British Columbia Report

Adverse Events Following Immunization with COVID-19 Vaccines

December 13, 2020 to July 24, 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 July 24, 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

No safety signals have been identified in association with the mRNA reports received in BC to date. These vaccines have demonstrated safety in clinical trials prior to authorization for use and in worldwide use.[2-4] BC is reporting higher rates of anaphylaxis than many other Canadian jurisdictions, but about half of these had lower level of diagnostic certainty and may reflect events such as anxiety or pre-syncopal (fainting) events, which are nevertheless managed as anaphylaxis out of an abundance of caution, and reported thereafter. Serious events have not been reported at rates higher than expected compared to background rates. Canada and BC are monitoring the occurrence of myocarditis and pericarditis following recognition of an association with mRNA vaccines in the USA in young adults and adolescents.[5-7]

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; three of these meet the definition of '. 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 at rates of about 1 in 50,000 to 1 in 100,000 recipients.[8,9]

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

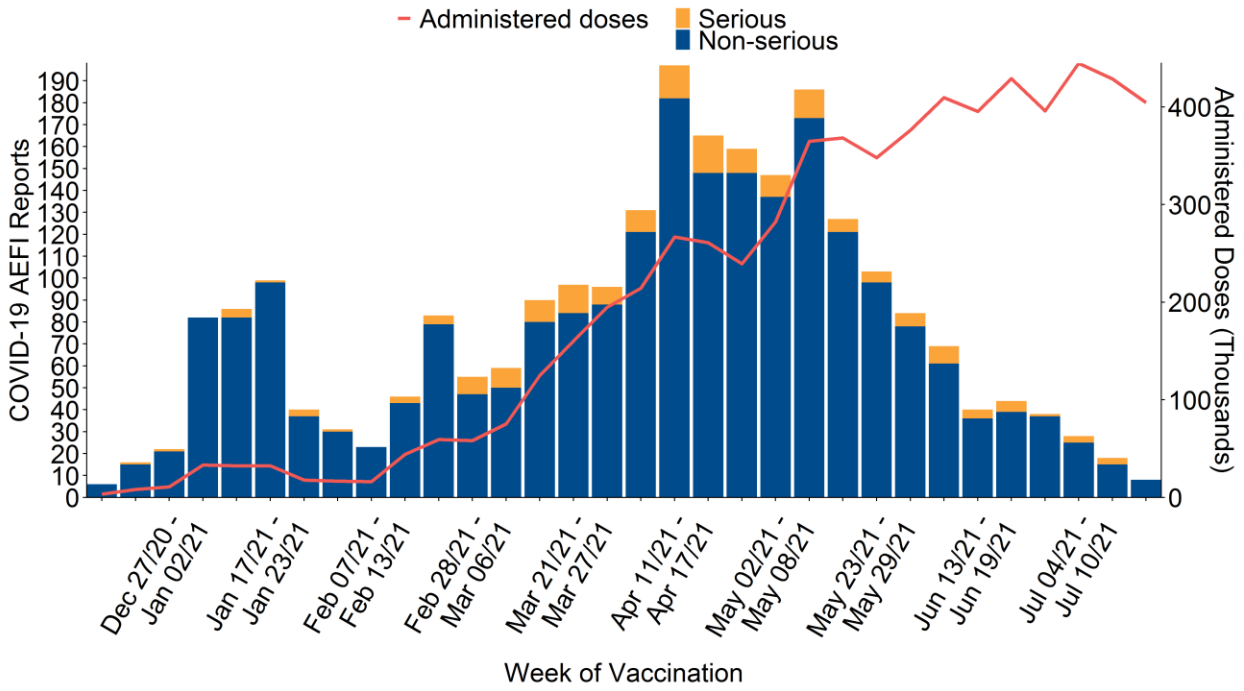
1. **Adverse event following immunization (AEFI)** - Any untoward medical event following immunization that is temporally (i.e., occurs within a biologically plausible timeframe after receipt of vaccine) but not necessarily causally associated.[13]
2. **Serious AEFI** - For the purpose of this report,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

Key Findings

- As of July 24, 2021, there have been 6,515,885 COVID-19 vaccine doses administered in BC and 2,475 COVID-19 AEFI reports (38.0 reports per 100,000 doses administered)
- 183 reports (7.4%) met the serious definition, for a rate of 2.8 per 100,000 doses administered
- The most frequently reported events were other allergic event, anaesthesia/paraesthesia, and event managed as anaphylaxis

Summary of AEFI Reports

Figure 1: Adverse event reports following receipt of a COVID-19 vaccine by week of vaccination, BC, Dec. 13, 2020 - Jul. 24, 2021 **(N=2,475)**



COVID-19 vaccinations of British Columbians began the week of December 13, 2020, and up to and including July 24, 2021, a total of 6,515,885 doses have been administered. During this period, there have been 2,475 AEFI reports following a COVID-19 vaccine, for a reporting rate of 38 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.

