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1. INTRODUCTION
An Adverse Event Following Immunization (AEFI) is defined as untoward event temporally associated with immunization that may or may not have been caused by the vaccine or immunization process. AEFIs are generally mild, serious ones are extremely rare. The benefits of preventing disease far outweigh the risks of immunization.

Most reported AEFIs occur in children, not because they are necessarily at greater risk of adverse events, but because of several other factors:

- Children receive the vast majority of immunization;
- Infants are seen frequently by healthcare professionals (HCPs) in the first year of life when they receive several immunizations, providing opportunity for reporting adverse events, and
- Viral and bacterial illnesses are very common in children and can result in signs and symptoms similar to those that may occur following immunization.

Vaccinators should be reminded to consider intercurrent illness and other potential causes when interpreting AEFIs.

2. PURPOSE
This document is intended to help HCPs who administer vaccines with the interpretation of AEFIs and their implications for subsequent immunization.

An understanding of basic mechanisms by which AEFIs occur will aid in the timely and accurate management of these events. Deferral of subsequent immunization because of incorrect or over-cautious interpretation of an adverse event may leave an individual at greater risk from the natural disease than from continued immunization.

3. FORMAT
Each category of an event includes the definition, criteria for reporting and implications regarding continuation, deferral or discontinuation of future immunizations. It is recommended that the Canadian Immunization Guide (the latest edition) be used as a reference to augment this document.

The AEFI definitions and the temporal criteria were developed by a group of experts at the Public Health Agency of Canada and World Health Organization.
4. LOCAL REACTIONS AT INJECTION SITE

4.1. Minor reactions

Pain, redness and swelling at the injection site are common reactions to vaccines. Local reactions are nearly universally reported in clinical trials. The injection of foreign material into the tissues and irritation of the tissues by the process of injection can produce an inflammatory response. These reactions tend to occur within 48 hours of vaccination.

Manage pain and swelling with cold compresses at the injection site, and acetaminophen, if required. Avoid pressure on the injection site.

**Reporting Criteria:**

- Redness, or swelling, or pain extends past the nearest joint; AND/OR
- Redness, or swelling, or pain persisting for 10 days or more.

**Implications:**

Local reactions are not a contraindication to further doses of vaccines. Recurrence risk with the same vaccine is moderate, and this declines with longer intervals between doses.

4.2. Major Reactions

4.2.1. Arthus Reaction

An Arthus reaction is a large, localized reaction characterized by pain, swelling, induration and edema. It usually begins within 48 hours following immunization and develops gradually over a period of hours. The reaction is due to circulating antigen-antibody complexes formed when there is a large amount of circulating antibodies prior to injection of the antigen. This results in massive swelling at the injection site that may involve the entire limb.

If a large local reaction occurs with the initial dose of vaccine in an infant younger than 4 months, it is probably due to high levels of maternal antibodies in the child’s blood. Arthus reactions may be seen with too frequent boosters of tetanus-containing vaccines, and they have been observed following repeat doses of pneumococcal polysaccharide vaccine after short internals.

Manage arthus reactions with cold compresses to the affected limb, acetaminophen and limb elevation. Most arthus reactions resolve within one week.

**Reporting Criteria:**

- Onset within 48 hours of immunization; AND
- Swelling extends past the nearest joint.
Implications:

If the reaction occurs with the initial dose in the primary infant series in a child younger than 6 months, deferral of subsequent doses of the same vaccine for several months may be recommended to wait for a decline of maternally acquired antibodies. If the child will be younger than 6 months when the second dose is due, this should be deferred until the child is 6 months; the third dose should be given 2 months later. Deferral is unnecessary if the next dose is due when the child is 6 months of age because circulating maternal antibodies will be greatly reduced.

If an arthrus reaction occurs with a tetanus-containing booster, future boosters can be spaced at longer intervals and anti-toxin levels monitored to determine when boosting is needed.

4.2.2. Abscess at injection site

An abscess is a fluctuant or draining fluid-filled lesion at the injection site, with or without fever, and generally seen within 7 days of vaccine receipt. Sterile abscesses are typically not accompanied by fever. An abscess at the injection site is a rare local reaction. Contamination of multidose vials (re-entering vial with a used needle, improper cleaning or improper storage) can result in infection and abscess formations.

Manage abscesses with analgesics (e.g., acetaminophen, and ice to injection site). Incision and drainage of infected abscess may be required.

Reporting criteria:

a) Infected abscess
   - Physician-diagnosed; AND
   - Material from the abscess is known to be purulent (positive gram stain or culture); OR
   - There are one or more signs of localized inflammation (erythema, pain to light touch, warmth to touch); AND
   - Evidence of improvement related to antimicrobial therapy.

b) Sterile abscess
   - Persists for more than 1 month, is more than 2.5 centimeters in diameter and/or drainage is evident; AND
   - Material from the mass is known to be non-purulent; AND
   - Absence of signs of localized inflammation (erythema, pain to light touch, warmth to touch) OR
   - Failure to improve on antimicrobial therapy

Implications:

No deferral of subsequent vaccines is necessary. Use an alternate site for the next dose and ensure sterile technique.
4.2.3. Nodule

A nodule is a firm, small mass of tissue at the injection site with discrete or well demarcated borders in the absence of abscess formation, erythema and warmth. Nodules are mainly associated with aluminum-adsorbed vaccines, particularly if the dose is deposited subcutaneously rather then intramuscularly. Sterile nodules can take up to 1 year or more to resolve, they are rarely permanent.

**Reporting criteria:**

- Nodule is more than 2.5 centimeters in diameter; AND
- Nodule persists for more than 1 month.

**Implications:**

No deferral of subsequent vaccines is necessary. Use an alternate site for the next dose. Use the correct length of needle for I.M injections.

4.2.4. Cellulitis

Cellulitis is an acute, infectious inflammatory condition of the skin, located in subcutaneous tissue, fat, fascia or muscle at the injection site. It is distinguished from post-injection erythema, tenderness and induration by the more intense erythema, tenderness to light touch, at least moderate induration, and substantial local warmth. Cellulitis is usually caused by infection with streptococci, staphylococci, or similar organisms. It can result from bacterial contamination of vaccine vial or injection equipment, or it can be due to introduction of surface bacteria into the deeper layers of the skin. Injection site cellulitis is generally seen within 7 days of vaccine receipt. Cellulitis is commonly treated with antimicrobials as it is generally a bacterial infection.

