Clinical Guidance on COVID- 19 Vaccines for People with Cystic Fibrosis

This guidance is intended for health-care providers. It is based on known evidence as of April 18, 2023.

The SARS-CoV-2 (i.e. COVID-19) pandemic has been of particular concern for the cystic fibrosis (CF) community. CF is a multisystem condition with comorbidities that are expected to increase vulnerability to COVID-19 infection.

Is COVID-19 immunization recommended for people with CF?

All Health Canada-approved COVID-19 vaccines should be actively encouraged for people with CF who do not have a contraindication, including those who have had COVID-19 infection. This recommendation is based on the following considerations for people with CF:

Chronic lung disease

Essentially all people with CF have a type of lung disease that is termed bronchiectasis. The basic defect in CF leads to chronic infection in the lungs by aggressive organisms such as *Pseudomonas aeruginosa*, which are difficult to eradicate despite appropriate antimicrobials and other therapies.

Over time, progressive and irreversible lung damage secondary to acute and chronic infection occurs. This is also associated with periodic acute infection flares termed pulmonary exacerbations, which require additional oral or intravenous (IV) antibiotic therapy. For the average adult with CF, two to three oral and one IV antibiotic course are received per year. In some patients, this will be much more frequent. For pediatrics with CF, lung disease in the early years is not as marked as in adults, and consistent use of appropriate treatment can slow lung disease progression. However, there are still patients who have frequent pulmonary exacerbations and need for oral and/or IV antibiotics.

This progression of lung disease accounts for the bulk of morbidity and mortality (approximately 50% of adults have a Forced Expiratory Volume in 1 second [FEV_1] <70%). The underlying lung disease complicated by difficult-to-treat infecting organisms is the primary reason for COVID-19 vulnerability.

Other reasons for COVID-19 susceptibility and poor outcomes in people with CF:

- Diabetes mellitus: Present in approximately 40% of adults with CF (dysglycemia is present in approximately 65%), and has been shown to be an independent factor for worse outcomes with COVID-19 infection.
- Nutritional deficiency: Approximately 85% of people with CF are pancreatic insufficient, with resultant undernutrition in a large proportion of adults with CF.
- Chronic liver disease: Affects approximately 30% of people with CF.

- Post-transplantation: In Canada, around 1,500 people with CF have received solid organ transplants (predominantly lung) since 2019. People who have received a solid organ transplant take immunosuppressant medications, which are believed to increase risk of serious disease from COVID-19 infection.

There is a growing evidence base available to understand the risk related to COVID-19 infection in people with CF. A recent publication based on data obtained prior to the introduction of COVID-19 vaccines from 22 countries reported on 1452 individuals with CF and confirmed COVID-19 infection. Of those included in the study, 1 in 5 patients required hospitalization, 1 in 30 required intensive care unit (ICU) admission, and 1 in 75 died.[1] Among non-transplanted individuals, worse outcomes were reported for those of older age, non-white race, lower lung function, low body mass index, and concomitant diabetes; this provides direct support for the postulated comorbidities/clinical features listed above. The CF Registry Global Harmonization Group published findings from a global study on the impact of COVID-19 on children with CF.[2] The study included 105 children with CF under the age of 18 from 13 countries; while infection was mild in most cases, a higher number of hospitalizations was noted in individuals with pre-existing advanced lung disease or poor nutrition.[3]

Impact of respiratory viruses in people with CF extrapolated from other data

People with CF commonly experience infections with a number of respiratory viruses including influenza, adenovirus, respiratory syncytial virus (RSV), enteroviruses, and rhinoviruses. These infections are a common cause of pulmonary exacerbations (estimated at >50%), which drive symptom morbidity and hospitalizations, accelerate lung function decline, and increase mortality. Viral infections may also be associated with acquisition of *Pseudomonas aeruginosa* pulmonary infection, which is independently associated with the aforementioned negative outcomes.

A previous meta-analysis showed that 50 to 70% of people with CF testing positive for influenza A (H1N1) required hospitalization, as compared to 7 to 20% of the general population.[4] Approximately 40% of patients never recover to their previous baseline lung function after a CF pulmonary exacerbation.

