PRACTICE POINT

Clinical guidance for youth with myocarditis and pericarditis following mRNA COVID-19 Vaccination

Principal author(s)

Peter D. Wong, Brian W. McCrindle, Kenny Wong, Michael Khoury, Kevin Chan, Marina Salvadori; Canadian Paediatric Society, Acute Care Committee (https://cps.ca/en/documents/authors-auteurs/acute-care-committee), Community Paediatrics Committee (https://cps.ca/en/documents/authors-auteurs/community-paediatrics-committee)

Abstract

This practice point aims to provide clinical guidance on myocarditis and pericarditis following mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna). The benefits of COVID-19 vaccination outweigh the risks, and the vaccine is recommended for all eligible individuals, including children and youth in their 12th year and over. A small increased risk of myocarditis and pericarditis (< 1 case per 10,000) has been reported following vaccination with COVID-19 mRNA vaccines in Canada and internationally, most often among adolescents and young adults < 30 years of age, males, and after the second dose. Although this safety signal is occurring at higher-than-expected background rates, most cases are mild. This document reflects expert opinion and available evidence, which is limited. It will be updated as further information becomes available and as younger individuals are immunized against COVID-19.

Keywords: *Myocarditis; pericarditis; COVID-19 vaccine; youth*

Abbreviations:

AEFI	Adverse Events Following Immunization
CBC	Complete Blood Count
CMR	Cardiac magnetic resonance
CRP	C-reactive protein
CT	Computer tomography
ECG	Electrocardiogram
ESR	Erythrocyte sedimentation rate
IMPACT	Canada's Immunization Monitoring Program Active
MIS-C	Multisystem Inflammatory Syndrome in Children
NACI	National Advisory Committee on Immunization
NSAIDs	Nonsteroidal anti-inflammatory agents
PCP	Primary care provider
PCR	polymerase chain reaction
PHAC	Public Health Agency of Canada
WBC	White blood cell

Background

Since May 2021, there have been international reports from Israel and the United States of myocarditis and pericarditis following mRNA COVID-19 vaccination (Pfizer-BioNTech and Moderna) [1]-[5]. Canada has also reported cases [6][7]. In early June 2021, the Public Health Agency of Canada (PHAC) communicated that the observed rates of myocarditis and pericarditis were not higher than would be expected in the general population, and that no clear causal relationship has been established [6][8][9]. However, subsequent increasing cases numbers (< 1 case per 10,000) suggest a statistically significant association [10]. Accurately estimating the true incidence has been challenging due to the broad spectrum of clinical presentation and limited ability to recognize a rare vaccine related event.

To reduce transmission of COVID-19 and prevent illness and complications, including multisystem inflammatory syndrome in children (MIS-C), vaccination continues to be recommended for all eligible individuals, including anyone in their 12th year and over. The benefits of reducing overall complications, deaths, and hospitalizations due to COVID-19 infections continue to outweigh the risks in eligible populations [6][8][9][11].

This practice point provides clinical guidance on myocarditis and pericarditis following mRNA COVID-19 vaccination. It will be updated as further information becomes available.

Identification

International reports of myocarditis and pericarditis following COVID-19 mRNA vaccination [1]-[3][10][12][13] indicate that:

- Cases were reported much more commonly after the second dose [8].
- Symptom onset was typically within several days (peak 1-3 and up to 7 days) after vaccination [8].
- Cases were mainly adolescents and young adults (< 30 years of age) [8].
- Cases were more often males compared to females [8].
- Cases were characterized by mild illness, which responded well to conservative treatment and rest, with rapid resolution of symptoms [8].

Pericarditis. The causes of pericardial disease can be both infectious and non-infectious. In developed countries, viruses are the most common etiological agent, whereas tuberculosis is the most frequent cause globally and in developing countries [14]. The diagnosis of acute pericarditis requires the presence of at least 2 of the 4 following [14]:

1. Pericardial chest pain (sharp, pleuritic, improved by sitting up and leaning forward)
2. Pericardial rub
3. Widespread ST-elevation or PR depression on ECG
4. Pericardial effusion (new or worsening)

Additional supportive findings include elevated inflammatory markers (CRP, ESR, WBC count) or evidence of pericardial inflammation on imaging techniques (CT, CMR). However, most reported cases of pericarditis after mRNA vaccination had normal or only mildly elevated inflammatory markers [15].

