Strategies For The Control Of Influenza Infections

While overall prevention of influenza infection is not yet possible, control strategies continue to improve. The most important strategy remains a vigilant awareness program, accompanied by a yearly vaccination program.

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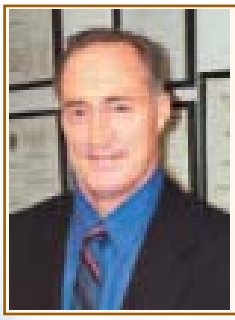
It has become common in winter months to see newspaper headlines about delays in access to medical care, patients being cared for in hallways, or difficulty ambulances have accessing overcrowded emergency departments. This frequently coincides with outbreaks of influenza virus infections, and these events remind us of how important the control of these infections is to our society.



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Overview Of Influenza Virus Infections

Clinically important influenza virus infections can be caused by influenza types A and B. Influenza type A and B infections cause annual winter outbreaks of respiratory infections in temperate climates. These infections are spread by droplets and by aerosol, with a short incubation period. Together, they result in the rapid spread of these infections through the community. Up to one-third of infected individuals may be asymptomatic, but can transmit infection.

Influenza

It is common for approximately 15% to 20% of a population to be infected annually in a relatively short period of time, usually within two months in any single community. Such a situation causes sudden, recognizable outbreaks of respiratory illness.

Typical symptoms of influenza infection include respiratory components, such as runny nose, sore throat, sneezing and coughing, and systemic symptoms, such as headache, fever, chills, muscle aches, fatigue and lethargy. In young children, however, common illness can include high fever, convulsions, croup, otitis and viral pneumonia. In the elderly, fever may be less prominent and individuals may present with extreme fatigue, to the point of incapacitation. Elderly people also may experience symptoms of respiratory or heart failure. Individuals may acquire secondary bacterial infection, most often caused by *streptococcus pneumoniae, staphylococcus aureus* or *hemophilus influenzae* as a cause of sinusitis and pneumonia.

The severity of clinical illness depends on host immunity, the age of the host and environmental factors, such as tobacco smoking. It also is critically dependent on the strain of organism.

Influenza A H1N1 infections tend to be milder than influenza A H3N2 infections. Influenza B infections are more commonly associated with gastrointestinal illness. Influenza viruses replicate with more mutations than any other viruses, except for human immunodeficiency (HIV) viruses and, consequently, every year substantial portions of our population are susceptible to infection.

Summary

Strategies For The Control Of Influenza Infections

- Clinically important influenza virus infections can be caused by influenza types A and B.
- It is common for approximately 15% to 20% of the population to be infected annually in a relatively short period of time, usually within two months in any single community.
- Typical symptoms of influenza infection include respiratory components, such as runny nose, sore throat, sneezing and coughing, and systemic symptoms, such as headache, fever, chills, muscle aches, fatigue and lethargy.
- Regular, thorough handwashing helps minimize the spread from person-to-person or from infected individuals to environmental objects that may become the source of exposure for other susceptible individuals.
- The use of anti-viral drugs is becoming a useful control strategy in institutional outbreaks.
- Vaccines are the major control strategy for influenza, targeting at-risk individuals. There are variable vaccine programs across Canada.
- Annually, it is estimated there are 6,000 excess deaths and 75,000 hospitalizations in Canada attributable to influenza infections.
- A key part of a comprehensive influenza control program begins with surveillance for influenza infections.
- For adults, the risk for complications from influenza infection begins at age 50.
- Health-care workers should be immunized annually with influenza vaccine.

Recombination between human and animal strains can result in totally novel strains. These strains result in the viruses with new surface proteins to which humans may have no immunity. Such events may be associated with pandemics (*i.e.*, worldwide epidemics of influenza infections that can spread very quickly and are associated with significant morbidity and mortality, depending upon the virulence of the strains). The most severe pandemics of influenza of the past century occurred in 1918-19, when the virus that originated from swine infected the human population. More than 20 million deaths were reported worldwide.

Control Strategies

Infection control. Regular, thorough hand washing helps minimize the spread of infection from person-to-person or from infected individuals to environmental objects that may become the source of exposure to other susceptible individuals. The use of masks minimizes droplet spread from individuals who are infectious. Individuals who are ill from their symptoms, or who are in the early stages of infection, should not be in the presence of individuals who are at high risk of influenza complications (*i.e.*, those with chronic heart disease, lung disease and the elderly). This is especially true for health-care providers, doctors and nurses, as they should voluntarily limit their exposure to patients if they think they have influenza infections.

Anti-viral drugs. Another potential control strategy is the use of anti-viral drugs. Influenza A infections can be prevented by prophylactic use of amantadine taken before exposure to influenza infections. No protection is offered for influenza B strains. Amantadine is relatively inexpensive and easy to administer, but has side effects, such as difficulty concentrating, nervousness and irritability. Also, its dosage must be monitored carefully in individuals with renal failure and should be adjusted for elderly individuals.

