Episode 97 – Viral Respiratory Infections November 24, 2023

Introduction

Respiratory diseases can be caused by several microorganisms, such as viruses, bacteria, and fungi.

Respiratory diseases caused by microorganisms [1] [2] [3] [4] [5] [6] [7] [8]

Organism*	Disease*
Viruses	
Respiratory syncytial virus	Bronchiolitis Pneumonia
Influenza	Pneumonia
Coronaviruses	
SARS-CoV-2	Coronavirus disease 2019 (COVID-19)
MERS-CoV	Middle East respiratory syndrome (MERS);
SARS-CoV	Severe acute respiratory syndrome (SARS)
Rhinoviruses	Common cold
Adenovirus	Pneumonia
Parainfluenza	Croup
Bacteria	
Streptococcus pneumoniae	Pneumococcal pneumonia
Bordetella pertussis	Pertussis
Haemophilus influenzae	Pneumonia
Fungi	
Histoplasma capsulatum	Histoplasmosis
Aspergillus	Aspergillosis

* Nonexhaustive list

In 2022, RSV, influenza, and SARS-CoV-2 caused a "tripledemic" pushing pediatric and adult hospitals beyond capacity across Canada. Public health measures used to reduce COVID-19 transmission also helped curb the spread of other respiratory viruses. As Canadian jurisdictions eased many public health measures, transmission of these other viruses increased. This, in combination with lower population-level immunity, led to higher rates of infection. Peak disease activity of the tripledemic lasted a few weeks, with indicators returning to expected levels by the end of December 2022. [9]

Belza et al. (2023) investigated severe respiratory disease among Canadian children with and without medical complexity during the COVID-19 pandemic. Children with medical complexity (e.g., cystic fibrosis,[1] congenital heart disease, sickle cell disease)

[1] Refer to Episode 83 for discussion on cystic fibrosis.

are at risk of severe acute illness from respiratory infections. The cross-sectional study found a substantial decrease in severe respiratory disease resulting in decreased hospitalizations, ICU admissions, and mortality during the first two years of the pandemic compared with the three prepandemic years. These findings suggest the need to evaluate the effect of public health interventions (e.g., masking, air filtration) in reducing circulating respiratory pathogens during nonpandemic periods to protect children at risk of hospitalization during seasonal respiratory viral surges. [10]

Viral respiratory infections

Viral infections commonly affect the upper or lower respiratory tract. Upper respiratory tract infections occur in the nose, nasal cavity, sinuses, pharynx, larynx, and trachea. Viral upper respiratory tract infections include the common cold and influenza. Infection of the upper respiratory tract is common and can spread to the lower respiratory tract, where they can cause serious complications. Lower respiratory tract infections occur from the bronchi to the alveoli of the lungs. Viral lower respiratory tract infections include bronchitis, bronchiolitis, and pneumonia.[2] [11] [12]

Respiratory infections can be classified by the causative virus (e.g., influenza virus) or according to the infection (e.g., common cold, croup, pneumonia). Although specific pathogens commonly cause characteristic clinical manifestations (e.g., RSV typically causes bronchiolitis), each virus can cause many types respiratory infections. [2]

Causes of common viral respiratory infections [2]

Infection	Common causes	Less common causes
Bronchiolitis	RSV	Influenza viruses Parainfluenza viruses Adenoviruses Rhinoviruses
Common cold	Rhinoviruses Coronaviruses	Influenza viruses Parainfluenza viruses Enteroviruses Adenoviruses Human metapneumoviruses RSV
Croup	Parainfluenza viruses	Influenza viruses RSV
Influenza-like illness	Influenza viruses	Parainfluenza viruses Adenoviruses
Pneumonia	Influenza viruses RSV Adenoviruses Coronaviruses (including SARS-CoV-2)	Parainfluenza viruses Enteroviruses Rhinoviruses Human metapneumoviruses

[2] Pneumonia is acute inflammation of the lungs. Symptoms may include cough that produces sputum (thick discoloured mucous), chest pain, chills, fever, shortness of breath, fatigue, confusion or changes in mental awareness (in adults ≥65 years), nausea, vomiting, and diarrhea. Symptoms may vary depending on how much of the lungs are infected and type of microorganism causing infection. [115] [116]

Severity of viral respiratory illness varies widely. Severe disease is more likely in infants and older adults. Morbidity may result directly from viral infection or may be indirect, due to exacerbation of underlying cardiopulmonary conditions or bacterial superinfection of the lung, paranasal sinuses, or middle ear. [2]

Symptom comparison

Respiratory syncytial virus (RSV), COVID-19, influenza, and the common cold are all contagious respiratory illnesses with similar symptoms, making it difficult to distinguish between these viral infections without a lab test. Seasonal allergies can also cause similar symptoms.

Symptom comparison [13] [14] [15] [16] [17] [18] [19] [20] [21] [22]

Symptom	RSV	COVID-19	Influenza	Cold	Seasonal allergy
Symptom onset	Gradual	Gradual	Sudden	Gradual	Maybe gradual or abrupt
Headache	Usually	Usually	Usually	Rare	Rare
Cough	Usually (dry)	Usually (dry)	Usually	Usually	Sometimes
Muscle aches	Rarely	Usually	Usually	Sometimes	Never
Fatigue	Sometimes	Usually	Usually	Sometimes	Sometimes
Sneezing	Usually	Rarely	Sometimes	Usually	Usually
Sore Throat	Usually	Usually	Usually	Sometimes	Rarely
Runny or stuffy nose	Usually	Usually	Usually	Usually	Usually
Fever	Sometimes	Usually	Usually	Sometimes	Never
Diarrhea	Rarely	Sometimes	Sometimes (more common in children)	Never	Never
Nausea or vomiting	Rarely	Sometimes	Sometimes (more common in children)	Never	Never
New loss of taste or smell	Rarely	Usually (early symptom, often without a runny or stuffy nose)	Rarely	Sometimes (especially with a stuffy nose)	Sometimes
Shortness of breath or difficulty breathing	Sometimes	Usually	Usually	Rarely	Rarely (unless a respiratory condition exists e.g., asthma triggered by pollen)
Wheezing	Often	Rarely	Rarely	Rarely	Sometimes (e.g., allergy-induced asthma)
Itchy nose, eyes, mouth, or inner ear	Rarely	Never	Rarely	Rarely	Usually
Conjunctivitis (pink eye)	Sometimes	Sometimes	Sometimes	Sometimes	Sometimes

Comparison of key features [23] [24] [25] [26] [27]

Key features	RSV	Seasonal influenza	SARS-CoV-2	Rhinovirus
Common symptoms	Similar to influenza.	Sudden onset of fever, cough, chills, headache, fatigue, sore throat, runny or stuffy nose, muscle pain or body aches.	Similar to influenza including shortness of breath. Other symptoms may include decreased or loss of taste and smell; and gastrointestinal symptoms (nausea, vomiting, diarrhea).	Runny nose, sneezing, cough, sore throat, muscle pain, fatigue, no or mild fever.
Severe complications	Pneumonia, bronchiolitis, death.	Pneumonia, worsening of underlying medical conditions, sepsis, cardiac involvement, neurologic involvement, death.	Similar to influenza with the addition of blood clots in lungs, heart, legs, or brain; and multisystem inflammatory syndrome in children (MIS-C), multisystem inflammatory syndrome in adults (MIS-A), long COVID, death.	Bronchitis; lower respiratory tract infection (pneumonia, bronchiolitis).
Risk groups for complications	Infants and children <2 years with congenital heart disease or chronic lung disease; premature infants; older adults; underlying medical conditions, including immunocompromised.	Young children; older adults; underlying medical conditions, including immunocompromised; obesity; pregnancy.	Older adults; underlying medical conditions, including obesity; immunocompromised.	Young children; immunocompromised; respiratory conditions.
Incubation period (time exposure to symptom onset)	3 to 7 days	1 to 4 days	1 to 14 days; median: 5 to 6 days Evidence suggests shorter incubation periods for COVID-19 variants of concern.	2 to 4 days
Communicable period	Usually until 3 to 8 days after symptom onset, but can sometimes be up to 4 weeks in infants and those with compromised immune systems.	1 day before and until about 5-10 days after symptom onset (peaks 24-48 hours after symptom onset). May be prolonged in people with compromised immune systems.	2-3 days prior to symptoms to ~10 days after symptom onset. May be prolonged in people with compromised immune systems.	1 to 3 weeks (peaks 2-3 days after symptom onset).

