British Columbia Report

Adverse Events Following Immunization with COVID-19 Vaccines

December 13, 2020 to September 18, 2021

This report summarizes the reports of COVID-19 vaccine adverse events following immunization (AEFI) reported to the BC Centre for Disease Control up to and including September 18, 2021. Please refer to the BCCDC website for reporting guidelines.[1] Events can be reported even when there is no certainty of a causal association. Please refer to the Data Notes section at the end of this report for additional information on the source data.

Summary

The COVID-19 vaccines demonstrated safety in clinical trials prior to authorization for use and in worldwide use.[2-4] During post-marketing surveillance, larger numbers of individuals are vaccinated, and this allows for detection of rare events undetected in clinical trials.

Anaphylaxis and allergic events are the most frequently reported events following all of the COVID-19 vaccines. About half of the cases managed as anaphylaxis had lower level of diagnostic certainty and may reflect events such as anxiety or pre-syncopal (fainting) events managed as anaphylaxis out of an abundance of caution.

In association with the mRNA vaccines, Canada and BC are monitoring the occurrence of myocarditis and pericarditis. This association was first recognized in Israel and the USA in young adults and adolescents, and has now also been seen in other countries.[5-7,22,23]

There have been four reports of thrombosis with thrombocytopenia syndrome reported in BC to date in association with over 350,000 doses of the ChAdOx1 (chimpanzee adenovirus vector vaccines AstraZeneca/COVISHIELD) administered. This syndrome was identified in March in Europe in association with the AstraZeneca vaccine, with a small number of cases accumulating in Canada associated with use of these vaccines; the rate of occurrence has been estimated at about 1 in 67,000 recipients following the first dose and 1 in 500,000 following the second dose.[8,9,22]

Background

AEFIs are reportable by health care providers to the local medical health officer under the regulations of the Public Health Act. Detailed reporting guidelines are available in the BC Immunization Manual.[10] When an AEFI report is received at a local public health unit, it is reviewed and reported in the public health information system aligned with the immunization registry which contains the information about the vaccine(s) administered on a specific date. Recommendations for further assessment and future doses are made by the medical health officer or designated public health professional. Expected side effects such as pain, redness, and swelling at the injection site which are commonly observed with many vaccines are not reportable as AEFI unless these meet specific severity thresholds.

AEFI reports are further investigated provincially with particular focus on serious AEFI and detection of potential safety signals (e.g., clusters of events, event rates occurring at a higher than expected frequency compared to background rates, or rare events with previously unknown association with vaccination). Additionally, BC submits AEFI reports to the Canadian Adverse Event Following Immunization Surveillance System where additional review and analysis for potential safety signals is performed at the national level.[11] The Public Health Agency of Canada also produces a weekly COVID-19 AEFI report.[12]