There is every reason to implicate SARS-CoV-2 infection with similar, if not greater, adverse events. Individuals with other chronic lung diseases also are negatively impacted by viral infections, including chronic obstructive pulmonary disease, severe asthma, and bronchiectasis. Although high-quality evidence is not available, influenza immunization is routinely recommended for people with CF worldwide.

Is the COVID-19 vaccine efficacious and safe for people with CF?

As CF is considered to be a severe underlying medical condition, people with CF were excluded from the Pfizer-BioNTech, Moderna, and AstraZeneca COVID-19 vaccine trials. Data is currently limited as to whether COVID-19 vaccines are as efficacious for people with CF as they were found to be for the clinical trial participants. There are data to suggest that the currently available COVID-19 vaccines have efficacy[5] and there is no reason to believe that the antibody response to immunization should be lower in CF compared to the general population.

CF transmembrane conductance regulator (CFTR) gene mutations, which are the cause of CF, do not have clinically relevant impacts on the host and innate immunity. There is no evidence of blunted immune response to other immunizations (e.g., influenza), and immunizations are a routine part of CF care. As well, the relatively younger age of people with CF supports a robust immunological response (<5% of patients are >65 years of age).

People with CF are most often not on maintenance/routine medications that would potentially blunt an immune response to immunization (e.g., oral corticosteroids or immunosuppressive therapies). If a patient has received a lung transplant or other solid organ transplant, please refer to the respective clinical guidance for these individuals.

There is no reason to believe that there are specific safety concerns for immunization in people with CF. A study involving 424 people with CF from Italy aged 12 years and older demonstrated that mRNA-based vaccines against SARS-CoV-2 were well-tolerated and safe in the short-term.[6]

Individuals with CF invariably have chronic lung disease, some more severe in nature. Therefore, if there was an anaphylactic reaction, there is the potential for more severe symptoms and complications. This would be similar to other patient populations with advanced lung disease (but perhaps less so in CF, as cardiovascular comorbidities are generally not present). As such, it is recommended that healthcare providers counseling people with CF follow the allergy contraindications and advice provided below closely, particularly for people with CF with most severe lung disease (i.e., FEV_1 <40% predicted).

Are there any specific contraindications or exceptions for people with CF?

Individuals who have had a severe allergic reaction to an ingredient of one type of COVID-19 vaccine are still able to receive future doses of the other type of vaccine.[7] BCCDC has a list of the individual components and their purpose in the vaccines. For a complete list of components in the vaccine, consult the vaccine monographs found at: www.bccdc.ca/health-info/diseases-conditions/covid-19/covid-19-vaccine/vaccines-for-covid-19.

People with a history of anaphylactic reaction to a previous dose of an mRNA COVID-19 vaccine, revaccination (i.e., administration of a subsequent dose in the series when indicated) may be offered with the same vaccine or the same mRNA platform if a risk assessment deems that the benefits outweigh the potential risks for the individual and if informed consent is provided. Prior to revaccination, consultation with an allergist or another appropriate physician (e.g., Medical Health Officer) is advised. If revaccination is going ahead, vaccine administration should be done in a controlled setting with expertise and equipment to manage anaphylaxis, with an extended period of observation of at least 30 minutes after revaccination.

Health Canada continues to monitor any adverse events following immunization through their post-authorization surveillance process.

Otherwise, there are no specific contraindications or exceptions for people with CF from a disease perspective.

COVID-19 vaccines can be given concomitantly with, or any time before or after any other live or inactivated vaccine.[8-11]

Are there specific recommendations or considerations for safe and/or most effective administration?

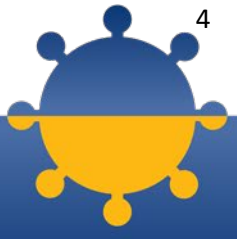
Out of abundance of caution, it is recommended that immunization be delayed in the following circumstances:

- If the patient is currently undergoing treatment, including antibiotics for a pulmonary exacerbation of CF;
- If patient is hospitalized for a CF-related complication like a bowel obstruction or acute pancreatitis.

Immunization delays in these circumstances would be decided on an individual basis by the CF clinician.

