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Enhanced Epidemiological Summary

Reports of events managed as anaphylaxis following COVID-19 vaccines in Ontario: December 13, 2020 to March 6, 2021

The report provides a summary of adverse events following immunization (AEFIs) managed as anaphylaxis that occurred following a COVID-19 vaccine and meet the provincial surveillance definition (i.e., confirmed).[1]

> Anaphylaxis is a rare but potentially life-threatening allergic reaction that is treatable with rapid recognition and management. It is a clinical syndrome characterized by sudden onset, rapid progression of signs and symptoms and involvement of multiple (two or more) organ systems.[1]

This epidemiologic summary describes AEFIs reported in the Public Health Case and Contact Management Solution (CCM) as of March 6, 2021. Vaccine doses administered up to and including March 6, 2021 were obtained from the Ministry of Health's COVID-19 webpage and from the $COVax_{ON}$ dashboard.[2] For a summary of all AEFIs associated with receipt of COVID-19 vaccines and more details on Ontario's vaccine safety surveillance system, please see Public Health Ontario's COVID-19 AEFI weekly summary.[3]

Brighton Collaboration definition

All reports of anaphylaxis that meet the provincial surveillance definition for 'events managed as anaphylaxis' are further assessed using the Brighton Collaboration case definition, which is an internationally recognized standard case definition for anaphylaxis following vaccination.[4] The Brighton Collaboration case definition for anaphylaxis is divided into levels of diagnostic certainty from level one to three, with level one being the most specific for the condition.[4] In this epidemiologic summary, only those reports that include sufficient clinical information required to conduct an assessment have been assigned a Brighton Collaboration level of diagnostic certainty. Some reports that meet the provincial surveillance definition of events managed as anaphylaxis may not meet Brighton Collaboration levels one to three of diagnostic certainty.

This epidemiologic summary describes all events managed as anaphylaxis that meet the provincial surveillance definition. Those reports that meet the Brighton Collaboration level of diagnostic certainty one to three are highlighted in Table 1.

Summary of reports

- A total of 665 AEFI reports (all event types) were received following 890,604 doses of COVID-19 vaccines administered in Ontario over the period of December 13, 2020 to March 6, 2021, for a reporting rate of 74.7 per 100,000 doses administered

- Among the 665 confirmed AEFI reports, there were 33 confirmed reports of events managed as anaphylaxis (5.0% of all AEFI reports)
    - Anaphylaxis has been associated with 0.004% of all COVID-19 vaccine doses administered in Ontario, representing a reporting rate of 37.1 per million doses of vaccine administered
- For the 33 confirmed reports of events managed as anaphylaxis:
    - 28 were reported after receipt of the Pfizer-BioNTech COVID-19 vaccine (84.8%)
    - Five were reported after receipt of the Moderna COVID-19 vaccine (15.2%)
    - One report was confirmed but still under investigation and could not be assessed using Brighton Collaboration criteria. The remaining 32 reports were assessed using the Brighton Collaboration standard case definition of anaphylaxis. Of the 32 reports:
        - Ten met Brighton definition at level 1 of diagnostic certainty (31.3%)
        - Five met Brighton definition at level 2 of diagnostic certainty (15.6%)
        - 17 reports had sufficient clinical information but did not meet Brighton Collaboration level of diagnostic certainty one, two or three (53.1%)

Table 1. Summary of reports of events managed as anaphylaxis received in Ontario, December 13, 2020 to March 6, 2021

	Pfizer-BioNTech	Moderna	All products combined
Doses administered	737,728	152,876	890,604
Reports of events managed as anaphylaxis that meet Brighton Collaboration case definition levels 1, 2 or 3			
Number of reports	14	1	15
Anaphylaxis reporting rate per 100,000 doses administered	1.9	0.7	1.7
Anaphylaxis reporting rate per million doses administered	19.0	6.5	16.8
All reports of events managed as anaphylaxis regardless of Brighton Collaboration case definition level			
Number of reports	28	5	33

	Pfizer-BioNTech	Moderna	All products combined
Anaphylaxis reporting rate per 100,000 doses administered	3.8	3.3	3.7
Anaphylaxis reporting rate per million doses administered	38.0	32.7	37.1

Note: The Brighton Collaboration case definition for anaphylaxis is divided into levels of diagnostic certainty from level one to three, with level one being the most specific for the condition.[4]
Data Source: CCM, MOH webpage, COVaxON dashboard (see technical notes for details on data sources)

Report Characteristics

Among the 33 confirmed reports of anaphylaxis (see Table 2 for details on each report of anaphylaxis):