Myocarditis. Myocarditis is an inflammatory disease of the myocardium [16][17]. It can present with a range of clinical symptoms, from mild chest pain with transient electrocardiogram (ECG) changes to arrhythmias, heart failure and cardiogenic shock [18][19]. The Brighton collaboration outlined case definition for definitive, probable, and possible cases of myocarditis based on clinical presentation and diagnostic criteria with key imaging findings [16]. Patients presenting with dyspnea, chest pain, diaphoresis and/or palpitations following COVID-19 mRNA vaccination should be evaluated for suspicion of myocarditis [2][16].

Investigations

Patients presenting especially within 2 weeks of a COVID-19 mRNA vaccination with a clinical suspicion of myocarditis/pericarditis should be assessed in person. It is important to maintain a broad differential regardless of the timing of receipt of the COVID-19 mRNA vaccination. Initial investigations should include an ECG, serum troponin level and inflammatory markers, such as CRP and ESR [12][15]. Other investigations will vary depending on the differential diagnosis and availability, such as septic work-up, nasopharyngeal swab for acute SARS-CoV (e.g., PCR testing) or serologic testing for prior SARS-CoV-2 infection (e.g., detection of SARS-CoV-2 nucleocapsid antibodies), rheumatologic workup and viral and microbiological testing for known causes of myocarditis/pericarditis [12][15].

For patients with an abnormal ECG (Table 1), elevated troponin level or high clinical suspicion of myocarditis/pericarditis, cardiology consultation and echocardiogram should be obtained [15]. Cardiac Magnetic Resonance (CMR) may be obtained if the clinical picture is unclear. Troponin levels may be exceedingly high (> 10,000 ng/L). It is important to rule out other potential causes of pericarditis [14] and myocarditis [16], and unwell patients should be monitored for features of cardiac failure, tamponade and arrhythmia. Consider consultation with infectious disease and/or rheumatology if other relevant diagnoses are being considered [12][15].

Table 1. Electrocardiographic changes of myocarditis and pericarditis

Pericarditis	• Widespread concave ST elevation and PR depression throughout most of the limb leads (I, II, III, aVL, aVF) and precordial leads (V2-6) • Reciprocal ST depression and PR elevation in lead aVR (± V1) • Sinus tachycardia
Myocarditis	• Paroxysmal or sustained atrial or ventricular arrhythmias (premature atrial or ventricular beats, and/or supraventricular or ventricular tachycardia, interventricular conduction delay, abnormal Q waves, low voltages) • AV nodal conduction delays or intraventricular conduction defects (atrioventricular block (grade I-III), new bundle branch block) • ST segment and T waves changes • Prolonged QRS • QT prolongation • Diffuse T wave inversion

Adapted from reference [15]

Management

Pericarditis. In general, most cases of acute pericarditis after COVID-19 mRNA vaccination are benign, self-limited and respond to nonsteroidal anti-inflammatory agents (NSAIDs). Only a small number have resulted in serious disease. For cases of mild pericarditis, ibuprofen (Dose: 10 mg/kg/dose q8h X 1 week (maximum 400 mg/dose, and maximum daily dose of 40 mg/kg/day up to 1200 mg/day), then 5 mg/kg/dose q8h X 1 week (maximum 200 mg)). Ambulatory setting follow-up may be appropriate after cardiology assessment. Colchicine can be considered in patients who do not respond to NSAIDs, as it has been found to be effective in relieving pain and preventing recurrent pericarditis [20]. Corticosteroids should be avoided as first-line treatment given the association of increased risk of recurrence of pericarditis [14]. Patients who present with high and persistent fever, large pericardial effusion or cardiac tamponade or poor response to NSAIDs or colchicine should be hospitalized for observation and management [15]. Other considerations for admission may include distance from care. Intravenous immunoglobulin is not recommended.

Myocarditis. In general, most reported cases of myocarditis following COVID-19 mRNA vaccination have been mild and have shown response to NSAIDs. However, admission or close ambulatory monitoring should be considered until the clinical course of the illness is established. Severe cases with heart failure, arrhythmia or other complications of myocarditis require hospitalization, critical care support with appropriate management and monitoring.

