

Episode #28 – COVID-19: What We Know So Far January 15, 2021

Overview

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the coronavirus responsible for the coronavirus disease 2019 (COVID-19), which was first observed in China in December 2019. On March 11, 2020, the World Health Organization (WHO) declared the situation a pandemic. Since the emergence of SARS-CoV-2, the virus has caused more than 88,000,000 infections and 1,900,000 deaths worldwide, with 223 countries, areas, or territories experiencing cases. [1] [2]

Coronaviruses are enveloped, single-stranded RNA viruses whose surface is covered by a halo of protein spikes, or “corona.” Other coronaviruses that have caused significant and lethal outbreaks in the past 20 years include SARS-CoV-1 and MERS-CoV that caused severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), respectively. SARS-CoV-2 is an enveloped β-coronavirus, with a genetic sequence very similar to SARS-CoV-1 (80%). The viral envelope is coated by spike glycoprotein, envelope, and membrane proteins. Host cell binding and entry are mediated by the spike protein. [3] [4]

To induce COVID-19, the spike 1 (S1) subunit attaches to angiotensin-converting enzyme-2 (ACE2) receptors on cellular surfaces such as the human respiratory tract. After binding to ACE2, the spike 2 (S2) subunit fuses the viral particle to the host cell membrane and releases its RNA into the cell, initiating viral replication. High concentrations of viral copies induce host cell lysis and the spread of infectious particles. During the infection, the immune response is activated to produce antibodies by plasma cells (activated B cells) specific to spike proteins (or other viral structural proteins) from SARS-CoV-2. Antibodies specific to S1 or S2 could neutralize and block the attachment and fusion of SARS-CoV-2 to the host cell, before its replication within the lungs and other tissue, including the gastrointestinal tract. Cleavage of the spike protein is an essential step for severe acute respiratory syndrome infection. Antibodies that bind to the spike protein interfere with this cleavage, inhibiting the fusion and the entry of SARS-CoV-2 into the host cell. Therefore, neutralizing antibodies play an important role in viral clearance. The production of these antibodies specific to S1 or S2 could help to protect against future COVID-19 infection. [5]

Asymptomatic and presymptomatic transmission

Many COVID-19 infections are asymptomatic or only mildly symptomatic, and SARS-CoV-2 is frequently transmitted by infected individuals before they develop symptoms. To a large extent, individuals with COVID-19 are most contagious 1–2 days prior to the

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onset of symptoms. One reason may be the ability of the virus to dampen the initial interferon-dependent innate immune response, which ordinarily coincides with symptom onset in many viral infections. Asymptomatic or presymptomatic transmission has complicated efforts to identify cases and prevent spread. Tracing chains of transmission in well-defined COVID-19 outbreaks in regions without previous widespread community transmission has provided direct evidence of presymptomatic and asymptomatic viral spread. Asymptomatic individuals often shed large quantities of virus in their respiratory secretions, and modelling studies have determined the usual incubation period of COVID-19 to exceed the serial interval between symptom onset in index and secondary cases, indicative of presymptomatic transmission. [6]

Johansson et al. (2021) used a decision analytical model to assess the level of transmission of SARS-CoV-2 from presymptomatic, asymptomatic, and symptomatic individuals. Using baseline assumptions for the model, the authors determined that 59% of all transmission came from asymptomatic transmission, comprising 35% from presymptomatic individuals and 24% from asymptomatic individuals. The study reinforces the importance of public health measures to reduce the risk of transmission from people with infection who are presymptomatic, asymptomatic, and symptomatic. [7]

Superspreading events

As observed during the SARS and MERS epidemics, episodic “superspreader events” are often associated with explosive COVID-19 transmission. Epidemiologists estimate that as few as 10% of infected persons are responsible for 80% of SARS-CoV-2 transmission, suggesting that recognition and prevention of events at high-risk for superspreading can have a major impact on limiting the epidemic. Analysis of superspreader events in settings as diverse as choir rehearsals, call centers, nightclubs, or research conferences has suggested common features to be avoided, i.e., closed poorly-ventilated indoor spaces, crowds, and close contact (the “three C’s”). A synthesis of current data suggests that exposure risk can be estimated on the basis of ventilation, density, face coverings, exposure duration, and activity. [6]