Key features	RSV	Seasonal influenza	SARS-CoV-2	Rhinovirus
Transmission	Direct person-to-person transmission and fomites.	Direct person-to-person transmission and fomites, and possibly small aerosols under certain conditions.	Primarily at short range through unprotected close contact and exposure to large and small respiratory particles and possible but less common transmission over longer distance under favourable conditions. Possibly fomites.	Direct person-to-person transmission and fomites.
Transmission based on symptoms	Uncertain, has not been well studied	Can transmit 24 hours before symptom onset. Asymptomatic people can transmit.	Evidence suggests 2-3 days before symptom onset. Can transmit while asymptomatic.	Uncertain, has not been well studied
Vaccine	Vaccine available for older adults. Synagis (palivizumab), a monoclonal antibody, for prevention in some high-risk infants.	Seasonal vaccine available and recommended annually.	Vaccines are available and recommended.	No vaccine
Antiviral medication	None routinely recommended	Used for treatment in those with moderate or severe illness or at risk for complications of influenza. Recommended for both treatment and prevention in outbreaks in closed settings, especially if residents are at high risk of complications. E.g., Tamiflu (oseltamivir) and Relenza (zanamivir)	Paxlovid (nirmatrelvir, ritonavir)	None

Signs and symptoms of illness caused by these respiratory viruses can be very similar and therefore cannot be distinguished without laboratory testing. These four viruses, along with other viruses, can cause outbreaks in facilities during the respiratory virus season.

Respiratory syncytial virus

Respiratory syncytial virus (RSV) is a common respiratory virus that usually causes mild, cold-like symptoms. In Canada, RSV causes yearly outbreaks of respiratory tract disease from late fall to early spring. Most individuals recover in one to two weeks. Reinfections occur throughout life and are relatively common in both children and adults as infection produces only partial and temporary immunity. Reinfection is usually less severe in adults and older children. Reinfection in older adults can cause serious health consequences.

RSV is the most common cause of acute lower respiratory infection in young children. Most children will have at least one RSV infection by the age of two. However, infants and older adults, particularly with existing health conditions (e.g., preterm birth in infants, asthma, chronic heart or lung disease, immunocompromised) are more likely to develop severe RSV and require hospitalization. Severe RSV can also escalate chronic health issues, such as asthma, chronic obstructive pulmonary disease (COPD), and congestive heart failure. In severe cases, an individual may require additional oxygen, IV fluids, or intubation with mechanical ventilation. [28] [29] [30]

Globally, RSV affects an estimated 64 million individuals and causes 160,000 deaths each year. In 2019, RSV caused an estimated 5.2 million cases, 470,000 hospitalizations, and 33,000 deaths in those aged ≥60 years in high-income countries. In 2019, RSV caused an estimated 33 million cases, 3.6 million hospitalizations, and 26,300 deaths in children ≤5 years globally. [31] [32] [33]

In Ontario, most deaths from RSV have occurred in individuals ≥60 years. Older adults in long-term care and retirement homes have longer hospital stays than the general population due to RSV. During peak RSV season, hospitals have seen a surge in emergency room visits and admissions of young children and older adults, putting a strain on hospital resources (e.g., beds, specialized units, staffing). [34]

Symptoms

Symptoms of RSV may include:

- Coughing
- Runny nose
- Sneezing
- Wheezing
- Fever
- Decrease in appetite and energy

In infants, symptoms may include:

- Irritability
- Difficulty breathing
- Decreased appetite or feeding
- Decreased activity [35] [36]

Transmission
RSV is very contagious and spreads by close contact (less than 2 metres apart) with someone with RSV who is coughing or sneezing. It may also be transmitted through contact with infected respiratory secretions on surfaces and objects. After exposure to the virus, it can take approximately 3 to 7 days before symptom onset. Individuals are usually contagious for up to 3 to 8 days. Children are often exposed to and infected with RSV outside the home (e.g., school, childcare centres) and can then transmit the virus to family members. [36]

Complications
RSV is the most common cause of bronchiolitis (i.e., inflammation, swelling, and obstruction of the bronchioles), an acute viral infection of the lower respiratory tract affecting infants <24 months. Bronchiolitis starts with cold-like symptoms (e.g., runny nose, sneezing, mild fever, coughing) but can progress to respiratory distress, worsening cough, wheezing, and/or crackles.

Treatment of bronchiolitis is supportive, and most children can be managed at home with hydration and comfort measures. Some infants with severe bronchiolitis require hospitalization for oxygen therapy and IV hydration. [30] [31] [37]

Research has shown hospitalization for respiratory illness due to RSV is complicated by cardiovascular events in up to 22% of adults, including worsening congestive heart failure, acute coronary syndrome, and arrhythmias. Underlying cardiovascular disease is associated with hospitalization in 45% to 63% of adults with confirmed RSV. [38]

Prevention in infants[3]
For decades the only RSV product available in Canada was Synagis (palivizumab), a monoclonal antibody used as a passive immunizing agent for infants at risk of severe RSV-associated outcomes. Synagis is delivered intramuscularly, preferably in the thigh, once a month for up to five months during RSV season to maintain effectiveness. [39] [40]

In April 2023, another passive immunizing agent, Beyfortus (nirsevimab), received Health Canada authorization for pediatric use.[4] It is given as a single intramuscular injection during infants' first RSV season. A second dose may be given to children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season (e.g., due to immunocompromised states, cystic fibrosis). [41] [42] [43]

Currently in Ontario, through the RSV Prophylaxis for High-Risk Infants Program, infants and children who are <2 years of age at high risk of severe illness from RSV may be eligible for Synagis to prevent serious lower respiratory tract infection caused by the virus, including:

- Infants born prematurely at or less than 32 completed weeks gestation and aged 6 months or younger at the start of, or during, the RSV season.