Follow-up

All suspected and confirmed cases of myocarditis and pericarditis following COVID-19 mRNA vaccination should be followed by their primary care physician (PCP), with specialist follow-up as determined by the clinical severity and course. For those not admitted to hospital, follow-up should be within a

week of presentation if symptoms are improving. Patients with a confirmed diagnosis of pericarditis should refrain from high intensity or competitive sports for 3-4 weeks or until resolution of symptoms and normalization of laboratory markers, ECG and imaging. Further, patients with a confirmed diagnosis of myocarditis and some cases of pericarditis may require exercise modification for at least 1 month or as recommended by their specialist [15]. While symptoms and signs of myocarditis and pericarditis resolve within a few days with supportive care, long-term effects are unknown and outcomes are expected to be good.

All cases of myocarditis and pericarditis following COVID-19 mRNA vaccination should be reported to public health authorities according to local/provincial/territorial reporting guidelines. Consider referral of the patient to a Special Immunization Clinic (SIC) [21] to discuss and advise on future COVID-19 vaccinations [8][9][22]. People with a history of myocarditis or pericarditis unrelated to mRNA COVID-19 vaccination should consult their clinical team for individual considerations and recommendations. The National Advisory Committee on Immunization (NACI) recommends deferral of the second COVID-19 vaccination for those with myocarditis/pericarditis after the first dose until more information is available [23].

Surveillance

Health Canada, PHAC and provincial/territorial health authorities continue to closely monitor the issue as part of the enhanced COVID-19 vaccine safety surveillance [7]. Provincial/territorial public health authorities report Adverse Events Following Immunization (AEFI) to PHAC as part of ongoing safety efforts [24]. Importantly, Canada's Immunization Monitoring Program Active (IMPACT), a paediatric national hospital-based surveillance network, provides active surveillance of myocarditis/pericarditis emergency visits and hospitalizations at tertiary centres [25].

Conclusions

1. There is a temporal association between receiving mRNA COVID-19 vaccination and myocarditis and pericarditis among youth. These events are very rare. The risk-benefit decision for mRNA vaccination is favourable, and the vaccine is recommended for all eligible populations.
2. Clinical evaluation should be in person and include a history, physical examination, and investigations (ECG, serum troponin and inflammatory markers).
3. Most cases are benign, respond rapidly to NSAIDs alone, and can be safely managed in the ambulatory setting.
4. All suspected and confirmed cases should be reported to local/provincial or territorial public health authorities (https://www.canada.ca/en/public-health/services/immunization/federal-provincial-territorial-contact-information-aefi-related-questions.html) as Adverse Events Following Immunization (AEFI)

Acknowledgements

This practice point was reviewed by Executives of the Community Paediatric and Paediatric Emergency Medicine Sections, and the Community Paediatric, Acute Care and Infectious Diseases and Immunization Committees of the Canadian Paediatric Society. It was also reviewed and endorsed by the Canadian Paediatric Cardiology Association.

CANADIAN PAEDIATRIC SOCIETY ACUTE CARE COMMITTEE (2021-2022)

Members: Carolyn Beck MD, Kevin Chan MD (Chair), Kimberly Dow MD (Board Representative), Karen Gripp MD (Past Member), Marie-Pier Lirette MD (Resident Member), Jonathan Sniderman MD, Evelyne D. Trottier MD, Troy Turner MD
Liaisons: Laurel Chauvin-Kimoff MD (Past Chair 2012-2019), CPS Paediatric Emergency Medicine Section; Sidd Thakore MD, CPS Hospital Paediatrics Section

CANADIAN PAEDIATRIC SOCIETY COMMUNITY PAEDIATRICS COMMITTEE (2021-2022)

Members: Tara Chobotuk MD, Michael Hill MD, Audrey Lafontaine MD, Alisa Lipson MD, Marianne McKenna MD (Board Representative), Julia Orkin MD (Past Chair), Peter Wong MD (Chair)
Liaison: Karen Cozens MD, CPS Community Paediatrics Section
Principal authors: Peter D. Wong[1,2] Brian W. McCrindle[3], Kenny Wong[4], Michael Khoury[5], Kevin Chan[6,7], Marina Salvadori[8]

Affiliations:

