COVID-19 Vaccine Testing & Administration Guidance for Allergists/Immunologists from the CSACI

Current as of November 14, 2021, and based on available evidence to date

COVID-19 vaccines have demonstrated efficacy and effectiveness against severe COVID-19 outcomes including hospitalizations, intensive care unit admissions, and fatality. They provide the first hope for mitigating the devastating health and economic impacts resulting from the pandemic. Two mRNA vaccines (Pfizer-BioNTech, Moderna), and two adenovirus vector vaccines (AstraZeneca/COVISHIELD, Janssen) are currently approved in Canada.[1]

Reports of reactions to COVID-19 vaccines have raised questions about their safety for use in individuals with allergies. In this document, we aim to address these concerns and provide guidance for CSACI members.

Suggested approach to vaccination in individuals with confirmed or suspected allergic conditions:

- **Assessment by an allergist is NOT WARRANTED prior to receiving COVID-19 vaccination for individuals with a history of unrelated allergic conditions or adverse reactions, INCLUDING ANAPHYLAXIS, such as:**
    - **Other vaccines**
    - **Foods**
    - **Insect venom**
    - **Environmental allergies**
    - **Unrelated oral/injected medication**
    - **Radiocontrast media (RCM), and**
    - **Asthma, allergic rhinitis, or atopic dermatitis**

  In these individuals, the available COVID-19 vaccines can be administered without any special precautions or investigations. The COVID-19 vaccines available do not contain any food products, antibiotics, latex, or thiomersal.[1] As with the routine administration of all vaccines, the COVID-19 vaccine should be administered in a healthcare setting capable of managing anaphylaxis, and individuals should be observed for a minimum of 15 minutes following vaccination (or 30 minutes if a history of injectable medication allergy or unrelated vaccine allergy).[1,2]

- **Assessment by an allergist is NOT WARRANTED for any individual who has a history of a mild, localized reaction to a prior dose of the COVID-19 vaccine, or to any of its components.** The risk of anaphylaxis is low and these individuals can be safely receive a subsequent dose of the same vaccine[3–5]. A prolonged 30-minute observation period may be considered.

- **Assessment by an allergist is WARRANTED for any individual with anaphylaxis following the COVID-19 vaccine or to any of its components.** This is strongly preferred over not being vaccinated or withholding vaccination, and includes anyone who has experienced a suspected severe immediate allergic reaction after administration of a

COVID-19 vaccine, or someone with a confirmed allergy to a component of the vaccine.[1] There is increasing evidence that these individuals can safely receive a subsequent dose of the same vaccine with low risk of a systemic reaction under the supervision of an allergist.[6–10] This recommendation is in keeping with the National Advisory Committee on Immunization (NACI) recommendations, which currently recommend that revaccination with the same vaccine or same mRNA platform may be offered in consultation with an allergist.[1]

- These recommendations will be updated as evidence evolves to reflect ongoing best practice.

Summary:

1. *There is a low risk for allergic reactions associated with vaccines. Non-allergic reactions to vaccines are much more frequent than allergic reactions.*
2. *The nature and cause of the reported allergic reactions to COVID-19 vaccines remain unclear, including what component of the vaccine those individuals may have reacted to.*
3. *The role of allergy testing for COVID-19 vaccines and their excipients is limited and not currently recommended.*
4. *In someone with anaphylaxis following a COVID-19 vaccine for whom an additional dose is required, revaccination with the same platform vaccine has been demonstrated to be safe under the supervision of an allergist. Graded dosing may be considered. A prolonged observation period of at least 30 minutes is recommended.*

1. <u>There is a low risk for allergic reactions associated with vaccines. Non-allergic reactions to vaccines are much more frequent than allergic reactions.</u>

Vaccines activate the immune system, which commonly result in minor local and systemic side effects, including fever and local inflammatory reactions (redness, swelling, pain and warmth) at the site of the injection.[12] As with other vaccines, local cutaneous reactions after vaccination with COVID-19 vaccines are common.[3,4] These reactions may include acute localized urticaria and/or angioedema[3,4] and tend to be mild and self-limiting. These reactions are not a contraindication to receiving the same vaccine in the future, as they do not pose a risk for future severe allergic reactions.[3,4]

Non-allergic reactions to vaccines also include immunization stress-related responses that can mimic allergic reactions, and may include breath-holding, hyperventilation, and vasovagal syncope (fainting).[13]

To date, there have been more than 250 million reported cases of COVID-19 worldwide and over 5 million deaths[14]*. By comparison, while approximately 7.5 billion COVID-19 vaccine doses have been administered*[14]*, there have been neither reported fatalities nor long-term morbidity associated with anaphylaxis following COVID-19 vaccine administration.*

2. **The nature and cause of the reported allergic reactions to COVID-19 vaccines remain unclear, including what component of the vaccine those individuals may have reacted to.**

The incidence of anaphylaxis following COVID-19 vaccination is estimated at about 7.91 cases per million doses administered (approximately 3 per million doses administered in Canada).[15,16] There have been no fatalities nor long-term morbidity described with these events. The nature and cause of the reported allergic reactions to these vaccines remain unclear, including what component of the vaccine those individuals may have reacted to.