**Reporting criteria:**

- Physician-diagnosed; AND
- Characterized by at least 3 of the following local signs or symptoms: pain or tenderness to touch, erythema, induration or swelling and warmth.

Laboratory culture results can confirm the diagnosis, but such results are seldom available.

**Implications:**

No deferral of subsequent vaccines is necessary. Ensure sterile technique with management of vaccine vial and injections.
5. SYSTEMIC REACTIONS

5.1. Fever

Fever is a common systemic reaction that generally occurs within 72 hours of immunization with inactivated vaccines. Injected protein can affect the body’s heat regulation. Fever following immunization with a live vaccine may occur at a later time (e.g. commonly 5-14 days after Mumps-Measles-Rubella (MMR) or Varicella vaccines). These delayed fevers result from a low grade infection produced by the live vaccine viruses.

A fever that begins within 24 hours after vaccination with inactivated vaccine or persists for more than 24 hours after vaccination should not be assumed to be due to the vaccine. Evaluate these new or persistent fevers for other causes unrelated to immunization, so that treatment is not delayed for serious conditions. Viral and bacterial illnesses are very common in children and can result in signs and symptoms similar to those that may occur following immunization. Consider intercurrent illness and other potential causes when interpreting an AEFI.

Antipyretics (e.g. acetaminophen 10-15 mg/kg/dose) are recommended for children who develop fever following an immunization. Tepid sponge bath and extra fluids will also aid in fever management. Products containing acetylsalicylic acid (ASA) should not be given to children because of their association with Reye syndrome.

Reporting criteria:

- Fever that occurs in conjunction with another reportable adverse event.

Implications:

Fever is not a contraindication to further doses of vaccines. There is usually only a moderate recurrence risk with the same vaccine.

5.2. Rash

Rashes following live attenuated vaccine are expected events and generally do not need to be reported.

MMR vaccine may produce a mild, non-transmissible measles-like illness that can be manifested by a generalized rash and fever. It occurs in 5-10% of persons following the first dose of MMR, usually within 7 days after vaccination. It is much less common following the second dose of MMR.

A localized varicella-like rash occurs at the injection site in 3-5% of individuals after a first dose of varicella vaccine, and in 1% of individuals after a second dose. A similar proportion of individuals will develop a small number of generalized Varicella-like papules or vesicles. Lesions usually appear within 5 to 26 days after immunization.

Most rashes occurring in children, even those temporarily related to immunization, are caused by intercurrent viral illness.
A generalized rash is more likely to be vaccine-associated if it is accompanied by a local reaction at the injection site. The absence of a local reaction weakens the likelihood of a relationship between the reaction and the vaccine.

**Reporting criteria:**

- Generalized rash, for which medical attention is sought, when the rash occurs within 7 days of immunization with an inactivated vaccine, is believed to be due to the vaccine, and for which no alternative cause has been identified;
- An expected rash following MMR (up to 30 days) or varicella vaccine (up to 42 days) that required hospitalization.

**Note:** a rash diagnosed as hives should be reported as an allergic reaction (refer to section 8b of the AEFI form)

**Implications:**

Rashes other than petechial ones are not a contraindication to further doses of vaccines. Petechial rashes should be referred for consultation to determine if further doses of the vaccine should be administered (see section 8.1 for Thrombocytopenia).

5.3. **Adenopathy / Lymphadenopathy**

Adenopathy / lymphadenopathy: enlargement of one or more lymph nodes.

Lymphadenitis: inflammation of one or more lymph nodes, usually caused by a primary focus of infection elsewhere in the body.

Lymphangitis (lymphatic streaking): painful and inflamed red streaks below the skin's surface (follows the path of lymph draining from the site of infection via lymphatic vessels to regional lymph nodes).

Regional adenopathy: abnormal enlargement of the lymph nodes closest to the injection site (e.g., inguinal adenopathy when associated with an IM injection in the thigh, axillary adenopathy associated with an IM injection in the deltoid).

Adenopathy was noted as a reaction following receipt of the adjuvanted pH1N1 (2009) vaccine. The adjuvant produces transient chemokine and cytokine stimulation, enhanced local activity of antigen presenting cells, and uptake by regional lymph nodes. This expected axillary or supraclavicular lymph node tenderness does not require reporting unless it meets the reporting criteria.

Live vaccines produce a low-grade infection that can include adenopathy. With any vaccine injections, if bacteria contaminate the injection site, adenitis may occur as part of the resulting infection. Adenitis in injection site-associated infections would usually occur first in the lymph nodes draining the injection site.
**Reporting criteria:**

- Enlargement of one or more lymph nodes 1.5 centimeters or more in diameter; AND/OR
- Draining sinus over a lymph node.

**Implications:**

Continue with further immunizations in a different limb.

### 5.4. Hypotonic-Hyporesponsive Episodes (HHE)

HHE is the sudden onset, in a child under 2 years of age, of reduced muscle tone, AND either hyporesponsiveness or unresponsiveness, AND either pallor or cyanosis.

With HHE, there is an acute decrease in sensory awareness or loss of consciousness, accompanied by pallor and muscle hypotonicity. Most reported episodes occur within 12 hours of immunization. Children are initially irritable and may be febrile. They then become pale, limp, and unresponsive or hyporesponsive. Respirations are shallow and cyanosis is frequently noted. As a result, parents may report that their child was not breathing. These episodes are usually transient (lasting a few minutes) and self-limiting, although it may be as long as 48 hours before the child returns to normal.

HHE has been documented to occur after immunization with diphtheria, tetanus, *Haemophilus Influenzae* type b, and hepatitis B vaccines. Most reported episodes have followed administration of pertussis-containing vaccines; there has been a decline in these reports with the use of acellular pertussis vaccines. HHE has also been observed most frequently during the primary immunization series, mainly after the first dose. The cause of these episodes is unknown, but they are most consistent with fainting spells. Some HHEs may represent atonic seizures, consisting of sudden loss of postural tone and consciousness, perhaps triggered by fever. Other cases have been confused with anaphylaxis or hypoglycemia. Follow-up of children who have had HHEs has demonstrated complete recovery without persistent neurologic or developmental defects. No treatment is necessary. If the HHE does not resolve spontaneously, other underlying problems should be sought and ruled out or treated.