[1]Division of Paediatric Medicine, Department of Paediatrics, University of Toronto
[2] Dalla Lana School of Public Health, University of Toronto
[3] Division of Cardiology, Department of Paediatrics, University of Toronto
[4] Division of Cardiology, Department of Paediatrics, Dalhousie University
[5] Division of Cardiology, Department of Paediatrics, University of Alberta
[6] Women and Children's Health, Trillium Health Partners
[7] Division of Emergency Medicine, Department of Paediatrics, University of Toronto
[8] Public Health Agency of Canada; Department of Pediatrics, McGill University

References

1. Vogel G, Couzin-Frankel J. Israel reports link between rare cases of heart inflammation and COVID-19 vaccination in young men 2021. https://www.science.org/news/2021/06/israel-reports-link-between-rare-cases-heart-inflammation-and-covid-19-vaccination (https://www.science.org/news/2021/06/israel-reports-link-between-rare-cases-heart-inflammation-and-covid-19-vaccination) (Accessed August 27, 2021).

2. Marshall M, Ferguson ID, Lewis P, Jaggi P, Gagliardo C, Collins JS, et al. Symptomatic acute myocarditis in seven adolescents following Pfizer-BioNTech COVID-19 vaccination. Pediatrics. 2021:2.

3. Kim HW, Jenista ER, Wendell DC, Azevedo CF, Campbell MJ, Darty SN, et al. Patients With Acute Myocarditis Following mRNA COVID-19 Vaccination. JAMA Cardiolo. June 29, 2021. https://jamanetwork.com/journals/jamacardiology/fullarticle/2781602 (Accessed August 27, 2021).

4. World Health Organization. COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety (GACVS): updated guidance regarding myocarditis and pericarditis reported with COVID-19 mRNA vaccines 2021. https://www.who.int/news/item/09-07-2021-gacvs-guidance-myocarditis-pericarditis-covid-19-mrna-vaccines (https://www.who.int/news/item/09-07-2021-gacvs-guidance-myocarditis-pericarditis-covid-19-mrna-vaccines) (Accessed August 27, 2021).

5. Mouch SA, Roguin A, Hellou E, Ishai A, Shoshan U, Mahamid L, et al. Myocarditis following COVID-19 mRNA vaccination. Vaccine. 2021 Jun 29; 39(29): 3790–3793. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8162819/ (Accessed August 27, 2021).

6. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Myocarditis and pericarditis following COVID-19 mRNA vaccines. Toronto, ON: Queen's Printer for Ontario; 2021. https://www.publichealthontario.ca/-/media/documents/ncov/vaccines/2021/06/covid-19-mrna-vaccines-myocarditis-pericarditis.pdf?la=en (https://www.publichealthontario.ca/-/media/documents/ncov/vaccines/2021/06/covid-19-mrna-vaccines-myocarditis-pericarditis.pdf?la=en)(Accessed August 27, 2021).

7. Health Canada. Reported side effects following COVID-19 vaccination in Canada. 2021. https://health-infobase.canada.ca/covid-19/vaccine-safety/ (Accessed August 27, 2021).

8. Public Health Agency of Canada. Communiqué to health practitioners Reports of Myocarditis/pericarditis after COVID-19 vaccination, June 3, 2021. https://www.cfpc.ca/CFPC/media/Resources/Communique-to-health-practitioners-Myocarditis-pericarditis-June-3-2021-FINAL.pdf (https://www.cfpc.ca/CFPC/media/Resources/Communique-to-health-practitioners-Myocarditis-pericarditis-June-3-2021-FINAL.pdf)(Accessed August 27, 2021).

9. BC Control for Disease Control. Myocarditis/ pericarditis in association with receipt of mRNA COVID-19 vaccine, June 11, 2021. http://www.bccdc.ca/Health-Info-Site/Documents/COVID-19_vaccine/Myocarditis-pericarditis-COVID-19-mRNA-vaccines.pdf (Accessed August 27, 2021).

10. Diaz GA, Parsons GT, Gering SK, Meier AR, Hutchinson IV, Robicsek A. Myocarditis and Pericarditis After Vaccination for COVID-19. JAMA. August 4, 2021.

11. Wallace M, Oliver S. COVID-19 mRNA vaccines in adolescents and young adults: Benefits-risk discussion. ACIP Meeting, June 23, 2021. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/05-COVID-Wallace-508.pdf (Accessed August 27, 2021).

