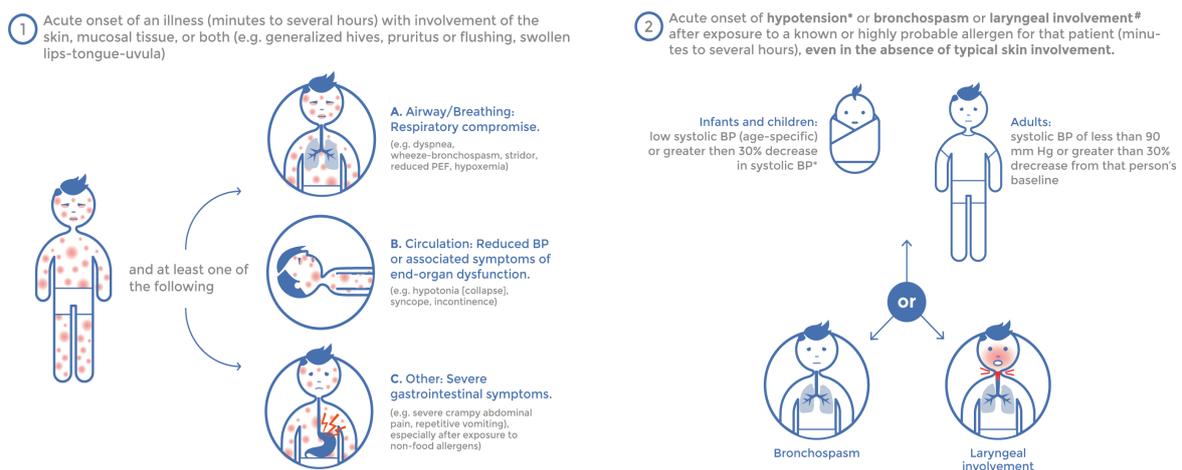


## APPENDIX A: MANAGEMENT OF ANAPHYLAXIS IN THE VACCINATION CLINIC

Vaccines often cause adverse events; however, the vast majority of adverse events following immunization (AEFI) are due to the vaccine stimulating a protective immune response, and not because of allergy. Anaphylaxis following vaccination is rare, occurring at less than 1 per million doses for vaccines.

The **World Allergy Organization** defines **anaphylaxis** as a serious systemic hypersensitivity (allergic) reaction that is usually rapid in onset and may cause death. Severe anaphylaxis is characterized by potentially **life-threatening compromise in airway, breathing and/or the circulation, and may occur without typical skin features or circulatory shock being present.**

Anaphylaxis is highly likely when any one of the following two criteria is fulfilled:



PEF, Peak expiratory flow; BP, blood pressure. #Laryngeal symptoms include: stridor, vocal changes, odynophagia.

**Fainting** is relatively common following vaccination. Symptoms should resolve rapidly on lying the patient flat. **If recovery is not rapid, consider the possibility of anaphylaxis and the need for IM epinephrine.**

	<b>Faint (vasovagal episode)</b>	<b>Anaphylaxis</b>
Onset	Before, during or within minutes of vaccination	Usually within 15 minutes, but can occur later
Features	<ul style="list-style-type: none"> <li>Generalized pallor, cold clammy or sweaty skin</li> <li>Normal respiration – may be shallow, but not labored</li> <li>Bradycardia, but with strong central pulse; Hypotension usually transient and responds to lying the patient down</li> <li>Sense of light-headedness/dizziness, improves once lying down. Transient jerking of the limbs and eye-rolling which may be confused with seizure.</li> </ul>	<ul style="list-style-type: none"> <li>Itchy skin rash / urticaria (wheals) or swelling (angioedema) e.g. lips. Face</li> <li>Facial erythema may be present</li> <li>Airway/Breathing symptoms (see above)</li> <li>Tachycardia, with weak/absent central pulse; hypotension – sustained</li> <li>Sense of “impending doom”; loss of consciousness – with no improvement once supine or head down position</li> </ul>

## MANAGEMENT

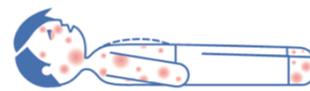
The treatment of anaphylaxis is based on general life support principles:

- Call for help immediately.
- Use an **Airway, Breathing, Circulation** approach to recognize and treat problems.

### Intramuscular (IM) epinephrine is the first-line treatment for anaphylaxis

- Give IM epinephrine to treat Airway/Breathing/Circulation problems
- Do not delay initial treatment if the diagnosis is unclear: a single dose of IM epinephrine (adrenaline) is well-tolerated and poses minimal risk
- **Repeat IM epinephrine every 5-15 minutes if features of anaphylaxis do not resolve.**

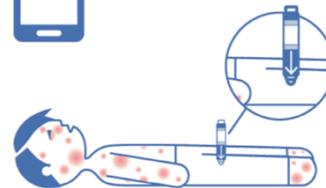
- 1 Assess the patient: Airway / Breathing / Circulation, mental status, skin and body weight (mass).



- 2 Call for help: resuscitation team (hospital) or emergency medical services (community) if available.