Table 1: Description of adverse event reports following receipt of a COVID-19 vaccine, BC, Dec. 13, 2020 - Jul. 24, 2021 **(N=2,475)**

		COVID-19 Vaccine*			
	All COVID-19 Vaccines	**AstraZeneca**	**COVISHIELD**	**Moderna**	**Pfizer**
Total reports	**2,475**	**210**	**63**	**744**	**1,457**
Non-serious reports	2,292	187	58	693	1,353
Serious reports	183	23	5	51	104
Proportion serious	7.4%	11%	7.9%	6.9%	7.1%

	COVID-19 Vaccine*				
	All COVID-19 Vaccines	**AstraZeneca**	**COVISHIELD**	**Moderna**	**Pfizer**
Dose 1 reports	2,153	202	62	637	1,251
Dose 2 reports	319	8	1	107	203
Total doses administered	**6,515,885**	**317,007**	**67,631**	**1,551,979**	**4,579,268**
Dose 1 administered	3,879,100	218,040	59,863	870,717	2,730,480
Dose 2 administered	2,636,785	98,967	7,768	681,262	1,848,788
Total reporting rate	**38.0**	**66.2**	**93.2**	**47.9**	**31.8**
Serious rate	2.8	7.3	7.4	3.3	2.3
Dose 1 rate	55.5	92.6	103.6	73.2	45.8
Dose 2 rate	12.1	8.1	12.9	15.7	11.0

Note: Rates calculated per 100,000 doses administered
* Some reports had an unspecified COVID-19 vaccine (n=1). Therefore, the total reports for all COVID-19 vaccines do not equal the sum of reports for each specific vaccine

Serious Reports

One hundred eighty-three reports (7.4%) were considered serious (refer to serious AEFI definition above). Of these, 170 individuals were admitted to hospital. These included 14 individuals hospitalized after anaphylaxis, 39 for a neurological diagnosis (including three for transverse myelitis, six for seizure, 20 for stroke, two intracerebral hemorrhage with one associated encephalopathy, another separate encephalopathy, one encephalitis, one meningitis, and five Guillain-Barre Syndrome), 37 for cardiac events (including 14 for myocardial infarction, 20 for myopericarditis, and three for an arrhythmia), and 16 for a respiratory condition (14 pulmonary embolism, one respiratory distress, and one for exacerbation of idiopathic pulmonary fibrosis). One hospitalization each occurred for a pregnancy related complication, capillary leak syndrome, and rhabdomyolysis. Eleven hospitalizations were for thrombocytopenia alone or associated with a concurrent condition, and 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.

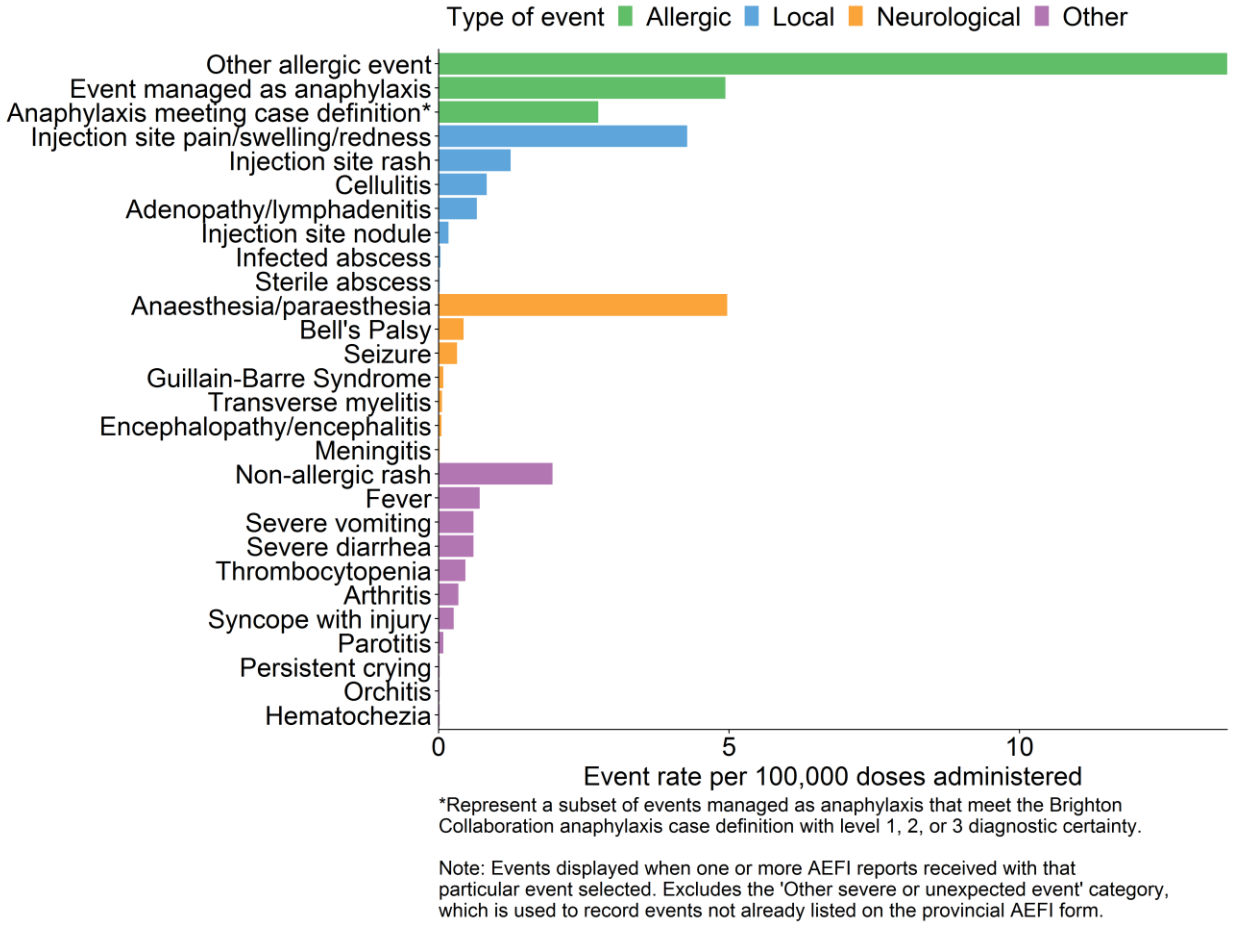
Death is reportable as an adverse event when it occurs within 30 days of vaccination and no other clear cause of death has been established.[10] Death may also be recorded as the outcome of a specific reportable event. Fourteen serious AEFI reports were received for individuals who died within 30 days of receiving a COVID-19 vaccine. For two of the deaths, vaccination was not considered to be a contributing factor by health care providers who attended and investigated the death based on the individuals' medical history. Two deaths occurred in elderly individuals with underlying medical conditions; the coroner deemed these deaths not unexpected and further investigation into the cause of death was not conducted. Another death occurred in a long term care resident following deterioration with reduction in oral intake, without a clear underlying cause of death identified.