Definitions

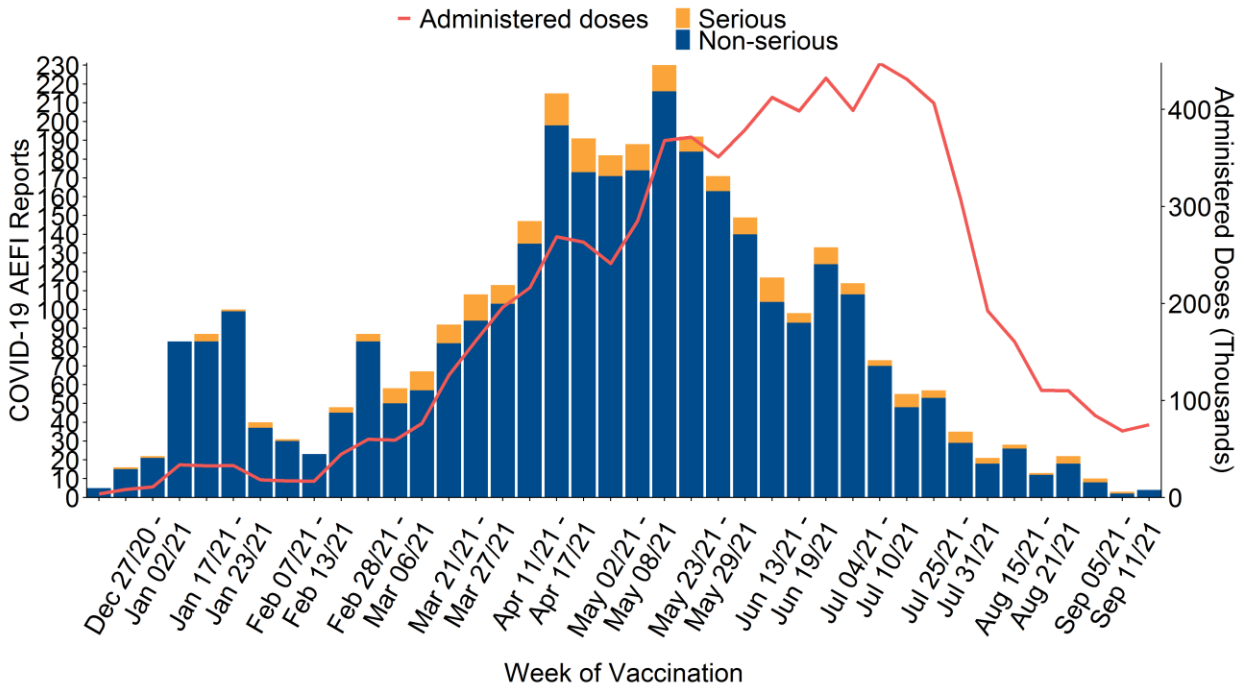
1. **Adverse event following immunization (AEFI)** - Any untoward medical event following immunization that is temporally (i.e., occurs within a biologically plausible timeframe after receipt of vaccine) but not necessarily causally associated.[13]
2. **Serious AEFI** - For the purpose of this report, a serious AEFI is one that resulted in hospitalization or a prolongation of hospitalization, permanent disability/incapacity, or death.

Key Findings

- As of September 18, 2021, there have been 7,679,036 COVID-19 vaccine doses administered in BC and 3,428 COVID-19 AEFI reports (44.6 reports per 100,000 doses administered)
- 247 reports (7.2%) met the serious definition, for a rate of 3.2 per 100,000 doses administered
- The most frequently reported events were other allergic event, anaesthesia/paraesthesia, and injection site pain/swelling/redness

Summary of AEFI Reports

Figure 1: Adverse event reports following receipt of a COVID-19 vaccine by week of vaccination, BC, Dec. 13, 2020 - Sep. 18, 2021 **(N=3,428)**



COVID-19 vaccinations of British Columbians began the week of December 13, 2020, and up to and including September 18, 2021, a total of 7,679,036 doses have been administered. During this period, there have been 3,428 AEFI reports following a COVID-19 vaccine, for a reporting rate of 44.6 reports per 100,000 doses administered (Table 1). Reports are delayed beyond the week of vaccination because of time to onset that varies by event and associated time to receive, investigate and process a report for submission. Weekly report counts, especially for recent weeks, are expected to increase over time as these are submitted, but Figure 1 shows that reports have declined as the immunization campaign has progressed, even as the doses administered have continued to increase. This is because the AEFI reporting rate associated with second doses of all COVID-19 vaccines administered has been substantially lower than the rate associated with the first dose.

Table 1: Description of adverse event reports following receipt of a COVID-19 vaccine, BC, Dec. 13, 2020 - Sep. 18, 2021 **(N=3,428)**

