TECHNICAL BRIEF

Adverse Events of Special Interest (AESIs) for COVID-19 Vaccines Surveillance

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Introduction

As vaccines for the novel Coronavirus Disease 2019 (COVID-19) are authorized for use in Canada, post-marketing surveillance is being conducted to monitor the safety of these new vaccines throughout implementation of the immunization program. Provincial reporting of adverse events following immunization (AEFIs) to Canada’s AEFI Surveillance System (CAEFISS) is an important component of post-marketing surveillance in Canada.

An AEFI is defined as any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of a vaccine. Reporting of adverse events of special interest (AESIs) for COVID-19 vaccines in the context of overall AEFI surveillance enables enhanced monitoring by pre-specifying events which may otherwise not be captured or readily analyzed from a passive surveillance system.

Purpose

This document outlines preliminary information and definitions (where available) related to Public Health Unit reporting of AESIs associated with administration of COVID-19 vaccine. This document should be used in conjunction with Appendix B: Provincial Case Definitions for Diseases of Public Health Significance for AEFIs, which sets out the overarching provincial case definitions for AEFI reporting for all vaccines.

This document includes a list of AESI for COVID-19 vaccines that have been identified to date by international health authorities, including the Public Health Agency of Canada (PHAC), Brighton Collaboration and World Health Organization (WHO). The AESIs that are described within this document have been selected based on a theoretical rationale for a possible association with COVID-19 vaccines, not due to events or other findings from COVID-19 vaccine clinical trials. For example, they include events that may occur during the clinical course of SARS-CoV2 infection or as complication of infection.

Given the rapidly evolving state of information related to COVID-19 disease and vaccines this document will be updated as new information becomes available, including forthcoming standardized case definitions from the Brighton Collaboration. If you have any questions regarding reporting of COVID-19 AEFIs, please contact the immunization team at Public Health Ontario (PHO) at ivpd@oahpp.ca.
Types of Adverse Events

Vaccine-associated Enhanced Disease

A physician-diagnosed illness occurring in an individual who receives a vaccine and is subsequently infected with the pathogen that the vaccine is meant to protect against.³

Discussion:

Vaccine-associated enhanced disease (VAED) may present as severe disease or modified/unusual clinical manifestations of a known disease presentation affecting an individual exposed to a wild-type pathogen after previously receiving a vaccination for the same pathogen.³

Clinical manifestations of VAED lie within the spectrum of natural disease, occurring more frequently and/or severely in vaccinated individuals.³ It is difficult to separate vaccine failure (occurrence of the specific vaccine-preventable disease in a person who is appropriately and fully vaccinated) from VAED in vaccinated individuals.³

VAED is a known adverse event associated with some vaccines, for example formalin-inactivated respiratory syncytial virus (RSV) vaccine, which was investigational only (e.g., never brought to market) and formalin-inactivated measles vaccine, which has not been used in decades.³ Randomized clinical trials have looked for VAED as a specific outcome and there is no evidence of an association between VAED and authorized COVID-19 vaccines.

Multisystem Inflammatory Syndrome in Children

A physician-diagnosed acute illness in children and young adults (under 21 years of age) characterized by a hyperinflammatory response including persistent fever and multi-organ involvement.⁴

Discussion:

Multisystem inflammatory syndrome in children (MIS-C) is a rare complication of COVID-19 infection. It is characterized by persistent fever and a constellation of symptoms, including multi-organ (e.g., cardiac, gastrointestinal, renal, hematologic, dermatologic, neurologic) involvement and elevated inflammatory markers.⁵ In children presenting with signs and symptoms consistent with MIS-C, the differential diagnosis is broad and includes other infectious and inflammatory conditions including Kawasaki disease (KD) and toxic shock syndrome.⁶ Further information and case definitions are available from the Centers for Disease Control and Prevention (CDC)⁷ and WHO.⁴

Acute Respiratory Distress Syndrome

An acute illness that is physician-diagnosed, characterized by progressive symptoms of dyspnea, tachypnea and hypoxemia.⁸

Discussion:

Acute respiratory distress syndrome (ARDS) is a manifestation of acute lung injury, commonly resulting from sepsis, trauma, and severe pulmonary infection.⁹ Clinically, it is characterized by dyspnea, profound
hypoxemia, decreased lung compliance and diffuse bilateral infiltrates on chest radiography. The fundamentals of therapy include supplemental oxygen, lung rest, and supportive care.