- 3 Inject epinephrine (adrenaline) intramuscularly in the mid-anterolateral aspect of the thigh, 0.01 mg/kg of a 1:1,000 (1 mg/ml) solution, maximum of 0.5 mg (adult) or 0.3 mg (child); record the time of the dose and repeat every 5-15 minutes, if needed. Most patients respond to 1 or 2 doses.



- 4 Place patient on the back or in a position of comfort if there is respiratory distress and/or vomiting; elevate the lower extremities; fatality can occur within seconds if patient stands or sits suddenly.



- 5 When indicated, give high-flow supplemental oxygen (6-8 L/minute), by face mask or oropharyngeal airway.



- 6 Establish intravenous access using needles or catheters with wide-bore cannula (14-16 gauge). Consider giving 1-2 liters of 0.9% (isotonic) saline rapidly (e.g. 5-10 ml/kg in the first 5-10 minutes to an adult; 10 ml/kg to a child).



- 7 If indicated at any time, perform cardiopulmonary resuscitation with continuous chest compressions.



- 8 At frequent, regular intervals, monitor patient's blood pressure, cardiac rate and function, respiratory status, and oxygenation (monitor continuously, if possible).



In addition

## Recommended doses for INTRAMUSCULAR epinephrine (adrenaline)

<b>0.01 mg/kg of body weight, to a maximum total dose of 0.5 mg</b> This is equivalent to 0.5ml of 1mg/ml (1:1000)* epinephrine (adrenaline) OR	
Infants under 10kg	0.01mg/kg = 0.01ml/kg of 1mg/ml
Children aged 1- 5 years	0.15mg = 0.15ml of 1mg/ml
Children aged 6-12 years	0.3mg = 0.3ml of 1mg/ml
Teenagers and adults	0.5mg = 0.5ml of 1mg/ml

\*Epinephrine 1mg/ml (1:1000) is recommended for intramuscular injections as this allows a more appropriate volume to be injected

In all vaccination settings, giving epinephrine by needle/syringe is preferred, since auto-injectors will only deliver a maximum of 300 micrograms epinephrine while **the appropriate dose in teenagers and adults is 500 micrograms**. Some settings may prefer to use an auto-injector for the first dose of epinephrine to treat anaphylaxis, for speed and ease. However, if further doses are needed, give these by needle/syringe in order to deliver the optimal dose.

### Training and equipment

All settings where vaccines are administered should be able to provide initial management of a patient with anaphylaxis. This includes:

- **Staff who are trained to recognize anaphylaxis**, call for help and administer IM epinephrine.
- Ability to **call for help**. A single responder must always ensure that help is coming. If there are several rescuers, actions can be undertaken simultaneously.
- **Equipment and drugs** for anaphylaxis. This includes (as a minimum):
  - Two ampoules of epinephrine (adrenaline) 1mg/ml (1:1000)
  - Four 23G needles and four graduated 1ml syringes
  - Equipment to provide ventilatory support e.g. bag/valve/mask ventilation. A risk assessment should be undertaken to assess whether an oxygen supply is appropriate (e.g. location, emergency services response times).

Do **not** stored equipment and emergency drugs in a locked cupboard or trolley. Drugs should be checked regularly to ensure they are within their expiry dates.

### Patient positioning

Death can occur within minutes if a patient stands, walks or sits up suddenly. Patients must NOT walk or stand during acute reactions. Use caution when transferring patients who have been stabilized.

- Patients with Airway and Breathing problems may prefer to sit up.
- Lying flat with or without leg elevation is helpful for patients with a low blood pressure (Circulation problem).
- Patients who are breathing normally and unconscious should be placed on their side (in the recovery position).
- Pregnant patients should lie on their left side to prevent aortocaval compression.



### Other supportive measures:

- Give further repeat doses of IM epinephrine every 5-15 minutes if symptoms do not resolve.
- Give oxygen.
- Severe upper airways obstruction is uncommon.
  - Seek urgent expert help if there is airway obstruction.
  - Nebulized epinephrine (5mL of 1mg/mL epinephrine) can be used to treat upper airways obstruction but **must not be prioritized over further IM epinephrine given every 5-15 minutes**.
- Bronchospasm - consider further inhaled bronchodilator therapy with salbutamol and/or ipratropium, but **must not be prioritized over IM epinephrine**.
- A reduction in blood flow is common in anaphylaxis, even in the absence of obvious circulatory compromise. Give a fluid bolus if there is an inadequate response to initial IM epinephrine, to support tissue perfusion and drug delivery.

### CARDIAC ARREST:

Patients with anaphylaxis must be monitored closely.

- Start chest compressions as soon as cardiac arrest is suspected (if the person becomes unresponsive or unconscious, and breathing is absent or abnormal)
- Ensure expert help (resuscitation team or ambulance) has been called.
- Follow standard cardiac arrest guidelines (use intravenous or intraosseous epinephrine in preference to IM route).

### Possible cross-reactivity between vaccines and drugs

Some oral medicines (e.g. antihistamines) used to treat more mild reactions contain the same substances as those which can cause allergic reactions to vaccines. Caution is recommended following allergic reactions to vaccines.