- **Gender**: 29 females (87.9%) and three males (9.1%); one had unknown gender (3.0%)
- **Age**: Age at vaccine administration ranged from 25 years to 100 years (median 49 years)
    - 28 individuals in the 18-64 year age group (84.8%)
    - Five individuals in the 65+ year age group (15.2%)
- **Healthcare utilization**: Four required in-patient hospitalization as well as a visit to the emergency department (ED) (12.1%), 23 involved a visit to the ED without in-patient hospitalization (69.7%), and six did not report either ED visit or hospitalization (18.2%)
- **Treatment**: 29 received epinephrine (87.9%)
- **Onset after receipt of vaccine**: 32 reports had known time between vaccine administration and onset of symptoms. Of the 32 reports, time between vaccine administration and onset of symptoms ranged from 2 minutes to 180 minutes, with 21 occurring in 15 minutes or less (65.6%)
- **Outcome**: 32 individuals were fully recovered (97.0%) and one individual (3.0%) was still hospitalized at the time of reporting
- **Past history of allergies**: 23 (69.7%) reported either a history of allergies and/or a history of previous anaphylaxis (e.g., food, drugs, other vaccines, other common allergens, etc.); of the 23 reports, nine individuals reported a history of previous anaphylaxis occurrence.

Anaphylaxis reporting rates for comparison

- The Canadian immunization guide reports that anaphylaxis has been causally associated with vaccines with an estimated frequency of 1.3 episodes per million doses of vaccine administered.[5]

- In 2018, there were ten reports of anaphylaxis reported as AEFIs in Ontario for all vaccines. Of those, five were after receipt of influenza vaccine at a rate of 1.2 per million doses distributed.[6] Vaccine safety surveillance data in Ontario between 2012 and 2019 are available from Public Health Ontario's Vaccine Safety Surveillance Tool.[7]

Anaphylaxis reporting rates specific to COVID-19 vaccines

- As of February 26, 2021, 46 reports of anaphylaxis following COVID-19 vaccines were reported to the Canadian Adverse Event Following Immunization Surveillance System (CAEFISS) in relation to 1,778,405 doses administered, for a reporting rate of 25.9 per million doses administered.[8] Only reports with Brighton levels 1, 2 and 3 are included in the CAEFISS reporting dashboard.

- As of January 18, 2021, estimated anaphylaxis reporting rates following COVID-19 vaccines in the United States based on the Vaccine Adverse Event Reporting System (VAERS) data are 4.7 cases per million doses administered for the Pfizer-BioNTech vaccine and 2.5 per million doses administered for the Moderna vaccine.[9] Only reports with Brighton levels 1, 2 and 3 are included. All 66 cases were treated in health care settings: 52% in the emergency department and 48% were hospitalized (including 18 intensive care).

- As of February 28, 2021, an estimated 21 million doses of COVID-19 vaccines had been administered in the United Kingdom (UK) with 214 and 194 reports of anaphylaxis or "anaphylactoid" reactions associated with the Pfizer-BioNTech and AstraZeneca vaccines, respectively.[10] This represents a reporting rate of 19 per million doses administered.

- Differences in surveillance systems, case definitions, reporting practices, and clinical severity of anaphylaxis cases are all possible explanations for variability in the reporting rates for anaphylaxis between Ontario and CAEFISS, and international comparisons with the United States and the UK.

Conclusions

- As of March 6, 2021, there were 33 reports of events managed as anaphylaxis in Ontario that were temporally associated with receipt of COVID-19 vaccine. Of those, 15 reports met the Brighton Collaboration case definition levels 1, 2 or 3, representing a reporting rate of 16.8 reports per million doses administered.

- Ontario's anaphylaxis reporting rate is within the range observed in other jurisdictions and remains a rare event, having been associated with fewer than 0.004% of all doses administered in Ontario.

- Anaphylaxis is a recognized but rare adverse event that is treatable with rapid and appropriate management. Advance preparation for emergency management of anaphylaxis is essential. COVID-19 vaccines should be administered in a healthcare setting capable of managing anaphylaxis and vaccine recipients should be observed for a minimum of 15 minutes for possible AEFIs. Some groups of individuals with a history of significant allergic reaction and/or anaphylaxis should be observed for an extended period post-vaccination for up to 30 minutes.[11] The Canadian Immunization Guide outlines the process for assessment and initial management of anaphylaxis in vaccine recipients.[5]

Table 2. Characteristics of reports of events managed as anaphylaxis following COVID-19 vaccine in Ontario, December 13, 2020 to March 6, 2021

Vaccine	Lot number	Age group (y)	Healthcare Utilization	Epinephrine received	Brighton level	Onset after receipt (minutes)	History of allergies	History of anaphylaxis
Mod.	300042460	18-64	Hosp, ED	Y	1	11		Non-COVID-19 vaccine
PB	EK4241	18-64	ED	Y	1	10	Food, drugs	Non-COVID-19 vaccine
PB	EL0203	18-64	ED	Y	1	18	No history	
PB	EL1404	18-64	ED	Y	1	10	No history	
PB	EL1404	18-64		N	1	6		Household product, food
PB	EL1406	18-64	Hosp, ED	Y	1	5		Drugs
PB	Unknown	18-64	ED	Y	1	10		COVID-19 vaccine dose 1
PB	EP6017	18-64	ED	Y	1	15	Food, drugs, non-COVID-19 vaccine	
PB	EN1194	65+	ED	Y	1	60		Drugs
PB	EP6775	18-64	ED	Y	1	5	No history	
PB	EK4245	65+	ED	Y	2	25	Food, drugs	
PB	EL0203	18-64	ED	Y	2	10	Food, drugs	