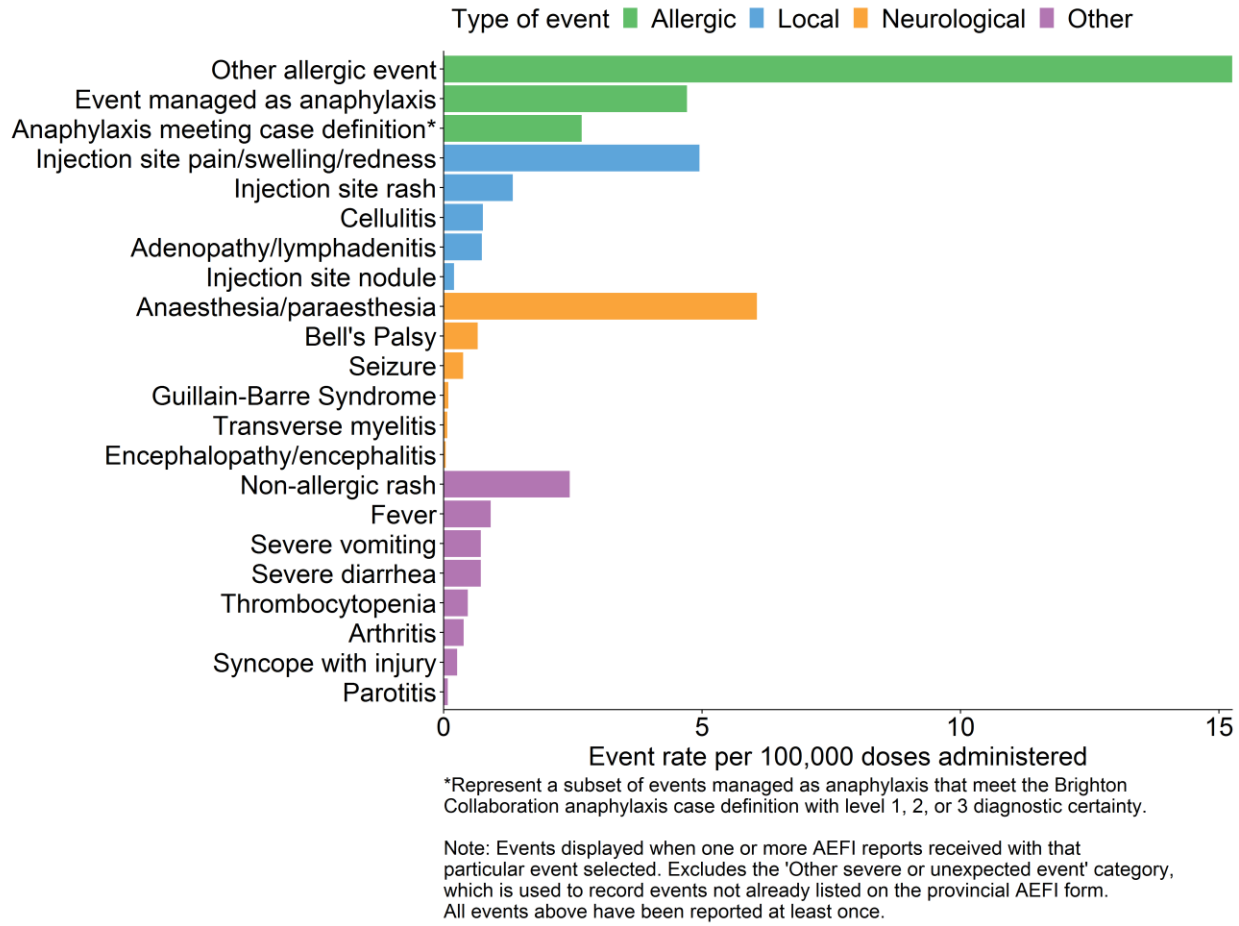
		COVID-19 Vaccine*			
	All COVID-19 Vaccines	**AstraZeneca**	**COVISHIELD**	**Moderna**	**Pfizer**
Total reports	**3428**	**246**	**66**	**1084**	**2032**
Non-serious reports	3181	218	60	1010	1893
Serious reports	247	28	6	74	139
Proportion serious	7.2%	11.4%	9.1%	6.8%	6.8%
Dose 1 reports	2781	222	65	862	1632
Dose 2 reports	645	24	1	222	398
Total doses administered	**7,679,036**	**323,979**	**67,434**	**1,883,353**	**5,404,270**
Dose 1 administered	4,175,758	222,561	59,116	979,744	2,914,337
Dose 2 administered	3,503,278	101,418	8,318	903,609	2,489,933
Total reporting rate	**44.6**	**75.9**	**97.9**	**57.6**	**37.6**
Serious rate	3.2	8.6	8.9	3.9	2.6
Dose 1 rate	66.6	99.7	110.0	88.0	56.0
Dose 2 rate	18.4	23.7	12.0	24.6	16.0

Note: Rates calculated per 100,000 doses administered

Summary of Reported Events

A single AEFI report may contain one or more adverse events. Reported events are temporally associated with vaccination (i.e., occur after vaccination within a biologically plausible timeframe) but not necessarily causally associated. The 3,428 AEFI reports received up to September 18, 2021 contained a total of 4,332 adverse events for a ratio of 1.3 events per COVID-19 AEFI report. The most frequently reported events were other allergic events (e.g., allergic rash, hives, pruritus, and gastrointestinal symptoms), anaesthesia/paraesthesia, and events managed as anaphylaxis (Figure 2).