12. Centers for Disease Control and Prevention. Myocarditis and Pericarditis. June 23, 2021. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html) (Accessed August 27, 2021).

13. Shimabukuro T. COVID-19 Vaccine safety updates. ACIP Meeting, June 23, 2021. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/03-COVID-Shimabukuro-508.pdf (Accessed August 27, 2021).

14. Adler Y, Charron P, Imazio M, Badano L, Barón-Esquivias G, Bogaert J. Guidelines for the diagnosis and management of pericardial diseases: Task Force of the European Society Cardiology. Endorsed: European Association for Cardio-Thoracic Surgery. Eur Heart J. 2015;36(42):2921-64.

15. SickKids. Myocarditis and pericarditis after mRNA COVID-19 vaccination in children: Interim guidance document, Version 3.3. August 6, 2021. https://www.sickkids.ca/contentassets/50c1bd3c95e74dcf9fa7c9f6fd707bd7/interim-guidance_myocarditis-pericarditis-after-mrna-covid-19-vaccination-in-children.pdf (https://www.sickkids.ca/contentassets/50c1bd3c95e74dcf9fa7c9f6fd707bd7/interim-guidance_myocarditis-pericarditis-after-mrna-covid-19-vaccination-in-children.pdf) (Accessed August 27, 2021).

16. Caforio AL, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J. 2013;34(33):2636-48, 48a-48d.

17. Law YM, Lal AK, Chen S, Čiháková D, Cooper Jr LT, Deshpande S, et al. Diagnosis and management of myocarditis in children: a Scientific Statement from the American Heart Association. Circulation. 2021:CIR. 0000000000001001.

18. Brighton Collaboration. Myocarditis Decision Tree. 2021. https://brightoncollaboration.us/wp-content/uploads/2021/05/Myocarditis-decision-tree_brief-

format_DRAFT_24May2021.pdf (Accessed August 27, 2021).

19. Maron BJ, Zipes DP, Kovacs RJ. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: preamble, principles, and general considerations: a scientific statement from the American Heart Association and American College of Cardiology. Journal of the American College of Cardiology. 2015;66(21):2343-9.

20. Imazio M, Brucato A, Pluymaekers N, Breda L, Calabri G, Cantarini L, et al. Recurrent pericarditis in children and adolescents: a multicentre cohort study. Journal of Cardiovascular Medicine. 2016;17(9):707-12.

21. CIRN. SIC Network Patient Referrals 2021. https://cirnetwork.ca/sic-network-patient-referrals/ (https://cirnetwork.ca/sic-network-patient-referrals/) (Accessed August 27, 2021).

22. Government of Canada. Reporting Adverse Events Following Immunization (AEFI) in Canada 2021. https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization/form.html (https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization/form.html) (Accessed August 27, 2021).

23. Health Canada, National Advisory Committee on Immunization (NACI). An Advisory Committee Statement (ACS): Recommendations on the use of COVID-19 vaccines. July 22, 2021. https://www.canada.ca/content/dam/phac-aspc/documents/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines/recommendations-use-covid-19-vaccines-en.pdf (https://www.canada.ca/content/dam/phac-aspc/documents/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines/recommendations-use-covid-19-vaccines-en.pdf)(Accessed August 27, 2021).

24. Public Health Agency of Canada, Vaccine Vigilance Working Group. Reporting Adverse Events Following Immunization (AEFI) in Canada: User guide to completion and submission of the AEFI reports. June 2021. https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization/user-guide-completion-submission-aefi-reports.html (https://www.canada.ca/en/public-health/services/immunization/reporting-adverse-events-following-immunization/user-guide-completion-submission-aefi-reports.html) (Accessed August 27, 2021).

25. Canadian Paediatric Society. IMPACT Canadian Immunization Monitoring Program Active, 2021. https://cps.ca/en/impact (https://cps.ca/en/impact)(Accessed August 27, 2021).

Disclaimer: The recommendations in this position statement do not indicate an exclusive course of treatment or procedure to be followed. Variations, taking into account individual circumstances, may be appropriate. Internet addresses are current at time of publication.

Last updated: Sep 16, 2021