Symptoms of COVID-19

Symptoms include:

- Fever (temperature of 37.8°C/100.0°F or greater)
- Cough (that is new or worsening [e.g., continuous, more than usual if chronic cough] including croup [barking cough, making a whistling noise when breathing]). Not related to other known causes or conditions (e.g., chronic obstructive pulmonary disease)
- Shortness of breath (dyspnea, out of breath, unable to breathe deeply, wheeze, that is worse than usual if chronically short of breath). Not related to other known causes or conditions (e.g., chronic heart failure, asthma, chronic obstructive pulmonary disease)
- Sore throat (painful swallowing or difficulty swallowing). Not related to other known causes or conditions (e.g., post nasal drip, gastroesophageal reflux)
- Rhinorrhea (runny nose). Not related to other known causes or conditions (e.g., returning inside from the cold, chronic sinusitis unchanged from baseline)

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- Nasal congestion (stuffy nose). Not related to other known causes or conditions (e.g., seasonal allergies)
- New olfactory or taste disorder (decrease or loss of smell or taste). Not related to other known causes or conditions (e.g., nasal polyps, allergies, neurological disorders)
- Nausea and/or vomiting. Not related to other known causes or conditions (e.g., transient vomiting due to anxiety in children, chronic vestibular dysfunction)
- Diarrhea. Not related to other known causes or conditions (e.g., irritable bowel syndrome, inflammatory bowel disease, side effect of medication)
- Abdominal pain that is persistent or ongoing. Not related to other known causes or conditions (e.g., menstrual cramps, gastroesophageal reflux disease)
- Chills
- Headache that is new and persistent, unusual, unexplained, or long-lasting. Not related to other known causes or conditions (e.g., tension-type headaches, chronic migraines)
- Conjunctivitis (pink eye). Not related to other known causes or conditions (e.g., blepharitis, recurrent styes)
- Fatigue, lethargy, or malaise (general feeling of being unwell, lack of energy, extreme tiredness) that is unusual or unexplained. Not related to other known causes or conditions (e.g., depression, insomnia, thyroid dysfunction, anemia, malignancy)
- Myalgias (muscle aches and pain) that are unexplained, unusual, or long-lasting. Not related to other known causes or conditions (e.g., fibromyalgia)
- Decreased or lack of appetite. For young children and not related to other known causes or conditions (e.g., anxiety, constipation) [8]

Older adults and COVID-19

Some adults, 65 years of age or older, may experience delirium, unexplained or increased number of falls, acute functional decline, and/or worsening of chronic conditions. [8]

Kennedy et al. (2020) investigated how frequently older adults (aged ≥65 years) with COVID-19 had presented to the emergency department with delirium. In their cohort study of 817 older emergency department patients with COVID-19, 28% had delirium at presentation, and delirium was the sixth most common of all presenting symptoms and signs. The top six symptoms at presentation were fever (56%), shortness of breath (51%), cough (50%), hypoxia (40%), weakness (30%), and delirium (28%). Among patients with delirium, 16% presented with delirium as a primary symptom and 37% had no typical COVID-19 symptoms or signs, such as cough or fever.