**Reporting criteria:**

- Physician-diagnosed HHE in a child younger than 2 years.

**Implications:**

HHE is not a contraindication to further doses of the same vaccine.

### 5.5. Screaming/persistent crying

Crying in children is a common reaction to painful stimuli. Most often, crying immediately following immunization is short-lived, has a familiar sound, and is viewed as normal by parents. However, parents are concerned when crying is prolonged, persistent, high-pitched, and the infant is inconsolable. Use analgesics e.g., acetaminophen in doses 10-15mg/kg every 4-6 hours as needed to
control pain. Products containing ASA should not be given to children because of their association with Reye syndrome.

**Reporting criteria:**

- Screaming or persistent crying [continuous, unaltered (i.e. the quality of the crying does not change throughout the episode)], with onset within 72 hours of vaccine receipt and lasting for 3 or more hours.

**Implications:**

Persistent crying is not a contraindication to further doses of vaccines.

5.6. Parotitis

Parotitis is an inflammation of the parotid gland(s) with accompanying pain and/or tenderness. The parotid glands lie at the side of the face just below and in front of the external ear. Parotitis is a common manifestation of mumps infection. Since the mumps-containing vaccine is a live virus vaccine, low-grade infection following immunization can occasionally produce the same manifestation. Parotitis is transient and self-limiting. Management includes antipyretics and analgesics as required and adequate fluid intake.

**Reporting criteria:**

- Physician-diagnosed parotitis occurring 5-30 days following immunization with MMR.

**Implications:**

Continue with further dose of MMR vaccine as needed.

5.7. Orchitis

Orchitis is an inflammation of one or both of the testes, characterized by swelling and pain. It is usually associated with MMR vaccine. Since this vaccine contains a live virus, immunization can produce the same manifestation. Management involved support and elevation of the scrotum, cold packs and analgesics.

**Reporting criteria:**

- Physician-diagnosed orchitis occurring 5-30 days following immunization with MMR.

**Implications:**

Continue with further dose of MMR vaccine as needed.
5.8. **Severe Vomiting/Diarrhea**
Nausea and vomiting have been particularly associated with oral typhoid vaccine, human diploid cell rabies vaccine (HDCV) and Japanese encephalitis vaccine. Treat severe vomiting/diarrhea symptomatically to prevent dehydration and electrolyte imbalance.

**Reporting criteria:**
- 3 or more episodes of vomiting or diarrhea in a 24 hour period; AND
- Vomiting and/or diarrhea is severe, i.e., projectile vomiting or explosive, watery diarrhea;

**Implications:**
Severe vomiting or diarrhea is not a contraindication to further doses of vaccines.

6. **ALLERGIC REACTIONS**
Allergic reactions constitute a spectrum, the extreme end of which is anaphylaxis. Milder forms of allergic reactions may involve both the dermatological/mucosal (e.g., urticaria, pruritus, rhinitis) and/or the respiratory systems (e.g. upper airway swelling, respiratory distress).

An allergic reaction is an acquired hypersensitivity to an antigen that does not normally produce such a reaction. Antigen-antibody complexes stimulate the release of chemicals, such as histamine, that produce overt signs and symptoms of hypersensitivity. An allergic reaction can occur in response to a component of a vaccine in a person previously sensitized (i.e. antibodies must be present from a previous exposure to the antigen). Allergic reactions are rarely seen following the first dose in a vaccine series, but they may be seen with the second dose or any subsequent dose.

Allergic reactions include:

I. **Skin manifestations:** hives (urticaria) are circumscribed, intensely itchy weals with erythematous raised edges and pale, blanched centers. Hives may be limited to the injection site (e.g. within a few centimeters of where immunization was given) and/or may be generalized, involving other body sites.

II. **Bronchospasm:** a whistling, musical or puffing sound on expiration.

III. **Local or generalized edema:** swelling may be localized to the injection site, or it may be in the deeper layers of the skin, subcutaneous tissues or mucosa lining the throat, airways and gut. Swelling may not be well circumscribed and is usually not itchy. Typical sites in anaphylaxis include the tongue, lips, around the eyes (periorbital) and eyelids.

**Reporting criteria:**
- Allergic reactions (hives, bronchospasm, edema) occurring within 48 hours of immunization.
Implications:

- Generalized hives occurring within 2 hours of immunization (cause and effect likely): refer to an allergist for assessment prior to further doses of the same vaccine or its components.

- Hives occurring within 48 hours following immunization (cause and effect less likely): consider providing next dose of the vaccine in a physician’s office or an emergency setting and observe the patient for one to two hours following immunization. If a hive-like rash reappears with this dose, particularly a generalized rash appearing within 48 hours of vaccination, refer to an allergist for assessment prior to further doses of the same vaccine or its components. If there is no reaction following this dose, further immunization can be given in the routine settings.

- Hives occurring 48 hours or later of immunization (cause and effect link unlikely): consider giving next vaccine dose under routine conditions. Consider other potential causes of the hives, particularly if there was no reaction at the injection site.

6.1. Anaphylaxis

Anaphylaxis is a rare but potentially life-threatening adverse reaction to immunization. It is characterized by sudden onset, rapid progression of signs and symptoms and involvement of multiple (more than 2) organ systems. The highest level of diagnostic certainty, Brighton Collaboration Level 1 is defined as:

- ≥ major dermatological; AND
- ≥ major cardiovascular; AND/OR
- ≥ major respiratory criterion.

Not all cases reported as anaphylaxis will meet Level 1 degree of certainty. Suspected anaphylaxis is managed appropriately and promptly, avoiding escalation of symptoms and progression to a more severe outcome.

Reporting criteria:

- All adverse events managed as anaphylaxis at the time of occurrence.

Implications:

A true anaphylactic reaction to a vaccine is a contraindication to receipt of further doses of the same vaccine or to a component of a vaccine. Consultation with an allergist may be sought to identify the component to which the client has hypersensitivity.
Table 1: Anaphylaxis

This table outlines major and minor signs and symptoms in the organ systems involved in an anaphylactic event.