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An important recent development is the availability of neuraminidase inhibitors. Some are administered by aerosol and others are available orally, in pill form. These also can be used for treatment, but the longer a symptomatic individ-

ual waits prior to initiating treatment, the less beneficial it is. In influenza outbreak situations in institutions, however, the prophylactic use of oral neuraminidase drugs has been observed to stop outbreaks. The development of resistance to neuraminidase inhibitors is being monitored carefully, but appears to be less frequent than resistance to amantadine.

Unfortunately, anti-viral drugs have no demonstrated efficacy in the general population.

Vaccines. Vaccines are the major control strategy for influenza, targeting at-risk individuals. There are variable vaccine programs across Canada.[1] The at-risk population includes the elderly, especially people over 65, and individuals with chronic underlying heart and lung disease. Influenza vaccine also is used to prevent infection in individuals who may transmit the virus to those at risk of complications. This has been an increasingly important area for influenza control strategies.[1]

The main compelling reason for these vaccine control programs is simple: they work. Multiple studies have shown that, even in the at-risk mobile elderly population, mortality rates are reduced by 39% to 60%.

For example, by using the vaccine for health-care providers, such as doctors, nurses and family members who look after those who are at risk of complications, we can provide a zone of protection. This helps minimize their potential exposure to influenza viruses and, thus, helps lower mortality rates.[2]

Why Do We Try To Control Influenza Infections?

The side effects of influenza infections in a population are substantial. Because 15% to 20% of individuals become infected, if only a small percentage of this group suffer complications there is a major impact on both the health of individuals and our health-care system as a whole. It is estimated there are 6,000 excess deaths and 75,000 hospitalizations in Canada annually that are attributable to influenza infections,[3] and in the United States, an average of 114,000 excess hospitalizations.[4] There also is a substantial impact of influenza infection on lost productivity at work, school and at home.

Another key feature of mobilizing an annual influenza immunization control program is that it prepares us in case any pandemic outbreak of influenza infection should occur. Historically, pandemics have been observed approximately every 30 years, so while it is unpredictable when the next one will occur, we know another pandemic is inevitable. There will likely be even less time to mobilize the delivery of influenza vaccine programs with pandemic influenza because novel vaccines must be designed, produced, tested and approved in a very short period of time. Consequently, it is necessary to have an efficient delivery and mobilization process for vaccine and this is best accomplished by annual vaccine programs.

The main reason for these vaccine control programs is simple: they work. Multiple studies have shown that, even in the at-risk mobile elderly population, mortality rates are reduced by 39% to 60% and hospitalization rates are reduced by over 20% in individuals who have been immunized, as compared to those who are not immunized.[5] Numerous studies show the impact of influenza vaccine is felt not only in reduced hospitalizations for pneumonia and

influenza illness, but also for reduced all-cause mortality. Studies also have shown immunization vaccine programs to be very cost-effective.[6]

How Are Influenza Controls Programs Organized?

A key part of a comprehensive influenza control program begins with surveillance for influenza infections. Through the use of sentinel physicians who provide both clinical information as well as swabs from individuals with influenza-like illness (ILI), public health organizations and public health laboratories have access to information and specimens that can be monitored on an annual basis. These symptoms and the results of laboratory studies provide the framework for regular Canada-wide surveillance of respiratory infections.

The awareness of influenza isolates in a community also is important information for physicians, patients, health-care administrators and health departments when planning an adequate response to influenza infections. When influenza infections are documented in the community, part of an effective control strategy is to alter the use of our health-care system to anticipate pressure on emergency departments and hospital beds. We must be prepared to curtail elective procedures (*i.e.*, elective surgery), so that resources can be allocated where there is likely to be the most important needs.

To achieve high rates of immunization promotion and awareness of influenza, control programs are needed. This requires enthusiasm and strong organizational skills. A variety of ways to increase the awareness of the general public and professionals, include television, radio and bus stop advertisements, as well as posters, newsletter articles, *etc.* No opportunity should be missed to encourage a high-risk individual to be immunized.

In-hospital patients can be immunized at the time of discharge. Individuals in out-patient clinics should be immunized. Immunizing health-care providers involves strategies, such as bringing the vaccine to the hospital clinics or wards while doctors and nurses are on duty.