The authors concluded that delirium was common and often was seen without other typical symptoms or signs. In addition, delirium was associated with poor hospital outcomes and death. These findings suggest the clinical importance of including delirium on checklists of presenting signs and symptoms of COVID-19 that guide screening, testing, and evaluation. [9]

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Children and COVID-19

COVID-19 is less prevalent in children as compared to adults and children infected with SARS-CoV-2 experience less severe symptoms. Commonly reported symptoms in children include abdominal symptoms and skin changes or rash. Children under one year of age and with underlying conditions may experience more severe illness than other children, but the case fatality rate for children is much lower than for adults. In very rare cases, children with COVID-19 have developed pediatric multisystem inflammatory syndrome in children (MIS-C), which can include symptoms of fever and inflammation and can affect cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, or neurological systems. Children who do experience more severe symptoms have a shorter hospital stay, decreased requirement for mechanical ventilation, and decreased mortality compared to adults. [3]

Preliminary case definition of MIS-C[1]

WHO has developed a preliminary case definition for multisystem inflammatory disorder in children and adolescents. The preliminary case definition reflects the clinical and laboratory features observed in children reported to date, and serves to identify suspected or confirmed cases both for the purpose of providing treatment and for provisional reporting and surveillance.

Preliminary case definition:

Children and adolescents 0-19 years of age with fever ≥3 days who have two of the following:

- Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet)
- Hypotension or shock
- Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP)
- Evidence of coagulopathy (by PT, PTT, elevated d-Dimers)
- Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain)

And

- Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin

And

- No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes

And

- Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19. [10]

[1] Consider this syndrome in children with features of typical or atypical Kawasaki disease or toxic shock syndrome. WHO will revise the case definition as more data become available.

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COVID-19 symptom progression

Larsen et al. (2020) hypothesized the order of symptom occurrence of COVID-19 to help healthcare professionals more quickly distinguish COVID-19 from other respiratory diseases. They determined the most likely path of seven common symptoms are fever, cough, sore throat, headache, myalgia, nausea/vomiting, and diarrhea. The most likely order of symptoms in influenza were cough, myalgia, headache, sore throat, fever, diarrhea, and nausea/vomiting.[2] [11]

Key features of influenza, SARS-CoV-2 and other common respiratory viruses[3]

Key Features	Seasonal Influenza	SARS-CoV-2 (COVID-19)	Respiratory Syncytial Virus (RSV)	Rhinovirus
Most common symptoms	Sudden onset of fever, cough, chills, headache, fatigue, sore throat, runny or stuffy nose, muscle pain or body aches	Similar to influenza with the possibility of other symptoms, including loss of taste and smell	Similar to influenza	Runny nose, sneezing, cough, sore throat, muscle pain, fatigue, no or mild fever
More severe manifestation/ complications	Pneumonia, worsening of underlying medical conditions, sepsis, cardiac involvement, neurologic involvement, death	Pneumonia, sepsis, blood clots, cardiac involvement, neurologic involvement, renal involvement, multisystem inflammatory syndrome in children (MIS-C), death	Pneumonia, bronchiolitis, death	Lower respiratory tract infection (pneumonia, bronchiolitis) in infants, bronchitis
Signs and symptoms of these illnesses can be very similar and therefore cannot be diagnosed without laboratory testing. [12]				

Disease severity

The severity of COVID-19 and range of symptoms can vary from person to person, with some people experiencing no symptoms or very mild symptoms. Some more serious manifestations of illness may be due to an immune response to SARS-CoV-2 rather than due to infection. In some patients an intense immune response results in a hyper-inflammatory reaction that can result in more severe outcomes. Advanced age, obesity, smoking, immunosuppression, and pre-existing conditions such as diabetes, hypertension, heart disease, or cancer increases the risk of requiring hospitalization or dying from COVID-19. Some groups may also be disproportionately affected by COVID-19 as a result of existing health inequities related to socioeconomic factors.

Research is ongoing to help explain the relationship between the viral load (the quantity of viral particles per unit of bodily fluid in the infected person) and severity of disease. Patients with a higher viral load appear to experience more severe symptoms

[2] Refer to Episode #16 – FAQs for more information on influenza versus COVID-19

[3] Key features of influenza, SARS-CoV-2 and Other Common Respiratory Viruses, Public Health Ontario, September 30, 2020 https://www.publichealthontario.ca/-/media/documents/ncov/ipac/2020/09/key-features-influenza-covid-19-respiratory-viruses.pdf?la=en