<table>
<thead>
<tr>
<th>COURSE OF REACTION</th>
<th>B. MAJOR CRITERIA</th>
<th>C. MINOR CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUDDEN ONSET OF SIGNS AND SYMPTOMS</td>
<td>Generalized urticaria (hives)</td>
<td>Injection site urticaria</td>
</tr>
<tr>
<td>RAPID PROGRESSION OF SIGNS AND SYMPTOMS</td>
<td>Generalized erythema</td>
<td>Red AND itchy eyes</td>
</tr>
<tr>
<td>SKIN</td>
<td>*Angioedema (general or localized)</td>
<td>Generalized prickle sensation</td>
</tr>
<tr>
<td></td>
<td>Generalized pruritus WITH skin rash</td>
<td>Generalized pruritus WITHOUT skin rash</td>
</tr>
<tr>
<td>RESP</td>
<td>Bilateral wheeze (by stethoscope)</td>
<td>Persistent dry cough</td>
</tr>
<tr>
<td></td>
<td>Stridor</td>
<td>Hoarse voice</td>
</tr>
<tr>
<td></td>
<td>≥ 2 indicators of respiratory distress:</td>
<td>Sensation of throat closure</td>
</tr>
<tr>
<td></td>
<td>o Tachypnea</td>
<td>Sneezing OR rhinorrhea</td>
</tr>
<tr>
<td></td>
<td>o Cyanosis</td>
<td>Difficulty breathing WITHOUT wheeze or stridor</td>
</tr>
<tr>
<td></td>
<td>o Grunting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o Chest wall retractions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o ↑ use of accessory muscles</td>
<td></td>
</tr>
<tr>
<td>CV</td>
<td>Documented hypotension</td>
<td>≥2 signs of reduced peripheral circulation</td>
</tr>
<tr>
<td></td>
<td>≥3 signs of uncompensated shock</td>
<td>o Tachycardia</td>
</tr>
<tr>
<td></td>
<td>o Tachycardia</td>
<td>o Capillary refill &gt;3 seconds</td>
</tr>
<tr>
<td></td>
<td>o Capillary refill &gt;3 seconds</td>
<td>o ↓ level or loss of consciousness</td>
</tr>
<tr>
<td></td>
<td>o Reduced central pulse volume</td>
<td></td>
</tr>
<tr>
<td></td>
<td>o ↓ level or loss of consciousness</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Documented MD diagnosis of shock</td>
<td></td>
</tr>
<tr>
<td>GI</td>
<td>Nausea</td>
<td>Vomiting</td>
</tr>
<tr>
<td></td>
<td>Abdominal pain</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>LAB</td>
<td>Elevated mast cell tryptase</td>
<td></td>
</tr>
</tbody>
</table>

Other terms:
- Bilateral red eyes
- Sore throat
- Difficulty swallowing
- Chest tightness
- Rash -generalized
- Rash – localized at non-injection site
- Pallor
- Dizzy
- Metallic taste
- Other (specify)
Table 2: Level of diagnostic certainty

This table can be used to determine level of diagnostic certainty in the review of an event managed as anaphylaxis. Check all boxes that apply based on Table 1. If criteria for more than one level of diagnostic certainty are met, choose Level 1 over Level II and Level II over Level III.

<table>
<thead>
<tr>
<th>Level</th>
<th>≥ 1 SKIN</th>
<th>≥ 1 RESP</th>
<th>≥ 1 CV</th>
<th>Additional Criteria needed to Meet Level II or III</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>☐ MAJOR</td>
<td>☐ MAJOR</td>
<td>☐ MAJOR</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>☐ MAJOR</td>
<td>☐ MAJOR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>☐ MAJOR</td>
<td>☐ MAJOR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td></td>
<td>☐ MAJOR</td>
<td>☐ MAJOR</td>
<td>&gt; 1 minor from skin, cardiovascular, gastrointestinal</td>
</tr>
<tr>
<td>II</td>
<td>☐ MAJOR</td>
<td></td>
<td>☐ MAJOR</td>
<td>&gt; 1 minor skin, respiratory, gastrointestinal</td>
</tr>
<tr>
<td>II</td>
<td>☐ MAJOR</td>
<td>☐ Minor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>☐ MAJOR</td>
<td>☐ Minor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>☐ Minor</td>
<td></td>
<td>☐ MAJOR</td>
<td>&gt; 1 minor criterion from at least 2 different systems</td>
</tr>
<tr>
<td>III</td>
<td>☐ Minor</td>
<td></td>
<td>☐ MAJOR</td>
<td>&gt; 1 minor criterion from at least 2 different systems</td>
</tr>
<tr>
<td>IV</td>
<td>☐ Reported anaphylaxis with insufficient evidence to meet case definition levels 1, 2 or 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>☐ Not a case of anaphylaxis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Web-based checklists can also be used to determine the diagnostic certainty according to a specific Brighton Collaboration case definition (registration with Brighton Collaboration is required).


7. NEUROLOGICAL EVENTS

7.1. Convulsion/seizure

Seizures are defined as paroxysms of generalized tonic skeletal muscle contractions and generalized clonic jerking, usually associated with decreased level of consciousness. They must be distinguished...
from vasovagal or fainting episodes, in which isolated muscle contractions may occur. Seizures may last for several minutes or more.

While fevers are usually benign, an abrupt rise in temperature is a risk factor for febrile convulsions in susceptible children. Febrile seizures are the most common seizure disorder of childhood, and are age-dependent. They are rare prior to 6 months of age and after 5 years of age, with peak onset at 14-18 months of age. Incidence in this age group approaches 2-5%, with greater risk in those with a family history. While simple febrile seizures are disturbing for the child and parents, they have a uniformly excellent prognosis without residual sequelae and remit on their own as the child ages. There are no long-term sequelae, such as permanent brain damage, associated with simple febrile seizures. Prophylactic antipyretics have not been shown to decrease the recurrence of febrile seizures, but these are often recommended by providers. Remind parents that children susceptible to febrile seizures may have a recurrence following immunization or following other events, such as viral infections.