[3] See page 25 for addition information on protection from respiratory viruses.
[4] As of November 2023, Beyfortus (nirsevimab) was not available yet in Canada, possibly due to the shortage in US where there has been unprecedented demand for the medication. [117] [124]

- Children younger than 24 months with certain comorbidities. [36]

See footnote below for the hyperlink to additional eligibility criteria.[5,6]

Prevention in adults[7]

On August 4, 2023, Health Canada approved the first RSV vaccine, Arexvy by GSK, for adults ≥60 years. One dose of the Arexvy RSV vaccine provides protection against RSV disease in adults ≥60 years for at least two winter seasons, when RSV normally circulates. During the first RSV season after vaccination, one dose of Arexvy was 83% effective in preventing lower respiratory tract disease caused by RSV in adults ages ≥60 years with healthy immune systems and 95% effective in those with underlying medical conditions. During the second RSV season after vaccination, one dose of Arexvy was still 56% effective against lung infections. Further evaluation is planned to assess how long protection lasts and whether additional doses are required. [44] [45] [46] [47]

For the 2023-2024 RSV season, adults ≥60 years residing in long-term care homes, Elder Care Lodges, and some retirement homes may be eligible for the RSV vaccine at no cost through the Ontario High-Risk Older Adult RSV Vaccine Program. If adults ≥60 years do not qualify for the free RSV vaccine, they can purchase the vaccine with a prescription from their medical provider.

Currently, as per the Ontario Immunization Advisory Committee (OIAC), as a precautionary measure, it is recommended eligible individuals who wish to receive the RSV vaccine receive it at least 14 days before or after receiving other vaccines, including COVID-19 and/or influenza vaccines. This is not due to any safety signals but instead to enable proper surveillance of potential vaccine effects.

Coadministration of the Arexvy vaccine with COVID-19 and influenza vaccines, or at a shortened interval (i.e., <14 days) should be considered in situations where, in the provider's best judgement, the benefits outweigh the risks, including if:

- There is an RSV, COVID-19, or influenza breakout within the home or nearby;
- Community activity of COVID-19, influenza, and/or RSV is high and increasing;
- There is a risk the individual will not receive the recommended vaccine doses. [25] [34] [36]

Treatment

Treatment for RSV generally involves supportive care to manage symptoms, such as:

- Using over-the-counter acetaminophen or ibuprofen for fever or pain. Ibuprofen should not be given to infants under six months old without prior medical

[5] Eligibility criteria for the monoclonal antibody for high-risk infants/children: https://www.ontario.ca/page/respiratory-syncytial-virus

[6] Note: In the US, Pfizer's bivalent vaccine Abrysvo has been licensed and recommended for use during RSV season for individuals who are 32 through 36 weeks pregnant (i.e., maternal vaccination) to protect infants from RSV. Infants born to individuals who receive this RSV vaccine at least two weeks before delivery will have protection and, in most cases, should not need RSV antibody products later. [118]

[7] Note: Two RSV vaccines, Arexvy by GSK and Abrysvo by Pfizer, have been licensed for use in adults ≥60 years. On April 14, 2023, Health Canada accepted for review Pfizer's Abrysvo vaccine for both older adult and maternal immunization. [119] [120]

consultation. Aspirin (acetylsalicylic acid [ASA]) should never be given to children and teenagers due to the chance of Reye syndrome.[8]
- Drinking fluids to prevent dehydration. For infants having trouble drinking, try to clear nasal congestion with a bulb syringe or with saline nose drops.
- A lukewarm bath or wet face cloths will not change someone's body temperature but may help increase comfort. Avoid cold baths because they can make the individual shiver, raising their temperature. Do not use rubbing alcohol to reduce fever.
- Dressing in light clothing to allow the body to cool down and to increase comfort. If the individual starts to shiver, add warmer clothing and remove when shivering stops.
- Consulting a medical provider before combining natural or herbal supplements with medications to avoid interactions.
- Consulting a medical provider for advice about appropriate over-the-counter medications for children (e.g., cough, cold medications) as some products contain ingredients that should be avoided.

Seek immediate medical attention for any of the following:
- Worsening symptoms.
- Difficulty breathing, pale skin, cyanosis (bluish skin, nails, or lips due to lack of oxygen), asthma, or wheezing.
- High fever, difficult to wake, or very sleepy.
- Repeated vomiting and unable to keep any liquids down for eight hours or more.
- Signs of dehydration (e.g., dry mouth, no urination for eight hours or more). [36] [48]

Influenza

Influenza is an acute respiratory infection caused by influenza viruses. It is common in all parts of the world. Each year, influenza results in up to one billion infections, five million hospitalizations, and 650,000 deaths worldwide. Prior to the pandemic, there was an average of 46,500 laboratory-confirmed cases of influenza in Canada each year, though the total number of cases is suspected to be higher. [49] [50]

There are four types of seasonal influenza viruses, types A, B, C, and D. Influenza A and B viruses circulate and cause seasonal epidemics of disease.
- Influenza A viruses are classified into subtypes based on two surface proteins (hemagglutinin [HA] and neuraminidase [NA]). Currently circulating in humans are subtype A(H1N1) and A(H3N2) influenza viruses. The A(H1N1) is also written as A(H1N1)pdm09 as it caused the pandemic in 2009 and subsequently replaced the seasonal influenza A(H1N1) virus which had circulated prior to 2009. Only influenza type A viruses are known to have caused pandemics.
- Influenza B viruses have evolved into two lineages: B/Yamagata and B/Victoria.

[8] Reye syndrome is a rare but serious condition that causes swelling in the brain and liver. It can occur at any age but usually children and teenagers recovering from a viral infection, most commonly influenza and chickenpox. It is not well understood, but studies have linked it to the use of aspirin or aspirin products during illnesses caused by viruses. Symptoms of Reye syndrome may include persistent or recurrent vomiting, listlessness, personality changes (e.g., irritability, combativeness), disorientation, confusion, delirium, convulsions, loss of consciousness. In rare cases, it can cause death within hours. [121] [122] [123]

- Influenza C virus is detected less frequently and usually causes mild infections, thus does not present public health importance.
- Influenza D viruses primarily affect cattle and are not known to infect or cause illness in humans. [27] [49] [51]

Antigenic drift

Antigenic drift (or antigenic variation) consists of small changes (mutations) in the genes of influenza viruses that can alter the surface proteins of the virus, HA (hemagglutinin) and NA (neuraminidase). The HA and NA surface proteins are antigens that trigger an immune response in the host, including production of antibodies to fight infection. The changes associated with antigenic drift happen continually over time as influenza viruses spread and replicate in infected hosts. Influenza vaccines are designed to target one or more of the surface proteins/antigens of influenza viruses.

Antigenic drift results in multiple strains within an influenza A subtype or B lineage. If antigenic drift changes the virus' antigenic properties enough, existing antibodies will not effectively recognize and neutralize the antigenically different influenza viruses, resulting in susceptibility to infection again. These new strains may cause seasonal epidemics because protection by antibodies generated to the previous strain is decreased.

Antigenic drift is a reason why individuals can get influenza multiple times over their lifetime. It is also a primary reason why the composition of influenza vaccines for use in the northern and southern hemispheres is reviewed annually and updated as needed to address evolving influenza viruses. In most seasons, one or more of the strains in influenza vaccines are changed from the previous season.

Also, vaccine-induced immunity wanes over time. Together, antigenic drift resulting in new vaccine formulations and waning vaccine-induced immunity are reasons why the influenza vaccine is recommended before each influenza season. [1] [27] [52]

Antigenic shift

While influenza viruses continuously evolve genetically and often undergo antigenic drift, antigenic shift happens infrequently. Antigenic shift occurs when two different influenza strains, one native to humans and one native to animals (commonly birds), exchange genetic material. This exchange creates an entirely new influenza strain with potential to infect humans. Since this influenza strain is completely novel, human immune systems do not have any memory to recognize it to mount an immune response. This is why antigenic shift can be dangerous, and why it has potential to cause pandemics.