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and shed more virus over a longer timeframe than mild cases and a higher viral load has been found to be associated with a higher rate of mortality rate among patients with COVID-19. [3]

Duration of illness and long-term sequelae

The duration of illness ranges from about two weeks for mild cases to between three and six weeks in severe to critical cases. Long-term sequelae that persist beyond six weeks have been observed in some patients. Age, chronic health conditions, and obesity have been found to be significant predictors of persistent symptoms and those who have been hospitalized may experience symptoms for longer. Persistent symptoms may include fatigue, cough, breathing difficulties, headache, and joint pain. Some people have also suffered damage to the heart muscle, scarring of the alveoli, endocrinological and metabolic dysfunction, psychiatric problems with cognitive deficits, strokes, and seizures. Children with MIS-C may experience long-term sequelae as well. [3]

Additional long-term sequelae that may be anticipated based on knowledge of SARS and MERS include anxiety, cardiovascular system abnormalities, depression, glucose metabolism disorders, hyperlipidemia, lipid metabolism dysregulation, post-traumatic stress disorder, and reduced lung capacity. There is some evidence that olfactory dysfunction (e.g., dysosmia) and gustatory dysfunction (e.g., dysgeusia) are relatively common long-term sequelae associated with COVID-19 infection. [13]

Stavem et al. (2020) conducted a cohort study to assess symptoms and their determinants 1.5 to 6 months after symptom onset in non-hospitalized individuals with confirmed COVID-19. The authors found a significant amount of symptom persistence such as dyspnea and disturbed or loss of taste and smell. Symptom persistence was associated with more comorbidities and number of initial COVID-19 symptoms. Most patients were symptom-free at 1.5 to 6 months. [14]

Lechien et al. (2021) investigated the prevalence and recovery of olfactory dysfunction in patients with confirmed COVID-19 according to disease severity. The study evaluated 2,581 ambulatory and hospitalized patients with COVID-19 identified at 18 European hospitals from March 22 to June 3, 2020. Characteristics of olfactory dysfunction that were assessed included hyposmia[4], anosmia[5], phantosmia[6], cacosmia[7], and aroma dysfunction. In total, 2,194 patients (85.0%) had mild disease, 110 (4.3%) had moderate disease, and 277 (10.7%) had severe-to-critical COVID-19. The authors found that olfactory dysfunction was more prevalent in mild COVID-19 forms (85.9%) than in moderate-to-critical forms (11.4%). At 2 months follow-up, 75% to 85% of patients recovered olfaction. Six months post-infection, olfactory dysfunction disappeared in 95% of patients. The main hypothesis underlying the higher prevalence of anosmia in mild COVID-19 was that milder cases develop a more robust local immune response to

[4] Hyposmia – decreased sense of smell or a decreased ability to detect odours
[5] Anosmia – complete loss of the sense of smell
[6] Phantosmia – an olfactory hallucination where smells are detected that are not present
[7] Cacosmia – hallucination or illusion of an unpleasant smell

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infection. The inflammation associated with that response may lead to stronger impairment of olfactory cells. [15]

Take home message
Research findings by Stavem et al. (2020) and Lechien et al. (2021) may be used by clinicians to provide reassurance to patients who may be experiencing persistent dyspnea or disturbed/loss of taste and smell symptoms.

Huang et al. (2021) investigated the long-term consequences of COVID-19 in patients after hospital discharge and identified the potential risk factors, including disease severity, associated with these consequences. Researchers examined data from 1,733 patients discharged from a Wuhan hospital from January 7 to May 29, 2020 and followed from June 16 to September 3, 2020. Patients were given physical examinations, interviewed about their quality of life, did a 6-minute walking test, and had blood drawn. Some patients also underwent pulmonary function tests and high-resolution chest CTs. Results indicated that 76% of patients reported at least one symptom at follow-up and a higher percentage was observed in women than men (81% vs. 73%). Fatigue or muscle weakness were by far the most common symptoms (63%), followed by sleep difficulties (26%), and 23% of patients reported anxiety or depression. Patients who were more severely ill during their hospital stay had more severe impaired pulmonary diffusion capacities and abnormal chest imaging manifestations. These results support that those with severe disease need post-discharge care. Longer follow-up studies in a larger population are necessary to understand the full spectrum of health consequences from COVID-19. [16]