**Reporting criteria:**

- Seizures (febrile or afebrile) that occur within 72 hours of inactivated vaccines, 5-30 days after MMR, or 5-42 days following varicella vaccine.

**Implications:**

If the febrile convulsions were multiple or prolonged (complex seizures; status epilepticus), there should be a consultation with a neurologist to rule out an underlying disorder. Afebrile seizures should be investigated by a neurologist. Uncomplicated febrile seizures (a single episode of short duration) are not a contraindication to further doses of vaccines.

**7.2. Encephalopathy/encephalitis**

Encephalopathy is a term used to describe a constellation of signs and symptoms reflecting a generalized disturbance in brain function.

Acute encephalopathy is the sudden onset of major neurological illness temporally linked with immunization and characterized by two of the following:

I. Severe alteration in level of consciousness or unresponsiveness, with or without generalized or focal convulsions. The symptoms must persist for more than a few hours, with failure to recover completely within 24 hours.

II. Increased intracranial pressure (as measured and diagnosed by a physician). A bulging fontanel as described by a parent to a nurse rather than observed by a physician is not sufficient to diagnose increase intracranial pressure. Intense crying can cause a bulging, pulsating fontanel.

III. Distinct change in behavior or intellectual functions lasting one day or more and felt by a physician to indicate an alteration in neurological function.
The following clinical features alone or in combination do not qualify as evidence of an acute encephalopathy: sleepiness, irritability (fussiness), high-pitched and unusual screaming, persistent inconsolable crying, and bulging fontanel. Seizures in themselves are not sufficient to constitute diagnosis of encephalopathy.

Encephalitis includes central nervous system inflammation AND either more than 24 hours depressed or altered consciousness with one or more signs or reduced responsiveness OR one or more signs of focal or multi-focal central nervous system abnormality.

Immunizations may very rarely lead to acute encephalitis, particularly in the setting of live-attenuated viral vaccines. The risk of encephalitis complications from viral infections (1/1000 cases of measles; 1/6000 cases of rubella) is greater than the risk following vaccination (1/1,000,000 following MMR). Encephalitis has occurred rarely following Yellow Fever immunization in young infants and thus this vaccine is not recommended for infants younger than 4 months.

**Reporting criteria:**

- Encephalopathy or encephalitis diagnosed by a physician.

Include appropriate non-nominal medical documentation, physicians’ assessments and test results, with the AEFI report. All reported cases of this severe but rare adverse event are reviewed by the Advisory Committee on Causality Assessment (ACCA).

**Implications:**

Encephalopathy itself is not a contraindication to further vaccination. Deferral of immunization may be considered until the neurologic condition has been diagnosed or is stable. If no other cause is found and the encephalopathy is temporally related to a combination vaccine, refer to a pediatric neurologist to determine which components of the vaccine may be continued.

7.3. **Meningitis**

Meningitis is an infection or inflammation of the membranes covering the brain and spinal cord. It is characterized by severe headache, vomiting, pain and stiffness in the neck.

Measles and mumps viruses were important causative agents of aseptic meningitis before introduction of measles and mumps vaccines. The postulated mechanism for aseptic meningitis following attenuated live virus vaccines is infection of the meninges with the vaccine virus. Such a causal relationship was established with the Urabe strain of mumps virus (1 case reported per 62,000 vaccinations), which is no longer used in vaccines in Canada. There is no evidence of a causal association with the Jeryl-Lynn strain of mumps used in MMR, or with any of the other routinely used live virus vaccines. Aseptic meningitis following immunization usually resolves without sequelae.
Reporting criteria:

- Physician- diagnosed meningitis occurring within 15 days of inactivated vaccines, 2-42 days following MMR, or up to 42 days following varicella vaccine, for which no other cause has been identified.

Include appropriate non-nominal medical documentation. Reports of this major, severe but rare adverse event will be subsequently investigated by the ACCA.

Implications:

Defer further vaccines until a determination is made as to the cause of the meningitis.

7.4. Anesthesia/Paresthesia

Anesthesia: the absence of normal sensation, especially sensitivity to pain, in an area of nerve distribution.

Paresthesia: numbness or tingling feeling in an area of nerve distribution.

The cause of anesthesia or paresthesia following vaccination is often not determined. An obvious cause could be an accidental injection of vaccine into a nerve, but this is ruled out in most reported cases. Anesthesia/paresthesia may occur early if it is related to injection technique. There are anecdotal reports of peripheral neuropathy associated with tetanus toxoid administration that are felt to be related to immune complex formation. Rubella vaccine may be rarely associated with peripheral neuropathy. There is no specific treatment. Investigation by a neurologist should be done to rule out permanent nerve damage.

Reporting criteria:

- Physician- diagnosed anesthesia or paresthesia lasting 24 hours or more, and occurring up to 7 days following administration of inactivated vaccines.

Supporting non-nominal medical documentation of the diagnosis should be included with adverse event report.

Implications:

If the cause is related to injection technique, avoid the site for future injections. In most cases, immunizations can continue.

7.5. Paralysis

Paralysis is characterized by a loss of muscle tone and function, with or without the loss of sensation. It may be caused by the administration of a live virus, and a causal relationship has been established only with oral polio vaccine (OPV) which is no longer in use.
OPV has been associated with paralytic disease in vaccine recipients and their close contacts when recipients excrete the virus in their stool for 3-4 weeks after immunization, and the transmission can occur with such activities as changing diapers. In Canada from 1965 through 1992, vaccine-associated paralysis occurred in recipients of OPV at a rate of 1 case per 11.7 million doses distributed, and in contacts of vaccinees at a rate of 1 case per 3.1 million doses distributed.

**Reporting criteria:**

- Physician-diagnosed paralysis occurring within 15 days following inactivated vaccine receipt, up to 42 days following MMR, OPV or varicella vaccine, and lasting more than 24 hours.

Supporting non-nominal medical documentation of the diagnosis should accompany the report.

**Implications:**

The decision to continue immunization must be made on a case-by-case basis. All cases should be evaluated by a neurologist.

7.6. Guillain-Barré syndrome (GBS)

GBS is an illness that includes acute onset of bilateral flaccid weakness/paralysis of the limbs with decreased or absent deep tendon reflexes. CSF test results, if available, must either be normal, or have <50 WBC/mm.