There have been six major influenza pandemics, typically named after the presumed location of origin:

- 1889: H2N2 (Russian influenza)
- 1900: H3N8 (Old Hong Kong influenza)
- 1918: H1N1 (Spanish influenza)
- 1957: H2N2 (Asian influenza)

- 1968: H3N2 (Hong Kong influenza)
- 2009: A(H1N1) (Swine influenza) [1]

In the spring of 2009, an antigenic shift occurred when an H1N1 virus with genes from viruses originating from North American swine, Eurasian swine, humans, and birds emerged. After early reports of influenza outbreaks in North America in April 2009, the new influenza virus (often called swine flu) spread rapidly around the world.

The World Health Organization (WHO) declared the H1N1 influenza to be a pandemic in June 2009. A total of 74 countries and territories had reported laboratory confirmed infections. Unlike typical seasonal influenza patterns, the new virus caused high levels of summer infections in the northern hemisphere, and then even higher levels of activity during cooler months. The new virus also led to patterns of death and illness not normally seen in influenza infections (e.g., only 20% of the deaths were in individuals >64 years, in contrast, about 90% of seasonal influenza deaths are in seniors.). The 2009 H1N1 influenza pandemic caused an estimated 284,400 deaths worldwide. In August 2010, WHO declared the pandemic over. The 2009 A(H1N1) virus continues to circulate as a seasonal virus and is included in vaccines against seasonal influenza. Fortunately, antigenic shift does not occur often, and influenza pandemics are rare. However, scientists predict another influenza pandemic will happen, although they cannot say exactly when. [52] [53] [54] [55] [56]

Transmission
Influenza is primarily transmitted by droplets and small particle aerosols spread through coughing, sneezing, talking, and breathing. It may also be transmitted through direct or indirect contact with infected respiratory secretions on surfaces and objects.

The incubation period of influenza can range from one to four days. Adults may be able to spread influenza from one day before symptoms start to approximately five days after symptoms onset. Children and adults who are immunocompromised may be infectious for longer. [27]

Symptoms
Infection usually lasts for about a week and is characterized by sudden onset of high fever, muscle and joint aches, headache, fatigue, nonproductive (dry) cough, sore throat, and rhinitis (runny or stuffy nose). Nausea, vomiting, and diarrhea may also occur, especially in children. Most individuals will recover on their own within one or two weeks. Medical care may be needed in severe cases and for those with risk factors. Influenza can worsen symptoms of other chronic diseases. Severe cases can lead to pneumonia, sepsis, and death. [49] [57]

High risk groups
All age groups can be affected but there are individuals at high risk of complications or hospitalization, including:
- Adults ≥65 years
- Children <5 years
- Pregnant individuals

- Individuals with chronic health conditions (e.g., cardiac or pulmonary disorders, diabetes, renal disease, obesity [BMI ≥40]; and neurodevelopmental, liver, or hematologic conditions)
- Children ≤18 years undergoing treatment with ASA (aspirin) because Reye syndrome is a risk
- Individuals with immunosuppressive conditions or treatments (e.g., HIV, receiving chemotherapy or steroids)
- Residents of long-term care and other chronic care facilities
- Indigenous peoples

Healthcare workers are at high risk of acquiring influenza due to increased exposure to patients, and at increased risk of spreading particularly to vulnerable individuals. Vaccination is important to protect healthcare workers and those around them.

Influenza epidemics can result in high levels of work and school absenteeism and productivity losses. Clinics and hospitals can be overwhelmed during peak illness periods. [1] [27] [49]

Treatment

Treatment should aim to relieve symptoms. Individuals with mild symptoms should:

- Rest
- Drink plenty of fluids
- Treat other symptoms (e.g., fever)
- Seek medical care if symptoms get worse

Antiviral treatment

Antiviral medications to reduce influenza morbidity and mortality are recommended for individuals with influenza symptoms in high-risk groups or who are severely ill. Antiviral medications are recommended for these individuals when influenza is circulating in the community. Antiviral medications are not a substitute for annual influenza vaccine.

There are currently two antiviral drugs licensed in Canada for the treatment and prevention (i.e., prophylaxis) of seasonal influenza, including Tamiflu (oseltamivir) and Ralenza (zanamivir).[9] Tamiflu is an oral medication for adults and children one year and older. Ralenza is dry powder for oral inhalation in adults and children 7 years of age and older. These medications are neuraminidase inhibitors, which block the exit of the influenza virus from the respiratory cells and prevent further viral replication. For this reason, when using antivirals for influenza treatment, they must be initiated as soon as possible within 48 hours of symptom onset. [25] [58] [59]

For individuals at very high risk of complications, early treatment started as soon as possible after exposure to an infectious case and before symptoms begin may be appropriate when influenza is prevalent. This strategy is preferred over post-exposure prophylaxis due to concerns regarding drug resistance. [25]

[9] Note: Although still licensed in Canada, amantadine is no longer recommended due to high rates of resistance observed among circulating influenza A viruses. [25]

Usual dose for treatment of influenza:

- Tamiflu is taken orally twice a day (morning and night) for five days.
- Ralenza is inhaled orally twice a day (morning and night) for five days.
- These medications work best when taken as soon as symptoms begin and no later than two days after influenza symptoms start.
- The entire treatment regime must be completed as recommended by the medical provider, even if feeling better.
- These drugs reduce duration of influenza symptoms by about 1 or 2 days. [58] [59]

Tamiflu is the primary agent in Canada for treatment of suspected or confirmed influenza. Ralenza is generally not recommended for elderly individuals, as they may have difficulty using the inhaler. Treatment with Ralenza should be considered for those not responding to Tamiflu therapy, those who have developed influenza while receiving Tamiflu prophylaxis, or those in whom influenza B infection is confirmed or strongly suspected. Ralenza is generally not recommended for treatment or prophylaxis of influenza in individuals with underlying respiratory conditions (e.g., COPD, asthma) due to the risk of bronchospasm. [59] [60]

Usual dose for prophylaxis (prevention) of influenza:

- Tamiflu should be taken within 2 days after contact with someone with influenza symptoms. It is taken once a day for 10 days or longer as prescribed by the medical provider.
- Ralenza is taken once daily for 10 or 28 days as prescribed by the medical provider. [58] [59]

Prevention

Vaccination is the best way to prevent influenza. Safe and effective vaccines have been used for more than 70 years. Vaccines are updated routinely to contain viruses that match those circulating. Several inactivated influenza vaccines and recombinant influenza vaccines are available in injectable form. Live attenuated influenza vaccines are available as a nasal spray. [49]

Inactivated influenza vaccines contain inactivated (killed) viruses and an adjuvant to enhance antibody response.

Live attenuated influenza vaccines are made with weakened (attenuated) viruses. These vaccines are not recommended for use in individuals who are pregnant, immunocompromised, or with certain medical conditions (e.g., severe asthma).

Egg-based vaccine manufacturing is used to make both inactivated vaccine and live attenuated vaccine. The egg-based production process begins with the candidate vaccine viruses grown in chicken eggs. These candidate vaccine viruses are then injected into fertilized chicken eggs and incubated for several days to allow the viruses to replicate. The fluid containing virus is harvested from the eggs. For inactivated influenza vaccines, the vaccine viruses are then inactivated, and the virus antigen is purified. For the live attenuated influenza vaccine, the starting vaccine viruses are used to make live, but weakened viruses that are then used in vaccine production. Egg-based

manufacturing process is the most common way influenza vaccines are made and has been used for more than 70 years. This production method requires large numbers of eggs to produce vaccine and may take longer than other production methods. The National Advisory Committee on Immunization (NACI) indicates egg allergy is not a contraindication for influenza vaccination and that egg-allergic individuals may be vaccinated against influenza using the full dose of any age-appropriate product.