Routes of transmission
SARS-CoV-2 infects a host cell by binding to ACE2 receptors that are present on tissues throughout the body including in epithelial cells of the airway, lungs, intestines, kidneys, blood vessels, and oral cavity. The virus replicates predominantly in the tissues of the upper respiratory tract. SARS-CoV-2 is primarily transmitted via prolonged unprotected close contact (<2 m) with an infected person. The vast majority of COVID-19 outbreaks have taken place indoors and are most often associated with close contacts in the home environment, or other indoor spaces where there is a high density of people and an extended period of contact in a poorly ventilated space. Most transmission appears to be due to exposure to the respiratory droplets and aerosols of an infected person. Other routes (e.g., fomites) may be possible but are not considered to be major routes of transmission. [3] [17] [18]

Relatively uncommon routes of transmission of SARS-CoV-2 include conjunctival, vertical (intrauterine), fecal-oral, and zoonotic. While these routes of transmission are possible, their contribution to the epidemiology of COVID-19 is unclear. Routes of transmission that are theoretically possible due to the detection of viral RNA, but that are very unlikely, are sexual transmission (via semen and vaginal secretions); bloodborne transmission (blood products, organ transplant); transmission through breast milk; transmission through urine; food-borne transmission; and transmission through contaminated wastewater. [19]

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Period of infectiousness
An infected person can transmit the virus to others both before they show any symptoms and when they are symptomatic. Pre-symptomatic persons can potentially infect others from one to about three days before symptom onset. Peak infectiousness is thought to occur about one day before symptom onset. The mean incubation period (time between exposure to the virus and the appearance of symptoms) has been estimated to be around five days, with modelling indicating a range of about two to 11 days. [3]

Treatment of COVID-19
Although global efforts to identify effective interventions for the prevention and treatment of COVID-19 have resulted in thousands of trials completed or underway, effective treatment remains limited.

Siemieniuk et al. (2020) created a living systematic review and network meta-analysis to compare drug treatments for COVID-19. The latest version of this study, updated on December 17, 2020, found that corticosteroids probably reduce mortality and mechanical ventilation in patients with COVID-19 compared with standard care, whereas azithromycin, hydroxychloroquine, interferon-beta, and tocilizumab may not reduce either. Whether or not remdesivir confers any patient-important benefit remains uncertain. The researchers noted that their article will be updated to reflect emerging evidence and updates may occur for up to two years from the date of original publication of July 30, 2020. [20]

Postinfection immunity
Understanding whether postinfection immunity exists, how long it lasts, and the degree to which it may prevent symptomatic reinfection or reduce its severity has major implications for the SARS-CoV-2 pandemic. Despite more than 88 million people infected worldwide and widespread ongoing transmission, reported reinfections with SARS-CoV-2 have been rare, occurring mostly after mild or asymptomatic primary infection, which suggests that SARS-CoV-2 infection provides some immunity against reinfection in most people.

Ongoing research has provided some evidence of postinfection immunity. For example, Figueiredo-Campos et al. (2020) conducted a cross-sectional study to determine seroprevalence of antibodies against SARS-CoV-2. The researchers monitored the antibody levels of over 300 patients hospitalized with COVID-19 and healthcare workers, 2,500 University of Lisbon staff, and 198 volunteers post-COVID-19 infection. The results of this 6 months study demonstrated a classic pattern with a rapid increase of antibody levels within the first three weeks after COVID-19 symptoms and a reduction to intermediate levels thereafter. In the early response phase, on average men produced more antibodies than women, but levels equilibrated during the resolution phase and were similar between the sexes in the months after SARS-CoV-2 infection. In the acute phase of the immune response, higher antibody levels in persons with more severe disease was observed. The results also indicated that age was not a confounding factor for the production of antibodies, as no significant differences were

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observed between age groups. Generally, 90% of study participants had detectable antibodies up to 7 months post contracting COVID-19.

