

Whooping cough is easily spread from person to person through coughing or sneezing, but its long incubation period (6-20 days) means that spread may not always be recognized. People infected with pertussis are infectious from just before they first get symptoms until three weeks after the severe coughing starts, or 5 days after they start taking erythromycin.

It is impossible to differentiate whooping cough from any other upper respiratory tract illness when it starts. By the time severe coughing starts, prescribing erythromycin has little or no effect on the severity or duration of coughing. Nonetheless, the diagnosis of pertussis is important, because prescribing erythromycin to the ill person reduces the spread of disease. In addition, household members and child care contacts are at high risk and should be given erythromycin (40-50 mg/kg/day daily, maximum 1kg per day, in four divided doses, for 10 days). Children aged more than one year and less than seven years do not need prophylaxis if their pertussis immunization is up-to-date (doses at 2,4,6,18 months, and 4-6 years).

Pertussis can be detected by culture, but the specimen must be a nasopharyngeal swab, and special media must be used. The best means to diagnosis pertussis is by PCR testing available at the Hospital for Sick Children, and the Central Public Health Laboratory. Nasopharyngeal aspirates or swabs (see Figure) must be collected, using a kit which can obtained from either institution (HSC: 416-813-6000; CPHL 416-235-5937). It is important to report all cases of pertussis to your local Public Health Unit so that contacts are identified and receive prophylaxis if necessary.

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