Allergic reactions to vaccines can be elicited by the active vaccine component, or more commonly, by one of the excipients in the vaccine.[17] Polyethylene glycol, commonly known as PEG, has been identified as the most likely potentially allergenic component of both Pfizer-BioNTech and Moderna COVID-19 vaccines, and polysorbate80 in the AstraZeneca/ COVISHIELD and Janssen vaccines.[1,18] Tromethamine (trometamol or Tris) in the Moderna COVID-19 vaccine has also been identified as a potentially allergenic excipient.[1] However, there is increasing evidence that either these are not the culprit excipients and/or the reactions are not IgE-mediated.[10,11,19] This remains under investigation.

3. **The role of allergy testing for COVID-19 vaccines and their excipients is limited and not currently recommended.**

Epicutaneous and intradermal testing protocols to COVID-19 vaccines and their excipients (PEG, polysorbate) have been published. However, there is emerging evidence that skin test results do not affect tolerance of a second COVID-19 dose even in individuals with an immediate reaction to the first dose.[19] There is a risk of an irritant response to testing.[19] As a result, testing is not currently recommended.

4. **In someone with anaphylaxis following the COVID-19 vaccine or to one of its components for whom an additional dose is required, revaccination with the same platform vaccine has been demonstrated to be safe under the supervision of an allergist. Graded dosing may be considered. A prolonged observation period of at least 30 minutes is recommended.**

For a patient with a history of a severe allergic reaction (anaphylaxis) to a COVID-19 vaccine or any of its components for whom an additional dose is required, allergy testing to the vaccine and its components is not currently recommended. A safe option for consideration as part of shared decision-making includes re-administration of the same vaccine with prolonged observation. This recommendation is also in keeping with NACI recommendations that in those with anaphylaxis following the COVID-19 vaccine, revaccination with the same vaccine platform or same vaccine may be offered in consultation with an allergist and with at least 30 minutes observation.[1] Several studies have demonstrated safe revaccination of individuals with an immediate reaction to the first dose of a COVID-19 vaccine, and it is increasingly recognized that these reactions may not be allergen-driven or IgE-mediated.[7,9–11]

A graded vaccine administration protocol may be considered, although almost all studies on revaccination among those with anaphylaxis used a single full dose protocol, noting it to be safe. For higher-risk patients who are hesitant to proceed with vaccine administration, allergy testing

remains an option after education that the predictive value of such testing is unknown. Allergy testing for lower-risk patients is NOT recommended and may unnecessarily delay administration of COVID-19 vaccines.

Guidance for the cautious graded administration of a vaccine in someone with a confirmed IgE-mediated allergy to that vaccine or one of its components has previously been published: administer 0.05 mL 1:10 dilution, 10%, 20%, 30%, and 40% of the full dose incrementally in alternate arms at 15-minute intervals, followed by a minimum 30-minute observation period.[17] Graded administration for adverse vaccine reactions determined not to be due to IgE-mediated allergy to the vaccine or one of its excipients may require an adjustment of this protocol as determined by the responsible physician.

Addendum: The prior CSACI guidance included a section on vaccination of individuals with immunocompromise as this was prior to the COVID-19 vaccines being recommended in these individuals. The National Advisory Committee on Immunization (NACI) now recommends a complete COVID-19 vaccine series in immunocompromised individuals. For moderately to severe immunocompromised individuals, NACI recommends a three-dose primary series with an mRNA vaccine. For information on vaccination of individuals with immunocompromise please refer to the National Advisory Committee on Immunization guidance[1].