GBS is also called acute afebrile polyneuritis or acute idiopathic polyneuritis. It is a subacute, usually symmetrical ascending paralysis, with associated sensory disturbances. It can appear as sequelea to a variety of infections after an interval of 1 to 8 weeks. Approximately two-thirds of patients with GBS report an antecedent infectious illness, most commonly a diarrheal or respiratory illness, and prior to the onset of neurologic signs. *Campylobacter Jejuni* is the most commonly reported pathogen in adults. GBS has been reported to occur sporadically in temporal association with a number of vaccines. A maximum degree of weakness is reached from 12 hours to 28 days after onset, followed by a clinical plateau and then either improvement or death. Overall, approximately 5-15% of patient die, and continued disability after 1 year has been estimated to be seen among 20% of patients.

There is limited evidence of an association between tetanus toxoid and GBS, or OPV and GBS, in addition to a swine influenza vaccine (1976) that is no longer in use. While cases of GBS have been reported temporally associated with other vaccines (e.g. Menactra), there is no evidence of a causal relationship.

**Reporting criteria:**

- Physician-diagnosed GBS occurring within 8 weeks of immunization with inactivated vaccines and within 3 month of immunization with live attenuated vaccines.

Provide non-nominal medical documentation confirming the diagnosis. GBS cases are regularly reviewed by ACCA.
Implications:

If GBS occurs in temporal relationship to Influenza or a tetanus-containing vaccine, subsequent doses of the same vaccine should only be given if the benefits of vaccination outweigh the risk of GBS recurrence if vaccine is given. There are no contraindications to immunization in persons with a previous history of GBS unrelated to vaccination; with the exception that history of GBS is a precaution to receipt of Menactra vaccine.

7.7. Bell’s palsy

Bell’s palsy is a unilateral paralysis or weakness of facial muscles. The cause of Bell’s palsy is not clear. There is a consideration that a viral infection such as viral meningitis or the herpes virus may be linked to Bell’s palsy since these infections can cause inflammation that can damage the nerve that controls muscles on the side of the face.

Although some variation in the prevalence of Bell’s palsy has been reported, it does not appear to occur in a seasonal pattern. Influenza infection does not appear to be a precipitating event for Bell’s palsy.

In only a single instance was Bell’s palsy known to be causally related to vaccine. An intranasal Influenza vaccine used only in Switzerland was removed from the market after an increase in cases of Bell’s palsy was noted (Mutsch, 2004).

Reporting criteria:

- Physician-diagnosed Bell’s palsy occurring within 8 weeks of immunization with inactivated vaccines and within 3 month of immunization with live attenuated vaccines.

Provide non-nominal medical documentation confirming the diagnosis. Bell’s palsy cases are regularly reviewed by ACCA.

Implications:

A temporal association between vaccine receipt and Bell’s palsy onset is expected to be coincidental. Bell’s palsy would not be a contraindicated to further doses of vaccines.

7.8. Subacute Sclerosing Panencephalitis (SSPE)

SSPE is a rare, degenerative central nervous system disease occurring as a late complication of measles (can be up to 10 years later) and characterized by behavioral and intellectual deterioration and convulsions due to inflammation of brain tissue. Seizures, blindness and dementia can occur. Remission occurs in only 4% of cases; it is otherwise fatal, and there is no treatment. For vaccine-associated cases there is no temporal criterion for reporting; as with cases following infection, the occurrence would be years following immunization. SSPE requires a physician diagnosis.

The association between natural measles infection and SSPE has led to concern that live attenuated measles vaccine virus could also cause a persistent infection of the CNS. Identification of the cause of SSPE as wild-type or vaccine-strain measles virus has not been possible.
Some reported cases of SSPE had history of measles vaccination and lacked a history of natural measles infection. If the vaccine indeed is associated rarely with SSPE, the risk following vaccination, if it exists, is estimated to be approximately one tenth or less of that noted after natural infection (less than 1/1,000,000 persons vaccinated versus 1/100,000 cases of measles). There has been a dramatic decline in the incidence of SSPE since the introduction of widespread measles immunization.

**Reporting criteria:**

- Physician-diagnosed SSPE.

Provide non-nominal medical documentation confirming the diagnosis. SSPE cases will be reviewed by ACCA.

**Implications:**

A diagnosis of SSPE is a contraindication to receipt of MMR vaccine.

### 8. MISCELLANEOUS

#### 8.1. Thrombocytopenia

Thrombocytopenia is defined as a platelet count of less than 150 x 10⁹/L accompanied by clinical signs and/or symptoms of spontaneous bleeding. Petechiae are small, purplish, hemorrhagic spots on the skin that do not blanch with pressure.

Normal platelet counts are 150-450,000/mm. Thrombocytopenia can occur in persons of all ages. Approximately 70% of cases occur following viral illness, often in children. It can also occur as a complication of a variety of medications. Many cases are idiopathic. Most cases in children are mild and transient, although hemorrhagic complications can occur. The cause of vaccine-associated thrombocytopenia is unknown.

Thrombocytopenia is a known complication of measles vaccination, occurring in 1 per 30,000 to 40,000 children following vaccination with the first dose of measles-containing vaccine. It may also occur following the second dose, even in persons who did not have a reaction after the first dose. However, thrombocytopenia after the first dose may increase the risk for recurrence with the second dose.

Corticosteroids and gamma globulin may be used to treat idiopathic thrombocytopenia. Precautions should be taken, particularly for young children, to avoid the risk and complication of bleeding (e.g. precautions to avoid serious head injuries). Control of bleeding may be necessary and transfusion of platelets may be required.

**Reporting criteria:**

- Physician-diagnosed thrombocytopenia occurring within 30 days following vaccination.
Laboratory results should accompany the report.

**Implications:**

Children with a history of thrombocytopenia may be at increased risk for developing thrombocytopenia after MMR vaccination. Such children should generally still be immunized because the benefits of immunization outweigh the risks. The risk of thrombocytopenia following natural measles or rubella infection is greater than the risk following immunization. Children who develop thrombocytopenia temporally related to their first dose of MMR should be assessed for immunity to measles. If the child is susceptible, discuss the benefits and risks of revaccination with the parent. If proceeding with vaccination, ensure that the parent is aware of the potential risk of recurrence, watches the child closely for development of petechiae in the 2-3 weeks post-vaccination, and is aware of the need for injury prevention.