Figure 2: Adverse events following receipt of a COVID-19 vaccine, British Columbia, Dec. 13, 2020 - Sep. 18, 2021 **(N=4,332)**



Event Descriptions

Three hundred sixty-two reports were received for events managed as anaphylaxis (i.e., the client received epinephrine for a suspected anaphylactic reaction). Of these, 205 (57%) met the Brighton Collaboration definition for anaphylaxis with diagnostic certainty levels of 1, 2, or 3.[14] Upon further review of these reports, many may reflect events such as anxiety or pre-syncopal (fainting) events.

Fifty-eight reports of cellulitis were received. Although most of these reports specified that antibiotics were provided, many appeared to represent a delayed onset local inflammatory reaction, a reaction described by “others”, rather than cellulitis.[15]

Ninety-nine reports contained a diagnosed neurological event. Fifty-one individuals experienced Bell’s palsy within 30 days following COVID-19 vaccination. Three individuals were admitted to hospital and diagnosed with transverse myelitis, including one with a history of multiple sclerosis. An additional two individuals were reported as having transverse myelitis, however, one had a clinical diagnosis unconfirmed by diagnostic imaging and the other’s workup was inconsistent with transverse myelitis. Twenty-nine individuals were reported with

seizures, including 13 with a history of a seizure disorder. Three individuals were admitted to hospital for an intracerebral hemorrhage, one of whom had a subsequent encephalopathy. One individual was hospitalized for aseptic meningitis and another for encephalitis presumed to be viral in nature. One individual developed encephalopathy attributed to a workplace toxin exposure and was hospitalized; this event was reported because of its coincidental temporal association to COVID-19 vaccine receipt. There were seven reports for individuals hospitalized with Guillain-Barre Syndrome (GBS), now all discharged. Three of these reports followed AstraZeneca vaccine. A possible infectious cause of GBS was not identified in five cases but followed an illness compatible with recent infection of unknown cause for the other two cases. GBS cases following COVID-19 vaccines have been identified in Canada and internationally, but rarely.[12,16,17] Finally, there have been three reports of sudden hearing loss verified by audiology testing. Two individuals had a sensorineural hearing loss (SNHL), and the other had either sensorineural or conductive hearing loss. Two individuals recovered their hearing with treatment and the third individual's hearing was still improving at the time of this report. One U.S. study has looked at an association between COVID-19 vaccines and SNHL and found rates after vaccination did not exceed background rates in the general population.[18]

There were 36 reports of thrombocytopenia without concurrent thrombosis. Two occurred in individuals with a single low platelet count followed subsequently by normal results; in both, the low platelet counts were assessed as due to laboratory error. The majority of reports were in individuals who had a previous history of thrombocytopenia or who had a concurrent condition (e.g., known infection, sepsis, cancer) or medication associated with thrombocytopenia. There were eleven reports of idiopathic thrombocytopenia (i.e., thrombocytopenia without a known cause). Seven of these were following the AstraZeneca vaccine, and in one case, the individual tested positive for the anti-platelet factor 4 antibody often observed with TTS. This individual did not meet the TTS definition as they had no signs or symptoms of thrombosis, and all imaging studies for a thrombus/thromboembolism were negative.7,8

Serious events:
Two hundred forty-seven reports (7.2%), including some of the events described above, were considered **serious** (refer to serious AEFI definition above). Of these, 231 individuals were admitted to hospital. These included 13 individuals hospitalized after anaphylaxis, 107 for circulatory system events (including 24 for stroke, 19 for pulmonary embolism, 15 for myocardial infarction, 47 for myopericarditis, and two for an arrhythmia), 21 for a neurological diagnosis (including three for transverse myelitis, six for seizure, two intracerebral hemorrhage with one associated encephalopathy, another separate encephalopathy, one encephalitis, one meningitis, and seven Guillain-Barre Syndrome), and 3 for a respiratory condition (one respiratory distress, and two for exacerbation of idiopathic pulmonary fibrosis). Two hospitalizations occurred for rhabdomyolysis, one of which was also suspected of having myocarditis. One hospitalization each occurred for a pregnancy related complication, and capillary leak syndrome. Nineteen hospitalizations were for thrombocytopenia alone or associated with a concurrent condition, of which four were for thrombosis with

thrombocytopenia syndrome (described further below). The remaining reports were for individuals who were hospitalized for monitoring of allergic, neurological, or cardiac symptoms but without a medically diagnosed event.