The research team also analyzed the neutralizing capacity of the antibodies produced by the patients and volunteers. Although they observed a reduction in the levels of antibodies over time, the results of the neutralizing assays showed a robust neutralization activity for up to the seventh month post-infection in a large proportion of previously virus-positive screened research participants. The authors concluded that since the SARS-CoV-2 response observed in their study was in line with well-known and detailed studied immune responses resulting in lymphocyte memory, it is very likely that SARS-CoV-2 protective immunity, reducing disease severity, will last for at least a few years. [21]

Lumley et al. (2020) conducted a study covering a 30-week period from April to November 2020 with 12,180 healthcare workers employed at Oxford University Hospitals. The healthcare workers were tested for antibodies to the virus to determine who had been previously infected. The researchers then followed whether staff who had been infected before had the same number of new COVID-19 infections as those who had not been infected before.

During the study, 89 of 11,052 staff without antibodies developed a new infection with symptoms. None of the 1,246 staff with antibodies developed a symptomatic infection. Staff with antibodies were also less likely to test positive for COVID-19 without symptoms, 76 staff without antibodies tested positive compared to just three with antibodies. The three healthcare workers with antibodies who tested positive for the virus were all well and did not develop symptoms of COVID-19 again.

The authors suggested that the results indicate that most people are unlikely to get COVID-19 again if they have already had it in the previous six months. The authors noted that they will continue to collect data for the study, with the goal of verifying how long protection from re-infection might last. [22]

Dan et al. (2021) analyzed multiple compartments of circulating immune memory to SARS-CoV-2 in 254 samples from 188 COVID-19 cases, including 43 samples at ≥ 6 months post-infection. The researchers measured antibodies, memory B cells, helper T cells and killer T cells. They found that virus-specific antibodies do persist in the bloodstream months after infection. Immunoglobulin G (IgG) to the Spike protein was relatively stable over 6+ months. Spike-specific memory B cells were more abundant at 6 months than at 1 month post symptom onset. SARS-CoV-2-specific $CD4^+$ T cells and $CD8^+$ T cells declined with a half-life of 3-5 months. They concluded that their data showed immune memory in at least three immunological compartments was measurable in ~95% of patients 5 to 8 months post-symptom onset, indicating that durable immunity against secondary COVID-19 is a possibility in most individuals.

The team cautioned that protective immunity did vary dramatically from person to person. In fact, the researchers saw a 100-fold range in the magnitude of immune memory. People with a weak immune memory may be vulnerable to a case of recurrent

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COVID-19 in the future, or they may be more likely to infect others. The researchers will continue to analyze samples from patients with COVID-19 in the coming months and hope to track their responses 12 to 18 months after the onset of symptoms. [23]

Take home messages
In general, most people infected with SARS-CoV-2 will have protective immunity against circulating viruses for many months after initial infection. However, how much protection still remains to be established.

COVID-19 vaccines[8]
To date, Health Canada has approved two vaccines Pfizer-BioNTech COVID-19 vaccine (Tozinameran or BNT162b2) and Moderna COVID-19 vaccine (mRNA-1273). Both are messenger RNA (mRNA) vaccines. mRNA vaccines are a new type vaccine. However, researchers have been studying and working with mRNA vaccines for decades. For example, they have been studied for flu, Zika, rabies and cytomegalovirus. Researchers have also used mRNA to trigger the immune system to target certain cancer cells. mRNA vaccines can be developed faster than traditional methods because they are made in a lab using materials that are easily available. [24] [25] [26] [27] [28]