Cell-based vaccines are grown in mammal cell cultures instead of chicken eggs. The vaccine is completely egg-free. Currently, cell culture-based manufacturing is used to make inactivated influenza vaccines.

Recombinant influenza vaccines are produced using recombinant DNA technology, a method that does not require an egg-grown vaccine virus and does not use chicken eggs at any stage of the production process. Manufacturers isolate the virus's gene that contains the genetic instructions for making the HA antigen. The HA gene is then combined with a baculovirus, a virus that grows well in insect cells. The resulting "recombinant" vaccine virus is then mixed with insect cells and allowed to replicate. The influenza virus HA surface protein is then harvested from these cells, purified, and packaged as recombinant influenza vaccine. This vaccine contains three times the antigen than other standard-dose inactivated influenza vaccines to help create a stronger immune response.[10] [50] [57] [61] [62] [63]

There are ten influenza vaccines authorized and available for use in Canada:
- Eight inactivated influenza vaccines,
- One recombinant influenza vaccine, and
- One live attenuated influenza vaccine.

Some vaccines protect against three strains of influenza (i.e., trivalent). Trivalent vaccines contain:
- One A(H1N1) strain,
- One A(H3N2) strain, and
- One influenza B strain from 1 of 2 lineages, Victoria or Yamagata.

Others protect against four strains of influenza (i.e., quadrivalent). Quadrivalent vaccines contain:
- Strains in the trivalent vaccine, and
- An influenza B strain from the other lineage. [64]

The WHO convenes technical consultations in February and September each year to recommend viruses for inclusion in seasonal influenza vaccines for the northern and southern hemispheres, respectively. Influenza in the northern hemisphere is often caused by viruses similar to those that spread in the southern hemisphere during their influenza season. Influenza season in the southern hemisphere goes from April until around September. The 2023 influenza season in the southern hemisphere peaked

[10] Refer to Episode 15 for additional information on the types of vaccines.

earlier than usual (April to May, compared to typical peaks in June to July) and was dominated by influenza A. [65] [66]

A Centers for Disease Control and Prevention (CDC) study by Fowlkes et al. (2023) of southern hemisphere countries, specifically Argentina, Brazil, Chile, Paraguay, and Uruguay, showed the 2023 influenza vaccine reduced risk for influenza-associated hospitalizations by 52%. Vaccine effectiveness was most pronounced among children and older adults. These early estimates suggest vaccination substantially reduced the risk for severe influenza illnesses, underlining the benefits of influenza vaccination. [67]

In Ontario, influenza season typically runs from late fall to early spring, so timing of the influenza vaccine is important. Ideally individuals should get vaccinated before influenza begins to spread. It also takes two weeks for the vaccination to take effect, making the fall the ideal influenza vaccination time. However, it is still better to get vaccinated later in the season than not at all. [68]

The Ontario Ministry of Health Universal Influenza Immunization Program (UIIP) offers influenza vaccine free of charge each year to all individuals six months of age and older who live, work, or go to school in Ontario. On October 30, 2023, individuals were able to start receiving their influenza vaccination and the new, most recent COVID-19 vaccine at local pharmacies, public health units, and primary care provider settings across Ontario. Individuals aged 6 months and over may receive influenza vaccination at the same time as, or at any time before or after a COVID-19 vaccine. [69] [70]

Vaccines available through UIIP for 2023-24 influenza season [50] [62]

Ages	Type of influenza vaccine	Influenza vaccine products
6 months – 64 years	Standard-dose inactivated quadrivalent (QIV)	• FluLaval® Tetra • Fluzone® Quadrivalent
≥65 years	High-dose quadrivalent inactivated (QIVHD)*	• Fluzone® High-Dose Quadrivalent
≥65 years	Adjuvanted trivalent inactivated (TIV-adj)	• Fluad®
≥65 years	Standard-dose inactivated quadrivalent (QIV)	• FluLaval® Tetra • Fluzone® Quadrivalent

*High-dose vaccine contains four times the amount of antigen as a regular influenza vaccine to help create a stronger immune response.
FluMist® Quadrivalent is authorized for use but it is not publicly funded in this 2023-2024 flu season. It is a live attenuated influenza vaccine given as an intranasal spray into both nostrils. [71]

COVID-19

SARS-CoV-2 is the virus that causes coronavirus disease 2019 (COVID-19) and led to a global pandemic with more than 6.9 million deaths and severe socioeconomic burden worldwide. As of November 2023, there have been over 4.8 million COVID-19 cases, and over 55 thousand deaths in Canada. [72] [73] [74]

Most individuals infected with the virus experience mild to moderate respiratory illness and recover without requiring special treatment. However, some individuals become

seriously ill and require medical attention. Older individuals and those with underlying medical conditions (e.g., cardiovascular disease, diabetes, chronic respiratory disease, cancer) are more likely to develop serious illness. However, anyone can become seriously ill or die from COVID-19. [51]

According to wastewater surveillance data from Public Health Ontario, COVID-19 has been on the rise in Ontario since early July 2023. These numbers are expected to increase with individuals moving indoors due to the colder weather. [75]

Symptoms

Symptoms of COVID-19 can vary depending on the individual, their age, and the COVID-19 variant. Commonly reported symptoms include:

- Fever
- Sore throat
- Congestion or runny nose
- Sneezing
- New or worsening cough
- Shortness of breath or difficulty breathing
- Feeling feverish or chills
- Fatigue or weakness
- Muscle or body aches
- New loss of smell or taste
- Headache
- Abdominal pain, diarrhea, vomiting [76]

Immediate medical attention should be sought for any severe symptom, including:

- Difficulty breathing or severe shortness of breath
- Persistent chest pain or pressure
- New confusion
- Difficulty waking or trouble staying awake
- Pale skin or cyanosis (blue-coloured skin, lips, or nail beds) [76]

Complications

Complications of COVID-19 include:

- Acute respiratory distress syndrome (ARDS)
- Heart disorders including arrhythmias, cardiomyopathy, and acute cardiac injury
- Coagulation disorders including thromboembolism and pulmonary emboli, disseminated intravascular coagulation, hemorrhage, and arterial clot formation
- Guillain-Barré syndrome (rare)
- Sepsis, shock, and multiorgan failure
- Multisystem inflammatory syndrome in children (MIS-C)[11]
- Multisystem inflammatory syndrome in adults (MIS-A)[12]
- Post COVID-19 condition (long COVID) [77]

[11] Refer to Episodes 28, 33, and 48 for additional information on MIS-C.
[12] Refer to Episode 33 for additional information on MIS-A.

Zhang et al. (2023) found individuals hospitalized with COVID-19 were more than twice as likely to develop new-onset persistent hypertension than those hospitalized with influenza. The retrospective observational study included over 45,000 participants with COVID-19 and nearly 14,000 with influenza without a history of hypertension. Persistent hypertension was more common among older adults, males, individuals with preexisting comorbidities (e.g., COPD, coronary artery disease, chronic kidney disease), and those who were treated with vasopressor and corticosteroid medications.