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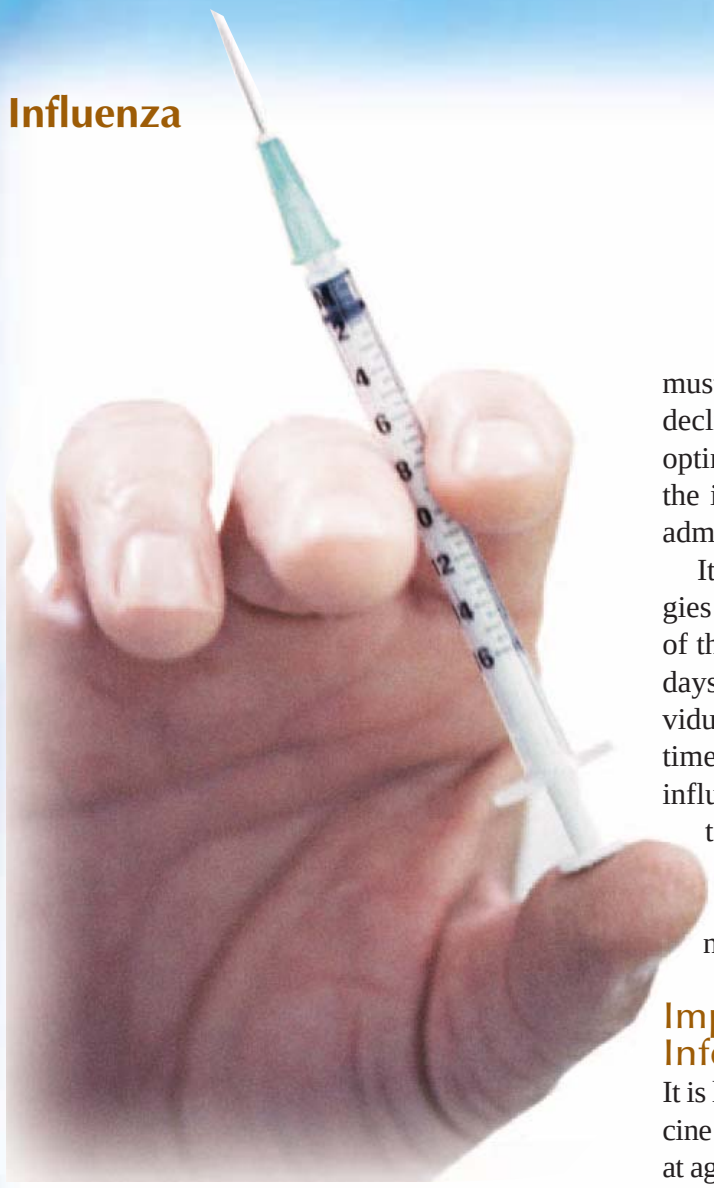
Post-marketing surveillance of influenza complications are important to ensure the vaccine has been safe. Generally, influenza vaccine is well tolerated. Aside from minimal local reactions from the intramuscular injection, occasionally some individuals will experience a low-grade fever and headache, which can be confused with mild influenza. Because it is a killed vaccine, however, it is impossible to acquire influenza infections from immunization.

In the winter of 2000-01, a mild clinical reaction called the oculorespiratory (ORS) syndrome was observed in approximately 1,000 Canadians out of approximately 10 million who were immunized. These reactions began within two to 24 hours of immunization and were associated with red eyes, facial swelling and difficulty breathing. The syndrome was very mild and resolved spontaneously within one or two days.



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Because of the new recognition of the syndrome, individuals who had this kind of reaction following last year's flu shot should be referred to public health departments or physicians for guidance regarding immunization this coming year. Further ORS surveillance will continue this year.

When Should Influenza Immunization Be Given?

The duration of immunity to a killed influenza vaccine is not longstanding and, consequently, it must be given annually. In addition, because of a decline in immunity following immunization, it is optimal to provide the vaccine in the fall prior to the influenza season. In Canada, it is common to administer the vaccine in October.

It is essential to have influenza control strategies in place prior to the influenza season because of the very short incubation period of one to three days, as well as the rapid virus spread from individual to individual. There usually is insufficient time to mobilize immunization programs once influenza has struck a community, because of the time required to establish such a program. In addition, it takes approximately one to two weeks for individuals who have been immunized to mount a protective immune response.

Improving Control Of Influenza Infections

It is likely the more widespread use of influenza vaccine will continue. The risk for complications begins at age 50. Recommendations in the U.S. are for individuals over age 55 to receive the influenza vaccine.

Ontario has expanded its influenza control program by offering free vaccines to individuals over the age of six months. In the winter of 2000, over half the population of Ontario was immunized for influenza. Studies are under way to evaluate the impacts of this enhanced immunization control program, as this is the first jurisdiction in the world that has made the vaccine so widely available as part of a public program.

In the future, the age of individuals offered immunization may be reduced to include routine childhood immunization. Recent publications from Japan have highlighted that, during childhood immunization programs in that country, there was a reduced mortality rate in the elderly.[7] This is a plausible explanation, given that children are observed to shed higher titres of virus for longer periods of time. Consequently, by reducing

the infections transmitted from children to high-risk populations, it is likely that greater opportunity for influenza control is possible.[8]

Other improvements include new vaccines. For example, live attenuated vaccine has been tested in children and adults with influenza infection, and has been found to produce excellent protection through an easily administered form of nasal spray. Many other improvements are being developed to improve the immune response, with both local and cellular immunity being stimulated through new vaccine formulations and adjuvants. Better vehicles for delivering vaccines by the use of novel routes (*i.e.*, nasal immunization) also are helping improve the immune response. Simultaneous, live intranasal and intramuscular killed vaccines reduce infections rates in the elderly.[9]

Summary

While overall prevention of influenza infection is not yet possible, control strategies continue to improve. It is important to emphasize that, although the vaccine has only 70% efficacy, if it is not used there will not be any benefit. Consequently, the more influenza vaccine is used, the greater will be the potential for influenza control. The same can be said for the potential for reducing complications of influenza infections. Health-care workers should be immunized annually with influenza vaccine.

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