References:

1. NACI: Recommendations on the use of COVID-19 vaccine(s) [Internet]. Available from: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines.html
2. CDC: COVID-19 ACIP Vaccine Recommendations [Internet]. Available from: https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html
3. McMahon DE, Amerson E, Rosenbach M, Lipoff JB, Moustafa D, Tyagi A, et al. Cutaneous reactions reported after Moderna and Pfizer COVID-19 vaccination: A registry-based study of 414 cases. J Am Acad Dermatol. 2021;85:46–55.
4. Robinson LB, Fu X, Hashimoto D, Wickner P, Shenoy ES, Landman AB, et al. Incidence of Cutaneous Reactions After Messenger RNA COVID-19 Vaccines. Vol. 157, JAMA dermatology. 2021. p. 1000–2.
5. Blumenthal KG, Freeman EE, Saff RR, Robinson LB, Wolfson AR, Foreman RK, et al. Delayed Large Local Reactions to mRNA-1273 Vaccine against SARS-CoV-2. Vol. 384, The New England journal of medicine. 2021. p. 1273–7.
6. Krantz MS, Kwah JH, Stone Jr CA, Phillips EJ, Ortega G, Banerji A, et al. Safety Evaluation of the Second Dose of Messenger RNA COVID-19 Vaccines in Patients With Immediate Reactions to the First Dose. JAMA Intern Med [Internet]. 2021;in press. Available from: https://doi.org/10.1001/jamainternmed.2021.3779
7. Kessel A, Bamberger E, Nachshon L, Rosman Y, Confino-Cohen R, Elizur A. Safe administration of the Pfizer-BioNtTech COVID-19 vaccine following an immediate reaction to the first dose. Allergy. 2021.
8. Krantz MS, Bruusgaard-Mouritsen MA, Koo G, Phillips EJ, Stone CAJ, Garvey LH. Anaphylaxis to the first dose of mRNA SARS-CoV-2 vaccines: Don’t give up on the second dose! Vol. 76, Allergy. 2021. p. 2916–20.
9. Kelso JM. Misdiagnosis of systemic allergic reactions to mRNA COVID-19 vaccines.

Vol. 127, Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology. 2021. p. 133–4.
10. Pitlick MM, Sitek AN, Kinate SA, Joshi AY, Park MA. Polyethylene glycol and polysorbate skin testing in the evaluation of coronavirus disease 2019 vaccine reactions: Early report. Vol. 126, Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology. 2021. p. 735–8.
11. Banerji A, Wolfson AR, Wickner PG, Cogan AS, McMahon AE, Saff R, et al. COVID-19 Vaccination in Patients with Reported Allergic Reactions: Updated Evidence and Suggested Approach. Vol. 9, The journal of allergy and clinical immunology. In practice. 2021. p. 2135–8.
12. Public Health Agency of Canada. Vaccine safety and possible side effects - Canada.ca. https://www.canada.ca/en/public-health/services/vaccination-children/safety-concerns-side-effects.html.
13. Public Health Agency of Canada. Anaphylaxis and other Acute Reactions following Vaccination: Canadian Immunization Guide - Canada.ca. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-2-vaccine-safety/page-4-early-vaccine-reactions-including-anaphylaxis.html
14. Johns Hopkins Coronavirus Resource Center [Internet]. Available from: https://coronavirus.jhu.edu/map.html
15. https://health-infobase.canada.ca/covid-19/vaccine-safety/#a3.
16. Greenhawt M, Abrams EM, Shaker M, Chu DK, Khan D, Akin C, et al. The Risk of Allergic Reaction to SARS-CoV-2 Vaccines and Recommended Evaluation and Management: A Systematic Review, Meta-Analysis, GRADE Assessment, and International Consensus Approach. J allergy Clin Immunol Pract. 2021;
17. Kelso JM, Greenhawt MJ, Li JT, Nicklas RA, Bernstein DI, Blessing-Moore J, et al. Adverse reactions to vaccines practice parameter 2012 update. J Allergy Clin Immunol. 2012;130:25–43.
18. Banerji A, Wickner PG, Saff R, Stone CAJ, Robinson LB, Long AA, et al. mRNA Vaccines to Prevent COVID-19 Disease and Reported Allergic Reactions: Current Evidence and Suggested Approach. J Allergy Clin Immunol Pr. 2020;in press.
19. Wolfson AR, Robinson LB, Li L, McMahon AE, Cogan AS, Fu X, et al. First-Dose mRNA COVID-19 Vaccine Allergic Reactions: Limited Role for Excipient Skin Testing. J allergy Clin Immunol Pract. 2021;
20. Warren CM, Snow TT, Lee AS, Shah MM, Heider A, Blomkalns A, et al. Assessment of Allergic and Anaphylactic Reactions to mRNA COVID-19 Vaccines With Confirmatory Testing in a US Regional Health System. JAMA Netw open. 2021;4:e2125524.