8.2. **Arthralgia/arthritis**

Arthralgia: joint pain
Arthritis: joint inflammation with swelling, redness and/or warmth

Arthritis is usually associated with arthralgia, which may occur without obvious arthritis. Rubella vaccine-associated arthralgia involves, in order of decreasing frequency, the joints of the fingers, knees, wrists, elbows, ankles, hips and toes. Arthralgia/arthritis has only been associated with rubella immunization.

Arthritis and Arthralgia can be manifestations of natural rubella infection in adults.

Transient acute Arthralgia or arthritis has been shown to occur 7-21 days post immunization in susceptible adolescent and adult women immunized with the RA 27/3 strain of rubella (the strain used in the MMR vaccine currently available in Canada). Arthritis/Arthralgia can also occur in children and adolescent and adult men, but at much lower rates. Persistence or recurrence of these symptoms is rare. There are case reports of chronic arthropathy following immunization, but in analytical reviews in control groups, MMR vaccine is not associated with chronic disease.

Analgesics/anti-inflammatories may be used to reduce inflammation, swelling and joint pain. Products containing ASA should not be given to children because of their association with Reye syndrome.

**Reporting criteria:**

- Arthralgia or arthritis occurring within 42 days following receipt of a rubella-containing vaccine, and lasting at least 24 hours.

**Implications:**

Transient arthritis/arthralgia is not a contraindication to a further dose of MMR vaccine. Since the joint symptoms are likely related to seroconversion, the risk following a second MMR dose is lower than that...
following the first dose. It is important to offer rubella vaccine to seronegative women of childbearing age to reduce the risk of congenital rubella syndrome.

8.3. Intussusception

Intussusception is the telescoping of one segment of the intestine with a neighboring segment, most often the ileum into the colon. The walls of the two sections of intestine press on each other, causing irritation, swelling and eventually decreased blood flow. If left untreated, intussusception can cause internal bleeding, severe abdominal infection, and death of intestinal tissue. Intussusception is the most common cause of acute intestinal obstruction in infants and young children. Hematochezia is red blood in the stool (described as “red currant jelly” material) that may be associated with Intussusception.

A rotavirus vaccine used in the United States was withdrawn from the market in 1999 because of the reported temporal association between the development of intussusception and receipt of the vaccine. New rotavirus vaccines have been licensed after undergoing large clinical trials to assess safety with regard to intussusception.

**Reporting criteria:**

- Intussusception or Hematochezia occurring within 42 days following rotavirus vaccine receipt.

**Implications:**

Intussusception is an uncommon, but naturally occurring event. Reports of intussusception following vaccination are not expected to exceed the number of cases that would be seen by chance alone. Intussusception is a contraindication for further doses of rotavirus vaccine.

8.4. Oculo-Respiratory Syndrome (ORS)

ORS is the onset of bilateral red eyes and respiratory symptoms (cough, wheeze, chest tightness, difficulty breathing, difficulty swallowing, hoarseness or sore throat) with or without facial edema.

**Reporting criteria:**

- Bilateral red eyes and respiratory symptoms, with onset within 24 hours of Influenza vaccine receipt.

**Implications:**

Most people who have had ORS after a previous dose of Influenza vaccine do not experience it again – about 5 to 34% experience another episode, but it is usually milder. Most people who have experienced ORS can be safely revaccinated. Persons who had severe symptoms such as wheeze, chest tightness/discomfort, difficulty breathing or throat constriction, difficulty swallowing should discuss the benefits and risk of immunization with their physician in order to make a decision about re-vaccination.
8.5. **Syncope with injury**

Syncope (vasovagal reaction), or fainting, is a temporary unconsciousness caused by diminished blood supply to the brain. It can be triggered by various stimuli, and it is observed to occur following immunization, perhaps triggered by pain or emotional reaction to the procedure. It happens suddenly, before, during or after immunization. Recovery occurs within 1-2 min. The risk of fainting is the more common reason to keep vaccinees under observation for 15 min post-immunization.

Syncope with injury has been reported following HPV vaccine and H1N1 vaccine receipt. These reports include head injuries after syncope-related falls, and motor-vehicle incidents where the individual lost consciousness while driving. Immunizers should be aware of presyncopal manifestations and take appropriate measures to prevent injuries if weakness, dizziness or loss of consciousness occurs. These events are potentially serious: life-threatening or resulting in death; requiring hospitalization or resulting in a residual disability. They are related to the process of immunization, rather than to a specific vaccine.

**Reporting criteria:**

- Syncope with injury within 24 hours following immunization.

**Implications:**

Syncope is not a contraindication to further immunizations.

8.6. **Other severe or unusual events**

**Definition/Criteria for reporting:**

Other severe and unusual events with a temporal association to immunization, and for which there is no other known cause and which are not covered under the categories previously described should be reported in this category. These must be clinically intriguing or epidemiologically interesting events and they usually require medical intervention to meet the criteria for reporting. Provide all details of the events, and include all necessary documentation with the report.

Any death of a vaccine recipient temporally linked (within 4 weeks) to immunization, where no other clear cause of death is established, should be reported. Fetal deaths or abnormalities following immunization of the pregnant woman should also be reported. Provide autopsy report when available.

Reporting of severe or unusual events is important not only to identify a possible causal relationship with vaccination, but also to rule out the vaccine as the cause. The severity of the adverse event and the plausibility of a causal association with vaccination will determine whether further doses of the implicated vaccine will be continued.
9. REFERENCES


Dobson S, Scheifele D, Bell A. Assessment of a universal school-based hepatitis B vaccination program. JAVA (1995); 274: 1212


Gidudu J et al. A local reaction at or near injection site: case definition and guidelines of data collection, analysis and presentation of immunization safety data. Vaccine (2008), Vol.26: 6800-6831


Note: all Brighton collaboration documents were retrieved from: http://www.brightoncollaboration.org/internet/en/index/definition_guidelines.html
10. SUMMARY OF REPORTING CRITERIA

The length of time between vaccine administration and onset of symptoms is an important consideration in causality assessment. Temporal criteria listed below are approximate timelines of which an applicable AEFI could occur.