References

1. Carr SB, McClenaghan E, Elbert A, Faro A, Cosgriff R, Abdrakhmanov O, Brownlee K, Burgel PR, Byrnes CA, Cheng SY, Colombo C, Corvol H, Daneau G, Goss CH, Gulmans V, Gutierrez H, Harutyunyan S, Helmick M, Jung A, Kashirskaya N, McKone E, Melo J, Middleton PG, Mondejar-Lopez P, de Monestrol I, Nährlich L, Padoan R, Parker M, Pastor-Vivero MD, Rizvi S, Ruseckaite R, Salvatore M, da Silva-Filho LVRF, Versmessen N, Zampoli M, Marshall BC, Stephenson AL; CF Registry Global Collaboration. Factors associated with clinical progression to severe COVID-19 in people with cystic fibrosis: A global observational study. J Cyst Fibros. 2022 Jul;21(4):e221-e231. doi: 10.1016/j.jcf.2022.06.006. Epub 2022 Jun 13. PMID: 35753987; PMCID: PMC9189103.
2. Cystic Fibrosis Registry Global Harmonization Group. First Global Study of COVID-19 in Children with Cystic Fibrosis Reports Reassuring Outcomes. Sept 9, 2021. https://www.cff.org/node/1426 Accessed 29 November 2021.
3. Bain, R, Cosgriff, R., Zampoli, M. et al. Clinical characteristics of SARS-CoV-2 infection in children with cystic fibrosis: An international observational study. Journal of Cystic Fibrosis, Volume 20, Issue 1, 2021, Pages 25-30 https://doi.org/10.1016/j.jcf.2020.11.021
4. Renk H, Regamey N, Hartl D. (2014). Influenza A(H1N1)pdm09 and Cystic Fibrosis Lung Disease: A Systematic Meta-Analysis. *PLoS ONE.* 9(1): e78583. https://doi.org/10.1371/journal.pone.0078583.
5. Azzolini E, Pozzi C, Germagnoli L, et al. mRNA COVID-19 vaccine booster fosters B- and T-cell responses in immunocompromised patients. Life Sci Alliance 2022;5(6)doi:10.26508/lsa.202201381, 10.26508/lsa.202201381.
6. Alicandro G, Daccó V, Cariani L, Contarini M, Morlacchi LC, Rosazza C, Sciarrabba CS, Ferraro F, Lanfranchi C, Orena BS, Gramegna A, Blasi F, Colombo C. Safety of mRNA-based vaccines against SARS-CoV-2 in people with cystic fibrosis aged 12 years and over. J Cyst Fibros. 2022 May;21(3):e173-e175. doi: 10.1016/j.jcf.2022.02.009. Epub 2022 Feb 16. PMID: 35256306; PMCID: PMC8847104.
7. BC Centre for Disease Control. COVID-19 Vaccine. Vaccine Considerations. Updated 12 May 2022. Available at: http://www.bccdc.ca/health-info/diseases-conditions/covid-19/covid-19-vaccine/vaccine-considerations. Accessed 8 August 2022.
8. BC Centre for Disease Control. Communicable Disease Control Manual Chapter 2: Immunization Part 4 - Biological Products. COMIRNATY. Updated 29 July 2022. Available at: www. http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual/immunization/biological-products. Accessed 8 August 2022.
9. BC Centre for Disease Control. Communicable Disease Control Manual Chapter 2: Immunization Part 4 - Biological Products. SPIKEVAX. Updated 8 August 2022. Available at: http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual/immunization/biological-products. Accessed 8 August 2022.
10. BC Centre for Disease Control. Communicable Disease Control Manual Chapter 2: Immunization Part 4 - Biological Products. VAXZEVRIA. Updated 8 July 2022. Available at: http://www.bccdc.ca/health-



professionals/clinical-resources/communicable-disease-control-manual/immunization/biological-products. Accessed 8 August 2022.

11. BC Centre for Disease Control. Communicable Disease Control Manual Chapter 2: Immunization Part 4 - Biological Products. NOVAVAX. 8 July 2022. Available at: http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual/immunization/biological-products. Accessed 8 August 2022.

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