The researchers highlighted pandemic-related factors that may have contributed to the association, including the effects of isolation, stress, less physical activity, unhealthy diet, and weight gain. The results should heighten awareness to screen at-risk individuals for hypertension after COVID-19 to enable earlier identification and treatment for hypertension-related complications. [78]

Long COVID[13]

Some individuals who become infected with COVID-19 may experience long-term symptoms, even after they recover from their initial infection. At least 65 million individuals worldwide are estimated to have post COVID-19 condition (also known as long COVID), with cases increasing daily.

Symptoms differ between individuals, and between adults and children and can be associated with poorer quality of life. More than 200 symptoms have been identified with impacts on multiple organ systems. Symptoms can last from weeks to months. Overall, the most common symptoms include:

- Fatigue
- Shortness of breath or difficulty breathing
- Memory, concentration, or sleep problems
- Persistent cough
- Chest pain
- Muscle aches
- Loss of smell or taste
- Depression or anxiety
- Fever

Most cases of long COVID are in nonhospitalized individuals with mild acute illness, as this population represents the majority of overall COVID-19 cases. Risk factors for developing long COVID may include more severe disease, older age, female sex, and preexisting lung disease. Taking measures to avoid COVID-19 infection is the most effective way to protect against long COVID. [77] [79] [80] [81]

Nayyerabadi et al. (2023) explored whether COVID-19 vaccination in individuals with long COVID could affect their symptoms, immune responses, and viral persistence. The study found that higher proinflammatory responses were associated with long COVID symptoms. However, vaccination helped mitigate symptoms, possibly by decreasing

[13] Refer to Episodes 28, 38, 48, and 71 for additional information on long COVID.

systemic inflammation. Vaccination did not reduce the persistence of viral products that could be involved in perpetuating inflammation through nonclassical monocytes.[14] [82]

Long colds

Vivaldi et al. (2023) found individuals who had an acute respiratory illness but test negative for COVID-19 may experience 'long colds' and a similar burden of lingering symptoms as those with long COVID. Researchers analyzed data from 10,171 UK adults. A total of 1,311 had COVID-19 and 472 had non-COVID-19 acute respiratory infection. Non-COVID-19 respiratory infection included pneumonia, influenza, bronchitis, common cold, etc. Both types of illness were associated with a range of long-term symptoms and decreased health-related quality of life.

Participants with COVID-19 had greater odds of problems with taste, smell, light headedness, and dizziness. Some of the most common symptoms of long cold included coughing, abdominal pain, and diarrhea more than four weeks after the initial infection. Both groups experienced breathlessness and fatigue.

Severity of symptoms following both COVID-19 and non-COVID-19 acute respiratory illnesses were found to be associated with severity of the initial infection. Those who experienced increased symptom severity were more likely to be female, a frontline worker, overweight, socioeconomically disadvantaged, or have comorbidities. The findings suggest there may be long-lasting health impacts following non-COVID acute respiratory infections that are currently going unrecognized. [83]

Risk factors

Some individuals are at higher risk of more severe disease or outcomes from COVID-19 infection, including:

- Older adults (increases with each decade, especially over 60 years)
- Pregnant individuals
- Those who have not received the recommended COVID-19 vaccine doses
- Those with a chronic medical condition, such as asthma (moderate to severe), dementia or other neurologic conditions, diabetes, hypertension, and cardiovascular, cerebrovascular, kidney, respiratory, or liver disease
- Individuals with obesity (BMI of ≥40)
- Individuals who are immunocompromised (e.g., cancer, untreated HIV/AIDS, undergoing chemotherapy, taking oral steroid medications, solid organ or blood stem cell transplant) [84] [85] [86]

Periodontitis and COVID-19[15]

A systematic review and meta-analysis by Al-Maweri et al. (2023) investigated the potential association between periodontitis and COVID-19 and its adverse outcomes. A total of 22 studies involving 92,535 participants from USA, Europe, Asia, the Middle East, and South America were included.

[14] Nonclassical monocytes are white blood cells that can have proinflammatory behaviour and secrete inflammatory cytokines in response to infection.

[15] Refer to Episodes 13 and 31 for additional information on COVID-19 and periodontal disease.

Research has linked periodontal disease to the risk and severity of COVID-19. The findings of the present systematic review support the results of previous systematic reviews. The mechanisms by which periodontitis contributes to COVID-19 adverse outcomes is still unclear. However, many theories have been suggested, such as:

- Aspiration of periodontopathogenic bacteria induces the expression of angiotensin-converting enzyme 2 (ACE-2), a receptor for SARS-CoV-2. This subsequently leads to production of inflammatory cytokines, such as IL-6 and IL-8 in the lower respiratory tract, thus aggravating the response.
- Periopathogenes have been reported to enhance the virulence of SARS-CoV-2 by cleaving its S glycoproteins, a matter that exacerbates COVID-19 complications.
- Chronic inflammation of periodontitis may play a role through triggering systemic inflammation, which aggravates the inflammatory response of many disease processes including COVID-19.
- Similarly, research has found a significant association between periodontal disease and exacerbation of other respiratory conditions, such as pneumonia and COPD.
- SARS-CoV-2 has been detected in periodontal pockets and caries lesions. These sites may act as virus reservoirs, making individuals more prone to COVID-19.

The findings of this study suggest a significant association between poor periodontal health and poor COVID-19 outcomes. However, the results should be interpreted with caution given the heterogeneity across the included studies along with some methodological limitations in some of the studies. Further prospective cohort studies with standardized methodologies are required to further explain the potential association between periodontal diseases and the risk of poor COVID-19 outcomes. [87]

Transmission

SARS-CoV-2 spreads through respiratory droplets and aerosols created from breathing, talking, coughs, and sneezes. It can be transmitted before symptom onset or through those who are asymptomatic. It may also be transmitted through contact with infected respiratory secretions on surfaces and objects. [88]

Rapid antigen tests

Testing is important to determine whether an individual has COVID-19. Currently in Ontario, individuals can access rapid antigen tests through their local public health unit. Healthcare providers across the province can order rapid antigen tests to share with their clients free of charge. [70]

Note: Independent dental hygienists can also access free rapid antigen tests for distribution to their clients through the Provincial Antigen Screening Program (PASP). This voluntary program will be in effect while provincial supplies last and prior to expiry. Please see details in the footnotes below.[16]

[16] Independent dental hygienists who are not currently enrolled in PASP and would like to distribute rapid antigen tests to their clients may register at https://covid-19.ontario.ca/provincial-antigen-screening-program. Ordering will continue through the PPE Supply Portal. For assistance in creating an account, accessing an existing account, or for any questions about orders and shipment, please contact sco.supplies@supplyontario.ca. For more information about the program, visit https://covid-19.ontario.ca/provincial-antigen-screening-program.