For 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. Finally, one death occurred in an individual with metastatic cancer who had been hospitalized for complications of thrombocytopenia and hemolytic anemia.

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 2,475 AEFI reports received up to July 24, 2021 contained a total of 3,162 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 - Jul. 24, 2021 **(N=3,162)**



*Represent a subset of events managed as anaphylaxis that meet the Brighton Collaboration anaphylaxis case definition with level 1, 2, or 3 diagnostic certainty.

Note: Events displayed when one or more AEFI reports received with that particular event selected. Excludes the 'Other severe or unexpected event' category, which is used to record events not already listed on the provincial AEFI form.

Event Descriptions

Three hundred twenty-two reports were received for events managed as anaphylaxis (i.e., the client received epinephrine for a suspected anaphylactic reaction). Of these, 179 (56%) 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-four 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 rather than cellulitis, a reaction described by others.[15] None of these reports were confirmed by microbial testing.

Sixty-six reports contained a diagnosed neurological event. Twenty-eight 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. One additional individual was investigated for transverse myelitis with a diagnosis made by clinical findings but not confirmed through diagnostic imaging. Twenty-one individuals reported seizures, including 13 with a history of a seizure disorder. Two 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 possibly related to a recent toxin exposure and was hospitalized. There were five reports for individuals hospitalized with Guillain-Barre Syndrome (GBS) who have since been discharged. Three of these reports followed AstraZeneca vaccine. A possible infectious cause of GBS was not identified in three cases but followed a 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 26 reports of thrombocytopenia without concurrent thrombosis. Two occurred in individuals with a single low platelet result followed subsequently by normal results; in both the low platelet counts were assessed as due to lab 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 nine reports of idiopathic thrombocytopenia (i.e., thrombocytopenia without a known cause). Six 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]

Some events may be reported as an "other serious" event when not its own discrete event on the provincial AEFI report form. Amongst these events, 87 were for various thrombotic/ thromboembolic conditions. These included 21 strokes and one cerebral venous sinus thrombosis without thrombocytopenia (i.e., not a TTS case), 14 myocardial infarctions, 18 pulmonary embolisms, 28 deep vein thromboses, and six 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. The individual has since been discharged after being treated in hospital. 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 46 reports of pericarditis/myocarditis. Twenty-three individuals had a diagnosis of pericarditis alone, six had myocarditis, and 17 had myopericarditis. Ages ranged from 16 to 95 with a median of 44.5 years, and 25 were male. Eighteen had received Moderna vaccine, 24 had Pfizer vaccine, and four had AstraZeneca/COVISHIELD; sixteen of the events occurred after a second dose (six Pfizer and ten Moderna). Some had alternate explanations including rheumatic diseases or genetic syndrome associated with cardiac disorders. Three met the diagnostic criteria to be considered a definite case of myocarditis according to the Brighton Collaboration myocarditis case definition, while 22 were either not a case or had insufficient details to be assigned a level.[21] Myopericarditis is 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.[4-7,12,22]

Data Notes

Data on COVID-19 AEFI reports and doses administered were extracted from Panorama, the provincial public health information system, on July 28, 2021. Only AEFIs reported and doses administered up to July 24, 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.

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