### BLOODS

A blood (serum) sample should be sent for mast cell tryptase measurement following suspected anaphylaxis. An initial sample should be taken 0.5-2 hours following onset of reaction, with a further convalescent sample at least 24 hours after complete resolution.

### SURVEILLANCE

The WAO is supporting a global surveillance program for allergic reactions to COVID-19 vaccines.

We encourage our colleagues to report anonymized information relating to possible reactions at:

<https://cutt.ly/wao-covid>

The information in this appendix is taken from the WAO 2020 Anaphylaxis Guidance, (available at [www.worldallergy.org/disease-focus/anaphylaxis#Guidelines](http://www.worldallergy.org/disease-focus/anaphylaxis#Guidelines)) and adapted from equivalent guidance from the Resuscitation Council UK.

## APPENDIX B: BRIGHTON COLLABORATION CRITERIA FOR ANAPHYLAXIS

The information in this appendix is a quick reference guide summarizing the Brighton Collaboration Anaphylaxis Working Group. Anaphylaxis: case definition and guidelines for data collection, analysis, and presentation of immunization safety data. *Vaccine*. 2007; 25(31):5675-84. doi: 10.1016/j.vaccine.2007.02.064.

The diagnostic certainty for anaphylaxis can be assessed by determining the number of major and minor criteria, as follows:

Organ System	Major Criteria	Minor Criteria
Skin or mucosal	<ul style="list-style-type: none"> <li>• generalized urticaria (hives) or erythema</li> <li>• angioedema, localized or generalized</li> <li>• generalized pruritus with skin rash</li> </ul>	<ul style="list-style-type: none"> <li>• generalized pruritus without rash</li> <li>• generalized prickle sensation</li> <li>• localized injection site urticaria</li> <li>• red and itchy eyes</li> </ul>
Cardiovascular	<ul style="list-style-type: none"> <li>• measured hypotension OR</li> <li>• shock (at least 3 of the following): <ul style="list-style-type: none"> <li>▪ tachycardia</li> <li>▪ capillary refill time (CRT) &gt;3 sec</li> <li>▪ reduced central pulse volume</li> <li>▪ decreased level of consciousness</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Reduced peripheral circulation (at least 2 of: <ul style="list-style-type: none"> <li>• Tachycardia</li> <li>• CRT &gt;3 sec without hypotension</li> <li>• decreased level of consciousness</li> </ul> </li> </ul>
Respiratory	<ul style="list-style-type: none"> <li>• Bilateral wheeze (bronchospasm)</li> <li>• Stridor</li> <li>• Swelling of upper airways</li> <li>• Respiratory distress (at least 2 of: tachypnoea; use of accessory respiratory muscles; recession; cyanosis; grunting)</li> </ul>	<ul style="list-style-type: none"> <li>• Persistent dry cough</li> <li>• Hoarse voice</li> <li>• Difficulty breathing without wheeze or stridor</li> <li>• Sensation of throat closure</li> </ul>
Gastrointestinal		<ul style="list-style-type: none"> <li>• Diarrhea</li> <li>• Nausea</li> <li>• Abdominal pain</li> <li>• Vomiting</li> </ul>
Laboratory		MC tryptase > upper normal limit

Note that all levels of diagnostic certainty **require the involvement the cardiovascular and/or respiratory systems.**

<p><b>Level 1 of diagnostic certainty</b></p> <ul style="list-style-type: none"> <li>• ≥1 major cardiovascular AND/OR ≥1 major respiratory criterion AND</li> <li>• ≥1 major dermatological criterion</li> </ul>
<p><b>Level 2 of diagnostic certainty</b></p> <ul style="list-style-type: none"> <li>• ≥1 major cardiovascular AND ≥1 major respiratory criterion OR</li> <li>• ≥1 major cardiovascular OR respiratory criterion AND</li> <li>• ≥1 minor criterion involving ≥1 different system (<i>other than</i> cardiovascular or respiratory systems) OR</li> <li>• (≥1 major dermatologic) AND (≥1 minor cardiovascular AND/OR minor respiratory criterion)</li> </ul>
<p><b>Level 3 of diagnostic certainty</b></p> <ul style="list-style-type: none"> <li>• ≥1 minor cardiovascular OR respiratory criterion AND</li> <li>• ≥1 minor criterion from each of ≥2 different systems/categories</li> </ul>

		Symptom One				
		DERM	CVS	RESP	Cvs	Resp
Symptom Two	CVS	1	-	2	-	2
	RESP	1	2	-	2	-
	Derm	-	2	2	3*	3*
	Cvs	2	-	2	-	3*
	Resp	2	2	-	3*	-
	GI	-	2	2	3*	3*
	Lab	-	2	2	3*	3*

CAPITALS: 1 or more MAJOR criteria in that system; Lower case: 1 or more minor criteria.

Columns or rows in CAPITALS indicate that 1 or more MAJOR criteria are present in that category. Columns or rows in Lower case indicate that 1 or more minor criteria are present. Level 3 diagnostic certainty requires 2 or more rows to be present in *either* the "cvs" or "resp" minor criteria column.

3\* = level 3 diagnostic certainty requires 2 or more minor criteria to be present in this column