Eligible individuals can access COVID-19 PCR testing at assessment centres and certain pharmacies. Eligibility criteria for PCR testing for those with symptoms include:

- Individuals ≥60 years
- Individuals ≥18 years who have at least one condition that puts them at higher risk of severe COVID-19 (e.g., cancer, diabetes, cystic fibrosis, etc.)
- Individuals who are immunocompromised
- Pregnant individuals
- Some individuals are also eligible with or without symptoms [24] [89]

Refer to footnote below for the hyperlink to the full list of eligibility criteria and the PCR testing locator.[17]

Treatment[18]

Treatment for mild COVID-19 is aimed at relieving symptoms and includes:

- Rest
- Fluids
- Pain relievers

Antiviral treatment

Antiviral treatments are available for individuals with symptoms (even if mild) who are at higher risk of severe COVID-19. Most treatments must be taken within the first five days of symptom onset. Refer to footnote below for the hyperlink to the COVID-19 antiviral treatment screener to determine risk of severe COVID-19.[19]

Individuals at higher risk include those who are:

- ≥60 years
- ≥18 years and are immunocompromised
- 18 to 59 years with one or more underlying medical condition(s) (e.g., diabetes, heart or lung disease), or inadequate immunity against COVID-19 from not receiving a full primary series of the COVID-19 vaccine or having received a full primary series but no COVID-19 vaccine or COVID-19 infection within the past six months.

The use of antivirals in children <18 years is not routinely recommended. Exceptions may be made on a case-by-case basis, such as for children who are severely immunocompromised and/or have multiple risk factors. [24]

Paxlovid

Paxlovid (nirmatrelvir, ritonavir) is an oral antiviral medication used to treat mild to moderate COVID-19 in adults (≥18 years) who had a positive SARS-CoV-2 viral test and who are at risk of severe COVID-19, including hospitalization or death. Treatment must begin within five days of the start of symptoms. Paxlovid can be prescribed by a physician, nurse practitioner, or participating pharmacist. Prescriptions can be filled at most pharmacies.

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[17] Eligibility criteria for PCR testing: https://www.ontario.ca/page/covid-19-testing-and-treatment
PCR testing locator: https://www.ontario.ca/assessment-centre-locations/
[18] Refer to Episode 57 for additional information on COVID-19 treatment.
[19] COVID-19 antiviral treatment screener: https://www.ontario.ca/covid-treatment-screener/

Paxlovid consists of two medications packaged together:
- Nirmatrelvir (pink tablet)
- Ritonavir (white tablet)

Dose
Usual dose is two pink nirmatrelvir tablets and one white ritonavir tablet. All three tablets are taken at the same time, twice a day (morning and evening) for five consecutive days.

Some adults with moderate kidney impairment require a lower dose of one pink nirmatrelvir tablet and one white ritonavir tablet taken at the same time, twice a day (morning and evening) for five consecutive days.

Paxlovid has the potential for numerous significant and serious drug interactions when taken with certain medications and may be contraindicated in some individuals. It is important the medical provider know the individual's medications (including natural health products or vitamins), medical conditions, or allergies before prescribing. [90]

Paxlovid is not approved to:
- Treat patients who are hospitalized due to severe or critical COVID-19.
- Prevent COVID-19.
- Be used for longer than five consecutive days.
- Treat children and adolescents <18 years. [90]

Paxlovid and COVID-19 rebound
In the Paxlovid clinical trial, a small number of participants had one or more positive SARS-CoV-2 PCR test results after testing negative, or an increase in the amount of SARS-CoV-2 detected by PCR, after completing their treatment course. This finding was observed in participants administered Paxlovid and in participants given placebo. There was no increased occurrence of hospitalization or death, and there was no evidence that the rebound in detectable viral RNA was the result of SARS-CoV-2 resistance to Paxlovid. [91]

In May 2022, the CDC issued an advisory about COVID-19 rebound after Paxlovid treatment. COVID-19 rebound is characterized by a recurrence of COVID-19 symptoms or a new positive viral test after having tested negative. CDC explained a brief return of symptoms may be part of the natural history of SARS-CoV-2 infection in some individuals, independent of treatment with Paxlovid and regardless of vaccination status. Limited information available from case reports suggests individuals treated with Paxlovid who experience COVID-19 rebound have had mild illness and there were no reports of severe disease. There is currently no evidence that additional treatment is needed with Paxlovid or other anti-SARS-CoV-2 therapies in cases where COVID-19 rebound is suspected. [92]

In January 2023, Health Canada issued a safety brief stating they were aware of cases of COVID-19 rebound reported worldwide following the use of Paxlovid. COVID-19 rebound appears to be generally mild in severity and may be a consequence of the

natural course of SARS-CoV-2 infection in some individuals. It has also been observed following treatment with other SARS-CoV-2 antiviral products and in placebo recipients in COVID-19 treatment clinical studies.

As of January 4, 2023, Health Canada had received 23 Canadian case reports of potential COVID-19 rebound with the use of Paxlovid in the Canada Vigilance database. Health Canada reviewed these case reports as well as findings from clinical trials and observational studies. Overall, there is no clear evidence to indicate COVID-19 rebound is Paxlovid-induced. The available information also suggests COVID-19 rebound does not change the benefits of Paxlovid, which include a reduction in hospitalization or death. Paxlovid use continues to be a safe and effective treatment for COVID-19 in outpatients at high-risk for progression to severe disease. At this time, it is not recommended that treatment be extended or repeated.

Healthcare professionals are encouraged to report adverse reactions suspected of being associated with COVID-19 treatments to the Canada Vigilance Program.[20] Health Canada will continue to monitor the safety of Paxlovid and will take appropriate action should new health risks be identified. [93]

Remdesivir
Remdesivir (Veklury) is an antiviral medication that must be taken intravenously at designated clinics. Remdesivir treatment must begin within seven days of the start of symptoms and requires a referral from a physician or nurse practitioner. Remdesivir is only prescribed to individuals who cannot take Paxlovid because they are on certain medications or have certain medical conditions. [24] [94]

Evusheld
Evusheld is a monoclonal antibody therapy that has been used to prevent COVID-19 in select individuals who are immunocompromised since April 2022. Evidence has indicated Evusheld is likely ineffective against multiple variants currently circulating in the province. As a result, Evusheld is no longer routinely recommended in Ontario for either the prevention or treatment of COVID-19. Individuals who have received Evusheld in the past, cannot rely on it for protection against COVID-19. [24]

Prevention
COVID-19 vaccines[21] help reduce the risks of severe illness, hospitalization, and death caused from COVID-19. In September 2023, Health Canada approved updated mRNA vaccines from Moderna and Pfizer-BioNTech that target the Omicron subvariant XBB.1.5, but are otherwise identical to previous mRNA vaccines. The latest formulations will protect better against currently circulating SARS-CoV-2 strains than the previous bivalent formulation. Both updated vaccines are approved for use in individuals aged six months and older. [95] [96]

[20] Report adverse reactions suspected of being associated with COVID-19 treatments to the Canada Vigilance Program here: https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html
[21] Refer to Episodes 15, 28, 34, 39, 40, 52, 56, and 71 for additional information on COVID-19 vaccines.

Fall 2023 Ministry of Health COVID-19 Vaccine Guidance
On October 6, 2023, the Ontario Ministry of Health released an update to its COVID-19 Vaccine Guidance to include recommendations for both Moderna Spikevax XBB 1.5 and Pfizer Comirnaty Omicron XBB 1.5 vaccines. The ministry strongly recommends individuals at high-risk from COVID-19, including those with a potential for greater impact from infection, receive a dose of the XBB vaccine this fall, if it has been six months since their last COVID-19 vaccine dose or confirmed SARS-CoV-2 infection.