Death is reportable as an adverse event when it occurs within 30 days of vaccination and no other clear cause of death has been established.[10] Death may also be recorded as the outcome of a specific reportable event. Sixteen serious AEFI reports were received for individuals who died within 30 days of receiving a COVID-19 vaccine.

- For five of the deaths, vaccination was not considered to be a contributing factor by the health care provider or coroner who attended and investigated the death and considered the individuals' medical history.
- One death occurred in a long term care resident following deterioration with reduction in oral intake, without a clear underlying cause of death identified.
- In six individuals, death was the outcome of cardiac arrest. Five of these were elderly individuals, many with multiple underlying medical conditions, while the other had cardiac risk factors and was hospitalized for a myocardial infarction.
- Two deaths occurred in elderly individuals following a stroke and hospital admission. Both had previous history of stroke along with other medical conditions.
- One death occurred in an individual with metastatic cancer who had been hospitalized for complications of thrombocytopenia and hemolytic anemia.
- One death occurred in an elderly individual who suffered from multiple serious comorbidities, with completion of a coroner's investigation pending.

'Other serious' events:

Some events may be reported as an "other serious" event when they do not have their own discrete event on the provincial AEFI report form. These are outlined in this section; some of these events have been described above in the **serious events** section. Amongst these events, 113 were for various thrombotic/ thromboembolic conditions. These included 25 strokes and one cerebral venous sinus thrombosis without thrombocytopenia (i.e., not a TTS case), 15 myocardial infarctions, 29 pulmonary emboli, 36 deep vein thromboses, and seven superficial vein thromboses. None of these events met the TTS criteria as none were associated with new onset thrombocytopenia.[8,9]

One "other serious" report was received for an individual with capillary leak syndrome with onset five weeks after AstraZeneca vaccine. Capillary leak syndrome is a very rare condition associated with the AstraZeneca vaccine. By June 2021 only six cases had been identified in Europe following over 78 million doses of AstraZeneca vaccine administered.[19] Health Canada has issued an advisory for this condition and its association with AstraZeneca/COVISHIELD vaccines.[20]

There have been four non-fatal confirmed cases of TTS reported in BC to date, three of which were adults in their 30s or 40s and the fourth was in their 60s. The first had onset four days

after receipt of the AstraZeneca vaccine with a low platelet count found upon presentation for care, and a diagnosis of pulmonary embolism. The second case had abdominal symptoms that progressed the week after receiving the AstraZeneca vaccine, with a diagnosis of abdominal venous thrombus and thrombocytopenia. The third case also had symptoms develop in the week after AstraZeneca vaccine. Upon presentation to care, thrombocytopenia was detected. The individual was assessed for possible TTS, and identification of an abdominal venous thrombus was made in hospital. All three of these individuals followed the first dose of AstraZeneca and had a positive anti-platelet factor 4 antibody test. The fourth individual suffered a stroke a week after the second dose of the AstraZeneca vaccine. Thrombocytopenia was identified in hospital; the anti-platelet factor 4 antibody test was negative.

There have been 97 reports of pericarditis/myocarditis. Forty-nine individuals were diagnosed with pericarditis alone, twenty with myocarditis alone, and 28 with myopericarditis. Ages ranged from 14 to 95 with a median of 40.4 years, and 63 were male. Thirty-six had received Moderna vaccine, 55 received Pfizer vaccine, and six received AstraZeneca/COVISHIELD. Forty-six of these events occurred after a second dose (22 Pfizer and 23 Moderna). Some had alternate explanations including rheumatic diseases or a genetic syndrome associated with cardiac disorders. Eighteen (out of 20) of the myocarditis cases met the diagnostic criteria for level 1, 2, or 3 of the Brighton Collaboration case definition. Twenty-three (out of 49) pericarditis cases met the diagnostic criteria for level 1, 2, or 3 of the Brighton Collaboration case definition. Eighteen (out of 28) myopericarditis cases met the diagnostic criteria for level 1, 2, or 3 of the Brighton Collaboration case definition for either myocarditis or pericarditis.[21] These conditions are being investigated as a possible safety signal after mRNA vaccines, with an association seen in several countries including the US and UK as well as in Ontario, especially in adolescent and young adult males and with the 2nd dose.[5-7,12]