Traditional vaccines typically involve injection with antigens such as purified proteins or polysaccharides or inactivated/attenuated viruses. mRNA vaccines work differently since they do not contain antigens. Instead, they contain a blueprint for the antigen in the form of genetic material, mRNA. In the case of Pfizer's and Moderna's vaccines, the mRNA provides the genetic information to synthesize the spike protein that the SARS-CoV-2 virus uses to attach to and infect human cells. Each type of vaccine is packaged in proprietary lipid nanoparticles to protect the mRNA from rapid degradation, and the nanoparticles serve as an adjuvant to attract immune cells to the site of injection. When injected into muscle, the lipid nanoparticles containing the mRNA inside are taken into the myocytes (muscle cells), where the cytoplasmic ribosomes detect and decode the mRNA resulting in the production of the spike protein antigen. It should be noted that the mRNA does not enter the nucleus, where the genetic information (DNA) of a cell is located, and cannot be reproduced or integrated into the DNA. The antigen is exported to the myocyte cell surface where the immune system's antigen presenting cells detect the protein, ingest it, and take it to regional lymph nodes where interactions with T cells and B cells results in antibodies, T cell–mediated immunity, and generation of immune memory T cells and B cells. A particular subset of T cells, cytotoxic or killer T cells, destroy cells that have been infected by a pathogen. [28]

The Pfizer-BioNTech COVID-19 vaccine is approved for people who are 16 years of age and older. The Moderna COVID-19 vaccine is approved for people who are 18 years of age and older. Safety and effectiveness in people younger than the stated ages have not yet been established. The vaccines are given by an injection into the muscle of the arm. Both require two doses, a single dose and then a second dose 21 days or 28 days later for the Pfizer-BioNTech vaccine and the Moderna vaccine, respectively. Both

[8] Refer to Episode #15 – Vaccines and SARS-CoV-2 for more information on vaccines

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vaccines were reported to produce about 95% protection against COVID-19 in their final analyses. [26] [27] [28]

It is important to note that recipients of the vaccine still need to follow public health guidance (e.g., masking[9], distancing, etc.) after receiving the vaccine because there is insufficient evidence at this time on the effectiveness of COVID-19 vaccines in preventing asymptomatic infection and reducing transmission of SARS-CoV-2. [29]

Vaccine side effects

Similar to medications and other vaccines, the Pfizer-BioNTech and Moderna COVID-19 vaccines can cause side effects. During the clinical trials, common side effects similar to other vaccines were reported (e.g., redness and pain at the injection site). These side effects do not pose a health risk. The most frequent adverse reactions were mild or moderate and resolved within a few days after vaccination. No major safety concerns were reported in the data submitted to Health Canada. [29]

Pfizer-BioNTech and Moderna mRNA COVID-19 vaccines side effects[10]

Vaccine	**Very common side effects** (may affect more than 1 in 10 people)	**Uncommon side effects** (may affect up to 1 in 100 people)
Pfizer-BioNTech	Pain at injection site Fatigue Headache Muscle pain Chills Joint pain Fever Diarrhea	Axillary swelling and tenderness (enlarged lymph nodes)
Moderna	Pain at injection site Fatigue Headache Myalgia Chills Nausea/Vomiting Axillary swelling and tenderness (enlarged lymph nodes)	Fever

COVID-19 vaccine safety

As of January 1, 2021, 115,072 total doses of COVID-19 vaccines have been administered across Canada, with 9 adverse events reported. Adverse events can range from common mild events such as soreness at the site of injection or a slight fever, to more rare serious events, such as a severe allergic reaction. Canada has a robust vaccine safety monitoring system in place and all serious events will be investigated. Four of the nine adverse events following immunization reports (AEFIs)

[9] Refer to Episode #25 – Community Use of Face Masks for more information on face covering to help prevent transmission of COVID-19

[10] COVID-19 About Vaccines Version 2.0, Ontario Ministry of Health, January 6, 2021 http://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/vaccine/COVID-19_about_vaccines.pdf