Healthcare providers should be aware of guidance updates, including:

- Change in terminology to align with NACI and the product monographs. The Ministry of Health is moving away from using the terms 'primary series' and 'booster dose(s)' and instead referring to an individual's vaccination status as 'not previously vaccinated' or 'previously vaccinated'.
- Update on XBB vaccine schedule recommendations is based on an individual's COVID-19 immunization history and health status.
- Unvaccinated individuals 12-29 years of age may receive either Pfizer or Moderna XBB vaccine.
- For individuals who are not able or willing to receive an mRNA COVID-19 vaccine, NACI recommends offering the Novavax COVID-19 vaccine. Health Canada is currently reviewing a submission from Novavax for its COVID-19 vaccine targeting the Omicron XBB.1.5 subvariant for individuals ≥12 years. [97]

All Ontarians six months and older can receive their next COVID-19 dose if it has been the recommended six months since their last dose or confirmed COVID-19 infection. Ontarians are encouraged to speak with a medical professional to help determine their appropriate vaccination schedule. [70]

Seasonality of COVID-19
As COVID-19 becomes endemic, infecting populations in successive waves, scientists are trying to determine whether the timing of these surges will ever be predictable. Knowledge of seasonal surges is crucial for healthcare and public health decision-making. According to a study by Townsend et al. (2023), the virus will likely settle into a seasonal rhythm similar to influenza, becoming most active during the colder months in northern climates and subsiding in summer. The researchers predicted future seasonality using historic infection data from coronaviruses with known seasonal patterns that are often attributed to causing colds. [98]

mRNA research
mRNA was first discovered in the 1960s by researchers François Jacob and Jacques Monod who were recognized with the Nobel Prize in Physiology or Medicine for their discovery. Since then, scientists have been studying mRNA given its potential to prevent and treat a wide range of diseases. Much progress was made in the early 2000s after years of continued research into mRNA, refinements, and technological advances. Independently, Pieter Cullis and Robert Langer developed lipid nanoparticles to deliver therapies and vaccines, a key enabler for mRNA technology. Research partners Katalin Karikó and Drew Weissman were able to engineer mRNA in a way that could get into cells without triggering the body's defenses. That breakthrough enabled

continued scientific advances that led to the development and authorization of the first mRNA vaccines for COVID-19 in 2020. [99] [100]

Fitzpatrick et al. (2022) estimated through to the end of November 2022, vaccines prevented over 3 million deaths and 18 million hospitalizations and saved more than $1 trillion in the US alone. [101] Worldwide, Watson et al. (2022) estimated 19.8 million out of a potential 31.4 million deaths were prevented in the first year after vaccines were introduced (December 2020 to December 2021), representing a global reduction of 63% in total deaths. [102]

Nobel Prize for mRNA
On October 2, 2023, biochemist Katalin Karikó and immunologist Drew Weissman won the Nobel Prize in Physiology or Medicine for discoveries that enabled the development of mRNA vaccines against COVID-19. The success with mRNA vaccines against COVID-19 comes from decades of previous research. [103]

New mRNA research
The success of COVID-19 mRNA vaccines generated an influx of funds to expand mRNA research and technology in areas such as infectious diseases, cancers, and rare genetic disorders. Current research is investigating:

- Vaccines against influenza, RSV, malaria, HIV, Zika virus, Epstein-Barr virus, cytomegalovirus, herpes, norovirus, Lyme disease, Nipah virus, *C. difficile*, leptospirosis, hepatitis C, tuberculosis, shingles, acne, chlamydia, and mpox virus.[22]
- Personalized cancer vaccines that train the immune system to fight cancer.
- Ways to improve delivery of gene-editing technologies.
- Therapies for rare diseases, such as cystic fibrosis and propionic acidemia (a rare metabolic disorder). [104] [105] [106]

In October 2023, Moderna and Pfizer-BioNTech separately announced positive results from their phase 1 and 2 trials of mRNA-based combination vaccines against influenza and COVID-19. Phase 3 trials are planned in the coming months. [107] [108]

Vaccine hesitancy[23]
In 2019, the WHO compiled a list of ten health threats to highlight their dangers to the global community. The ten threats were selected because of their potential to cause significant illness, death, societal disruption, and public health impact as well as considering their likelihood of occurring. The list included vaccine hesitancy and a global influenza pandemic.

Vaccine hesitancy is the reluctance or refusal to vaccinate despite vaccine availability. Vaccine hesitancy threatens to reverse progress made in tackling vaccine-preventable diseases. Vaccination is one of the most cost-effective ways of avoiding disease. Currently, it prevents 2-3 million deaths a year, and a further 1.5 million could be avoided if global vaccination coverage improved. [109]

[22] Refer to Episode 65 for discussion on mpox.
[23] Refer to Episode 40 for discussion on vaccine hesitancy.

The National Foundation for Infectious Diseases commissioned an annual survey to better understand beliefs about influenza, COVID-19, RSV, and pneumococcal disease, as well as attitudes and practices around vaccination. Overall, the 2023 survey found many adults in the US underestimate the seriousness of these respiratory diseases. As a result, many do not plan to get vaccinated and are not confident in the safety and effectiveness of vaccines. These findings underscore the need to raise awareness of the benefits of vaccines and highlight the importance of strong vaccine recommendations from healthcare professionals. [110]

Protection from respiratory viruses

The use of multiple prevention strategies provides the best protection against respiratory viruses for oneself and others. Prevention strategies include:

- Staying up to date with vaccinations (e.g., COVID-19, influenza, RSV if eligible)
- Consider wearing a tight-fitting, well-constructed mask in indoor public settings, especially if at higher risk of severe infection.
- Following any requirements for masking in hospitals, long-term care homes, other congregate living settings, and other healthcare spaces.
- Staying home when ill and wearing a tight-fitting, well constructed mask until day 10 from symptom onset in all public settings.
- Washing hands often (soap and water, or hand sanitizer if soap and water is not available).
- Covering coughs and sneezes with a tissue and discard immediately or cough into the upper sleeve if a tissue is not available.
- Cleaning high touch surfaces regularly.
- Optimizing indoor air quality (fresh outdoor air into rooms, improving air flow, etc.).
- Speaking with a medical provider about antiviral treatment if at high risk of severe illness. [68] [111] [112]

New research

Gargling and nasal rinsing with saltwater several times a day appeared to be associated with significantly lower COVID-19 hospitalization rates in a small, randomized, double-blind, controlled study. The findings were presented in a poster at the November 2023 American College of Allergy, Asthma and Immunology (ACAAI) Annual Meeting.

Adults aged 18-65 years who tested positive for SARS-CoV-2 between 2020 and 2022 were randomly selected to use low- or high-dose saltwater regimens for 14 days. To be included in the study, 14 days had to have elapsed since the onset of any COVID-19 symptoms. The low dose was 2.13 grams of salt dissolved in 8 ounces of warm water, and the high dose was 6 grams. Participants gargled the saltwater and used it as a nasal rinse for 5 minutes four times a day.

Low- and high- saline regimens were associated with similar frequency and duration of COVID-19 symptoms. Both saline regimens were associated with lower hospitalization rates compared to the control population. If confirmed, this simple intervention could be beneficial for individuals with COVID-19, particularly in low resource settings. [113] [114]

Take home messages:

- Staying up to date on vaccinations continues to be the best way for individuals to stay healthy during respiratory virus season and to avoid hospitalization.
- It is important to be aware of the links between periodontal diseases and respiratory conditions.
- Canada has a significant respiratory virus season. It is essential for oral health professionals to be cognizant and take appropriate precautions as respiratory viruses can be a workplace hazard in oral healthcare.

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