Table 2: Number of Myocarditis/Pericarditis reports following receipt of an mRNA COVID-19 vaccine, British Columbia, Dec.13, 2020 – Sep. 18, 2021 **(N=91)**

Vaccine / Dose		Age (years)					
		12-17	18-24	25-29	30-39	40+	All Ages
Moderna mRNA-1273	**N (% Total)**	**0**	**9 (9.9%)**	**6 (6.6%)**	**8 (8.8%)**	**13 (14.3%)**	**36 (39.6%)**
Dose 1	N (% Total)	0	2 (2.2%)	2 (2.2%)	4 (4.4%)	5 (5.5%)	13 (14.3%)
Dose 2	N (% Total)	0	7 (7.7%)	4 (4.4%)	4 (4.4%)	8 (8.8%)	23 (25.3%)
Pfizer mRNA BNT162b2	**N (% Total)**	**9 (9.9%)**	**10 (11%)**	**3 (3.3%)**	**9 (9.9%)**	**24 (26.4%)**	**55 (60.4%)**
Dose 1	N (% Total)	5 (5.5%)	3 (3.3%)	1 (1.1%)	7 (7.7%)	17 (18.7%)	33 (36.3%)
Dose 2	N (% Total)	4 (4.4%)	7 (7.7%)	2 (2.2%)	2 (2.2%)	7 (7.7%)	22 (24.2%)
Total	**N (% Total)**	**9 (9.9%)**	**19 (20.9%)**	**9 (9.9%)**	**17 (18.7%)**	**37 (40.7%)**	**91 (100%)**

Data Notes

Data on COVID-19 AEFI reports and doses administered were extracted from Panorama, the provincial public health information system, on September 22, 2021. Only AEFIs reported and doses administered up to September 18, 2021 were included in this report. Any AEFI report with a status of “Does not meet reporting criteria” or “Disregard - Entered in error” was excluded.

Delays exist between the time an AEFI occurs, is reported to public health, and is entered into Panorama. As AEFI investigations progress from draft version to being submitted for review and finally completed, there may be changes to the data, or reports may be removed from analysis if reflective of events that are not reportable (e.g., expected local reaction). This may lead to fluctuations in AEFI counts and rates, and subsequent weekly reports cannot be directly compared to previous reports of AEFI reported in BC.

References

1. BC Centre for Disease Control. Adverse events following immunization [Internet]; 2021 [cited 2021 Mar 23]. Available from: http://www.bccdc.ca/health-professionals/clinical-resources/adverse-events-following-immunization
2. Wollersheim S. Vaccines and Related Biological Products Advisory Committee December 10, 2020 Presentation - FDA Review of Efficacy and Safety of Pfizer-BioNTech COVID-19 Vaccine Emergency Use Authorization Request; 2020 Dec 10. Available from: https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-december-10-2020-meeting-announcement
3. Zhang R. Vaccines and Related Biological Products Advisory Committee December 17, 2020 Meeting Presentation - FDA Review of Efficacy and Safety of Moderna COVID-19 Vaccine EUA; 2020 Dec 17. Available from: https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-december-17-2020-meeting-announcement
4. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Weekly summary: adverse events following immunization (AEFIs) for COVID-19 in Ontario [Internet]. Toronto, ON: Queen's Printer for Ontario; 2021 [cited 2021 Apr 7]. Available from: https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-aefi-report.pdf?la=en
5. World Health Organization. COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety (GACVS) reviews cases of mild myocarditis reported with COVID-19 mRNA vaccines [Internet]; 2021 [cited 2021 Jun 2]. Available from: https://www.who.int/news/item/26-05-2021-gacvs-myocarditis-reported-with-covid-19-mrna-vaccines
6. Centers for Disease Control and Prevention. Myocarditis and Pericarditis Following mRNA COVID-19 Vaccination [Internet]; 2021 [cited 2021 Jun 2]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html
7. Shimabukuro, T. Update on COVID-19 vaccine safety, including myocarditis after mRNA vaccines. Presentation to the US Advisory Committee on Immunization Practices. June 23, 2021 [Internet]; 2021 [cited 2021 Jun 30]. Available from: https://www.cdc.gov/vaccines/acip/meetings/slides-2021-06.html
8. Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. N Engl J Med. 2021. Available from: https://www.nejm.org/doi/full/10.1056/NEJMoa2104840
9. Brighton Collaboration. Case finding definition of thrombosis with thrombocytopenia syndrome (TTS) v9.0 [Internet]; 2021 [cited 2021 Apr 21]. Available from: https://brightoncollaboration.us/thrombosis-with-thrombocytopenia-syndrome-case-finding-definition/
10. BC Centre for Disease Control. Communicable disease control manual. Chapter 2: Immunization. Part 5 - Adverse events following immunization [Internet]; 2019 [cited 2021 Mar 23]. Available from: http://www.bccdc.ca/resource-

gallery/Documents/Guidelines%20and%20Forms/Guidelines%20and%20Manuals/Epid/CD%20Manual/Chapter%202%20-%20Imms/Part_5_AEFI.pdf