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were non-serious. The most frequently reported non-serious adverse events were vaccination site reactions, nausea, paraesthesia, pruritis, and urticaria. Five of the nine AEFIs were considered serious and will continue to be investigated. The 9 individual AEFI reports represent 9 people who experienced one or more adverse events. Among the 9 AEFI reports, 5 were identified as serious; the adverse events included anaphylaxis (2), headache (1), severe allergic reaction (1), facial paralysis (1), chills (1), syncope (1), pain in extremity (1). No deaths were reported and there have been no vaccine safety issues identified to date.[11] [30] [31]

Contraindications for COVID-19 vaccine

The authorized COVID-19 vaccine is contraindicated in individuals with a history of anaphylaxis after previous administration of the vaccine. Vaccine is also contraindicated in persons with proven immediate or anaphylactic hypersensitivity to any component of the vaccine or its packaging. Clinical trials of the authorized COVID-19 vaccines excluded individuals with a history of severe adverse reaction associated with a vaccine and/or severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine. Individuals with a history of severe allergic reaction to a component of the COVID-19 vaccine should not receive the COVID-19 vaccine. [32]

SARS-CoV-2 variants

The Government of Canada is aware that the United Kingdom (UK) is investigating a new SARS-CoV-2 variant, which has been identified in cases in areas where there is also a high incidence of COVID-19. They are also aware that another variant of the SARS-CoV-2 virus has been detected in South Africa, and that this variant shares one of the same mutations found in the variant identified in the UK.

Genetic variations of viruses such as the one that causes COVID-19 are not uncommon and many other variants of the SARS-CoV-2 virus have been previously observed around the world in the past year. Both new variants include mutations (i.e., changes to the genetic material in the virus) on the “spike” protein, which may result in the virus becoming more infectious and spreading more easily between people. While early data suggest that these new variants may be more transmissible, to date there is no evidence that these variants cause more severe disease symptoms or have any impact on antibody response. More research is required to confirm these findings.

Further, at this time, there is no evidence that these variants might affect vaccine efficacy. The Pfizer-BioNTech and Moderna vaccines have been tested against a number of other viral variants, without impact on efficacy. Health Canada is monitoring the emerging variants closely and work with manufacturers and international regulators to assess the impact of the new variants on vaccine efficacy.

Additionally, there is no evidence at this time that these variants affect the ability of Health Canada authorized diagnostic tests to confirm COVID-19 cases. However, given

[11] COVID-19 vaccine safety in Canada webpage provides information about any adverse events following immunization that individuals have experienced after receiving a COVID-19 vaccine in Canada. These adverse events are not necessarily related to the vaccine. The webpage will be updated every Friday at 4:00 PM Eastern Time. https://health-infobase.canada.ca/covid-19/vaccine-safety/#a6

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the limited data on the new variants, more research is needed in Canada and around the world. Health Canada is working with other regulators and manufacturers of COVID-19 test devices to determine what, if any, impact these variants may have on the effectiveness of diagnostic tests. If an issue is identified, Health Canada will work quickly with the manufacturers and public health laboratories to mitigate those risks. [33]

Health Canada continues to monitor for virus variants that may be associated with an increased risk of spread. As of January 8, 2021, there have been 14 cases of the variant virus first reported in the UK (ON 6; AB 4; BC 3; QC 1) and no reports of other variants of concern, including none of the variant first reported in South Africa. [31]

Take home messages

In addition to identification and isolation of persons with symptomatic COVID-19, effective control of spread will require reducing the risk of transmission from people with infection who do not have symptoms. Also, measures such as wearing masks, hand, cough and surface hygiene, social distancing, and strategic testing of people who are not ill will continue to be foundational to slowing the spread of COVID-19 until the COVID-19 vaccines are widely implemented.

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Client Resources

CANImmunize - free digital tool for Canadians that securely stores vaccination records
https://www.canimmunize.ca/en/home

What you need to know about the COVID-19 vaccine for Canada – *Offers a downloadable factsheet available in multiple languages
https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/awareness-resources/know-vaccine.html

Resources from the Federal and Provincial Governments

Coronavirus disease (COVID-19): For health professionals
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