Vaccine	Lot number	Age group (y)	Healthcare Utilization	Epinephrine received	Brighton level	Onset after receipt (minutes)	History of allergies	History of anaphylaxis
PB	EL0203	18-64	ED	Y	2	12	No history	
PB	EK4245	65+		Y	2	11	No history	
PB	EL0203	65+	ED	Y	2	180	Unknown	
PB	EK4241	18-64	ED	Y	D/M	15	Drugs	
PB	EK4241	18-64	ED	Y	D/M	35	Food, drugs	
PB	EK4241	18-64		Y	D/M	5	Drugs	Food
PB	EK4241	18-64	ED	Y	D/M	30	Yes (details unknown)	
PB	EK4241	18-64	ED	N	D/M	8	No history	
Mod.	300042460	18-64	ED	Y	D/M	5	Food, drugs, latex	
PB	Unknown	18-64		Y	D/M	2	Food, environmental	
PB	Unknown	18-64	ED	Y	D/M	10		Non-COVID-19 vaccine
Mod.	300042460	65+	Hosp, ED	Y	D/M	5		Food
Mod.	300042698	18-64		N	D/M	36	Drugs	
PB	EJ1686	18-64	ED	Y	D/M	60	Food, environmental	

Vaccine	Lot number	Age group (y)	Healthcare Utilization	Epinephrine received	Brighton level	Onset after receipt (minutes)	History of allergies	History of anaphylaxis
PB	EK4241	18-64	ED	Y	D/M	5	Drugs	
PB	Unknown	18-64	ED	Y	D/M	175	Environmental	
PB	EP6017	18-64		N	D/M	50	Unknown	
PB	EP6017	18-64	ED	Y	D/M	30	Environmental	
PB	EL1406	18-64	ED	Y	D/M	3	Food, drugs	
PB	EP6775	18-64	ED	Y	D/M	15	No history	
Mod.	300042722	18-64	Hosp, ED	Y	NA*	unknown	Unknown	

Notes: Mod.=Moderna; PB=Pfizer-BioNTech; Hosp=in-patient hospitalization; ED=seen in emergency room; D/M=did not meet Brighton Collaboration case definition levels of diagnostic certainty one, two or three; NA*= reports are still under investigation and have not yet been assigned a level of diagnostic certainty.
Data Source: CCM

Technical Notes

Data Sources

- The data for this report were based on:
    - Information from the Public Health Case and Contact Management Solution (CCM) extracted on **March 8, 2021 at 9:00 a.m.**
    - Doses administered data were sourced from the Ministry of Health's COVID-19 webpage on **March 7, 2021** and from the Vaccine Management Dashboard from $COVax_{ON}$ on **March 6 at 8:00 p.m**.[2]

Data Caveats

- Data presented in this report only represent AEFIs reported to public health units and recorded in CCM. As a result, all counts will be subject to varying degrees of reporting bias. Including underreporting, particularly for mild or common reportable events, as well as stimulated (elevated) reporting, which can occur in response to media coverage and increased public awareness.
- CCM is a dynamic reporting system which allow ongoing updates to data previous entered. As a result, data extracted from CCM represent a snapshot at the time of data extraction and may differ from previous or subsequent reports.
- Doses administered data are subject to reporting lags as there may be delays in entering data into the information system.

Methods

- For provincial surveillance reporting, an adverse event must occur after receiving the vaccine and meet the MOH AEFI case definition.[1] Data presented in this report only includes AEFI reports with a confirmed case classification and an association with a COVID-19 vaccine in CCM at the time of data extraction.
- AEFI reports from CCM where the Disposition was reported as ENTERED IN ERROR, DOES NOT MEET DEFINITION, or CLOSED – DUPLICATE – DO NOT USE, or any variation on these values have been excluded.
- AEFI reports with a missing date of vaccine administration have been excluded.
- Each AEFI report refers to an individual who reported an AEFI after receiving a dose of COVID-19 vaccine. An AEFI report may contain multiple adverse events. Therefore, the total number of adverse events can exceed the number of individual AEFI reports reported in a given time frame.
- AEFI reporting rates are calculated using the number of COVID-19 vaccine-specific AEFIs reported in a given time period in Ontario divided by doses of COVID-19 vaccines administered in the same time period in Ontario.

- All reports of events managed as anaphylaxis are further assessed using the internationally recognized case definition for anaphylaxis following vaccination from the Brighton Collaboration.[4] An independent review of these cases is completed and a preliminary score is assigned based on this case definition. This score is not a measure of severity but rather reflects the level of diagnostic certainty, with level 1 being the most highly specific for the condition.

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For Further Information

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