11. Government of Canada. Canadian adverse events following immunization surveillance system (CAEFISS) [Internet]; 2019 [cited 2021 Mar 23]. Available from: https://www.canada.ca/en/public-health/services/immunization/canadian-adverse-events-following-immunization-surveillance-system-caefiss.html
12. Government of Canada. Reported side effects following COVID-19 vaccination in Canada [Internet]; 2021 [cited 2021 Mar 23]. Available from: https://health-infobase.canada.ca/covid-19/vaccine-safety/
13. Council for International Organizations of Medical Sciences (CIOMS). Definition and application of terms for vaccine pharmacovigilance [Internet]. Geneva, Switzerland: WHO Press; 2012 [cited 2021 Mar 23]. Available from: https://vaccine-safety-training.org/tl_files/vs/pdf/report-of-cioms-who-working-group.pdf
14. Ruggeberg JU, Gold MS, Bayas J-M, Blum MD, Bonhoeffer J, Friedlander S, et al. Anaphylaxis: case definition and guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine. 2007;25(31):5675-84. Available from: https://doi.org/10.1016/j.vaccine.2007.02.064
15. Blumenthal KG, Freeman EE, Staff RR, Robinson LB, Wolfson AR, Foreman RK, et al. Delayed large local reactions to mRNA-1273 vaccine against SARS-CoV-2. N Eng J Med. 2021;384(13). Available from: https://www.nejm.org/doi/full/10.1056/NEJMc2102131
16. Patel SU, Khurram R, Lakhani A, Quirk B. Guillain-Barre syndrome following the first dose of the chimpanzee adenovirus-vectored COVID-19 vaccine, ChAdOx1. BMJ Case Rep. 2021;14:e242956. Available from: https://casereports.bmj.com/content/bmjcr/14/4/e242956.full.pdf
17. Waheed S, Bayas A, Hindi F, Rizvi Z, Espinosa PS. Neurological complications of COVID-19: Guillain-Barre Syndrome following Pfizer COVID-19 vaccine. Cureus. 2021;13(2):e13426. Available from: https://www.cureus.com/articles/52295-neurological-complications-of-covid-19-guillain-barre-syndrome-following-pfizer-covid-19-vaccine
18. Formeister EJ, Chien W, Agrawal Y, Carey JP, Stewart CM, Sun DQ. Preliminary analysis of association between COVID-19 vaccination and sudden hearing loss using US Centers for Disease Control and Prevention Vaccine Adverse Events Reporting System data. JAMA Otolaryngol Head Neck Surg. 2021;147(7):674-676. Available from: https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2780288
19. European Medicines Agency. Vaxzevria: EMA advises against use in people with history of capillary leak syndrome [Internet]; 2021 [cited 2021 Jun 23]. Available from: https://www.ema.europa.eu/en/news/vaxzevria-ema-advises-against-use-people-history-capillary-leak-syndrome
20. Health Canada. AstraZeneca COVID-19 vaccine and COVIDSHIELD: risk of capillary leak syndrome [Internet]; 2021 [cited 2021 Jun 30]. Available from: https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2021/75947a-eng.php

21. Brighton Collaboration. Draft myocarditis case definition (version_1.4.2_30.May.2021) [Internet]; 2021 [cited 2021 Jun 2]. Available from: https://brightoncollaboration.us/myocarditis-case-definition-update/
22. Government of the United Kingdom. Medicines & Healthcare Products Regulatory Agency. Coronavirus vaccine - weekly summary of Yellow Card reporting. [Internet]; 2021 [cited 2021 Aug 5]. Available from: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting
23. European Medicines Agency. Meeting Highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 5-8 July 2021. [Internet]; 2021 [cited 2021 Aug 19]. Available from: https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-5-8-july-2021