**Acute Cardiovascular Injury**

Acute cardiovascular injury that is physician-diagnosed.

**Discussion:**

Acute cardiovascular injury refers to a broad spectrum of cardiac pathology including microangiopathy, heart failure, stress cardiomyopathy, coronary artery disease, myocarditis, pericarditis and cardiac arrhythmias. Of particular interest for AESI surveillance for COVID-19 vaccines are: myocarditis, pericarditis.

**Coagulation Disorders**

A condition characterized by abnormalities in the body’s ability to control blood clotting that is physician-diagnosed.

**Discussion:**

Coagulation disorders affect the body’s ability to control blood clotting and can include disseminated intravascular coagulation (DIC), thromboembolism, and haemorrhage. Severe COVID-19 has been associated with coagulation abnormalities that mimic other systemic coagulopathies associated with severe infections (e.g., DIC or thrombotic microangiopathy).

**Acute Kidney Injury**

Acute impairment of kidney function characterized by a decline in urine output and an elevation of creatinine levels that is physician-diagnosed.

**Discussion:**

Acute kidney injury is a broad clinical syndrome encompassing various aetiologies including specific kidney diseases (e.g. acute interstitial nephritis) and non-specific conditions (e.g. renal ischaemia).

**Acute Liver Injury**

An acute illness that is physician-diagnosed and occurs without preceding chronic liver disease.

**Discussion:**

Acute liver injury is loss of liver function that occurs rapidly usually in a person who has no pre-existing liver disease.
Anosmia and/or Ageusia

Complete loss of smell (anosmia) and/or taste (ageusia).^{14}

Discussion:

Smell and taste disorders may be attributable to a number of causes including, inflammatory conditions of the nasal sinuses, infections (e.g., COVID-19), head trauma, medication side effects, neurological disorders and aging.^{14,15}

Chilblain–like Lesions

A physician-diagnosed cutaneous manifestation resembling chilblains, characterized by erythematous, edematous or blistering skin lesions that mostly commonly affect the toes and extremities.^{16}

Discussion

Chilblain-like lesions are a dermatological finding that has been described in relation to COVID-19 disease.^{16} Chilblains (perniosis) are an inflammatory skin condition typically occurring as an abnormal vascular response to the cold^{17} whereas chilblain-like lesions are attributed to inflammatory or embolic microvascular occlusion,^{18} occurring in the toes, feet, fingers and/or hands.^{19} The lesions have been described as erythematous, purplish patches and papules, sometimes evolving towards erosions, pigmentation and scaling.^{20} Chilblain-like lesions have been reported to occur predominantly in younger, otherwise asymptomatic patients^{18} and may represent a post-viral or delayed-onset process, as developing lesions occur after the onset of other symptoms.^{21}

Single Organ Cutaneous Vasculitis

A condition diagnosed by a physician as single organ cutaneous vasculitis.

Discussion:

Cutaneous vasculitis (CV) encompasses a wide range of entities characterized by inflammation of cutaneous (skin) blood vessels, with the term “single-organ vasculitis” referring to vasculitis affecting arteries/veins of any size in a single organ, without features suggesting systemic vasculitis.^{22} Typically cases manifest as palpable purpura or erythematous macules; however, hives, hemorrhagic vesicles, and shallow ulcers have also been observed.^{23} Single organ cutaneous vasculitis may be challenging to distinguish from systemic vasculitis.^{24}

Erythema Multiforme

An acute, physician-diagnosed, immune-mediated dermatologic condition, with or without mucosal involvement.^{25}

Discussion:

Erythema multiforme is characterized by the appearance of distinctive target lesions, with concentric colour variations, sometimes accompanied by oral, genital, and/or ocular mucosal erosions.^{25} The clinical manifestations of erythema multiforme can vary and target lesions may not be present in all patients.^{25} The earliest lesions are typically round, erythematous, edematous papules surrounded by
areas of blanching.\textsuperscript{25} The papules can enlarge and develop concentric alterations in morphologic features and color, which results in the well-known target lesions. Lesions typically appear over three to five days and resolve over one to two weeks.\textsuperscript{25}

Erythema multiforme is most commonly caused by herpes simplex virus (HSV) infection and certain medications. Laboratory testing can be used to support infectious associations. Although usually self-limiting, in a subset of individuals frequent episodes of erythema multiforme over many years can lead to recurrent disease.\textsuperscript{25}
Adverse events of special interest (AESIs) for COVID-19 vaccine

References