<table>
<thead>
<tr>
<th>AEFI</th>
<th>Reporting criteria</th>
<th>Inactivated</th>
<th>Live attenuated</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOCAL REACTION AT INJECTION SITE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor reactions</td>
<td>• Redness or swelling or pain extends past the nearest joint; AND/OR • Redness or swelling or pain persists for 10 days or more.</td>
<td>0-48 hours</td>
<td>0-48 hours</td>
</tr>
<tr>
<td>Major reactions: Arthus reaction</td>
<td>• Onset within 48 hours of immunization; AND • Swelling extends past the nearest joint.</td>
<td>0-48 hours</td>
<td>0-48 hours</td>
</tr>
<tr>
<td>Infected abscess</td>
<td>• Physician-diagnosed; AND • Material from the abscess is purulent (positive gram stain or culture); OR • Signs of localized inflammation (erythema, pain to touch, warmth); AND • Evidence of improvement with antimicrobial therapy.</td>
<td>0-7 days</td>
<td>0-7 days</td>
</tr>
<tr>
<td>Sterile abscess</td>
<td>• Persists for &gt;1 month, is &gt;2.5cm in diameter and/or drainage is evident; AND • Material from the mass is non-purulent; AND • Absence of localized inflammation; OR • Failure to improve on antimicrobial therapy.</td>
<td>0-7 days</td>
<td>0-7 days</td>
</tr>
<tr>
<td>Nodule</td>
<td>• Is &gt;2.5cm in diameter; • Persists for &gt;1 month.</td>
<td>0-7 days</td>
<td>0-7 days</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>• Physician-diagnosed; AND • Characterized by at least 3 local signs or symptoms: pain or tenderness to touch, erythema, induration or swelling, warmth;</td>
<td>0-7 days</td>
<td>0-7 days</td>
</tr>
</tbody>
</table>
### SYSTEMIC EVENTS

<table>
<thead>
<tr>
<th>Event</th>
<th>Definition</th>
<th>Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Fever that occurs in conjunction with another reportable event.</td>
<td>0-72 hours 0-42 days</td>
</tr>
<tr>
<td>Rash</td>
<td>Generalized rash for which urgent medical attention is sought and believed to be related to vaccine; Any rash requiring hospitalization or treatment in ER.</td>
<td>0-7 days 5-26 days</td>
</tr>
<tr>
<td>Adenopathy/lymphadenopathy</td>
<td>Enlargement of one or more lymph nodes, ≥1.5cm in diameter; AND/OR Draining sinus over a lymph node.</td>
<td>0-6 days 1-6 months</td>
</tr>
<tr>
<td>HHE</td>
<td>Physician-diagnosed; AND Reduced muscle tone; AND Hyporesponsiveness; AND Pallor or cyanosis; AND Child &lt;2 years of age.</td>
<td>0-48 hours 0-48 hours</td>
</tr>
<tr>
<td>Screaming/Persistent crying</td>
<td>Continuous, unaltered crying lasting for 3 or more hours.</td>
<td>0-72 hours 0-72 hours</td>
</tr>
<tr>
<td>Parotitis/Orchitis</td>
<td>Physician-diagnosed following immunization with MMR.</td>
<td>5-30 days</td>
</tr>
<tr>
<td>Vomiting/Diarrhea</td>
<td>3 or more episodes in 24-hour period; AND Severe (i.e., projectile vomiting or explosive, watery diarrhea).</td>
<td>0-72 hours 0-72 hours</td>
</tr>
</tbody>
</table>

### ALLERGIC REACTIONS

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Definition</th>
<th>Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergic reactions</td>
<td>Any allergic reaction (hives, bronchospasm, edema) occurring within 72 hours of immunization.</td>
<td>0-48 hours 0-48 hours</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>All adverse events managed as anaphylaxis at the time of occurrence.</td>
<td>0-24 hours 0-24 hours</td>
</tr>
<tr>
<td>ORS</td>
<td>Bilateral red eyes and respiratory symptoms with onset within 24 hours of Influenza vaccine receipt</td>
<td>Influenza: 0-24 hours</td>
</tr>
</tbody>
</table>

### NEUROLOGIC EVENTS

<table>
<thead>
<tr>
<th>Event</th>
<th>Definition</th>
<th>Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Convulsion/seizure</td>
<td>Seizures (febrile or afebrile) if they meet the temporal criteria.</td>
<td>0-3 days 5-42 days</td>
</tr>
<tr>
<td>Encephalopathy/encephalitis</td>
<td>Physician-diagnosed encephalopathy or encephalitis.</td>
<td>0-15 days 2-42 days</td>
</tr>
<tr>
<td>Meningitis</td>
<td>Physician-diagnosed meningitis for</td>
<td>0-15 days 2-42 days</td>
</tr>
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### Adverse Events Following Immunization: Interpretation and Clinical Definitions Guide

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<tr>
<td>GBS</td>
<td>Physician-diagnosed GBS.</td>
<td>0-8 weeks</td>
</tr>
<tr>
<td>Bell’s palsy</td>
<td>Physician-diagnosed Bell’s palsy.</td>
<td>0-8 weeks</td>
</tr>
<tr>
<td>SSPE</td>
<td>Physician-diagnosed SSPE.</td>
<td>0-8 weeks</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Physician-diagnosed occurring within 30 days post-immunization.</td>
<td>0-30 days</td>
</tr>
<tr>
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<td>Any arthralgia or arthritis that follows the receipt of MMR and lasting at least 24 hours.</td>
<td>0-42 days</td>
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<tr>
<td>Intussusception</td>
<td>Intussusception or Hematochezia following rotavirus vaccine receipt.</td>
<td>0-42 days</td>
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<tr>
<td>Syncope with injury</td>
<td>Any syncope with injury following immunization.</td>
<td>0-24 hours</td>
</tr>
<tr>
<td>Death</td>
<td>Any death of a vaccine recipient temporally linked to immunization where no other clear cause of death can be established.</td>
<td>Within 1 month</td>
</tr>
<tr>
<td>Fetal death or abnormality</td>
<td>Any fetal death or abnormality that follows immunization of a pregnant woman.</td>
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**Miscellaneous:**

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