Anaphylaxis

Key changes

- Use of adrenaline by health professionals for the immediate management of anaphylaxis or suspected anaphylaxis following vaccination

Anaphylaxis: Immediate Management in the Community

Anaphylaxis is likely if a person exposed to an allergen develops systemic changes which affect the skin, respiration and circulation, and which usually progress over several minutes

Remove exposure to allergen (e.g., discontinue administration of drugs/therapeutic agent)

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Assess skin, airway, breathing and circulation

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Rash, stridor, wheeze, respiratory distress, hypotension or clinical signs of shock?[1]

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Get help
Call an ambulance[2]

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Lie patient flat with legs raised (unless vomiting or respiratory distress increases)[3]

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Give adrenaline 1:1,000 (1mg/mL) IM immediately into the middle third of anterolateral thigh (use 25mm needle)[4]

Aged less than 6 months	*0.1mL (100 micrograms)*
Aged 6 months-5 years	*0.15mL (150 micrograms)*
Aged 6-12 years	*0.3mL (300 micrograms)*
Aged over 12 years	*0.5mL (500 micrograms)*[5]

For those over 100kg use 38-40mm needle

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Up to 3 doses may be given at 5 minute intervals
Remember urgency of hospital transfer
Alternate legs for multiple doses

1. Give CPR/BLS if necessary.
2. Ambulance will be equipped with oxygen and fluids
3. If respiratory distress present, place in semi recumbent position
4. The anterolateral thigh is preferred to injection into the deltoid muscle or subcutaneously
5. Two 300 microgram doses may be used if neither 1mg/ml vial or 500 microgram auto-injector are available

NOTE: **There are no contraindications to adrenaline.** Immediate administration of adequate doses of adrenaline will decrease patient mortality and morbidity. All patients with signs of a systemic reaction, especially hypotension, airway swelling or difficulty breathing, should receive immediate intramuscular (IM) adrenaline in the anterolateral thigh.

Adrenaline auto-injectors are not recommended as first line treatment by health professionals for the immediate management of anaphylaxis or suspected anaphylaxis following vaccination unless they are the only source of adrenaline available, as they may not allow IM delivery of an age appropriate dose.

Suggested Anaphylaxis Kit

The availability of protocols, equipment and drugs necessary for management of anaphylaxis should be checked before each vaccination session

- Copy of "Anaphylaxis: Immediate Management in the Community" from Immunisation Guidelines for Ireland
- 3 x 1 ml ampoules of adrenaline (1:1000, 1mg/ml)
- 3 x 1 ml syringes
- Needles (3 x 25 mm, 3 x 38-40mm)
- 1 pocket mask
- Sphygmomanometer (optional)
- Stethoscope (optional)
- Pen and paper to record time of administration of adrenaline.

The kits should be kept closed to ensure the drugs are not exposed to light and stored at room temperature. The kits require regular checking to replace drugs before their expiry date.

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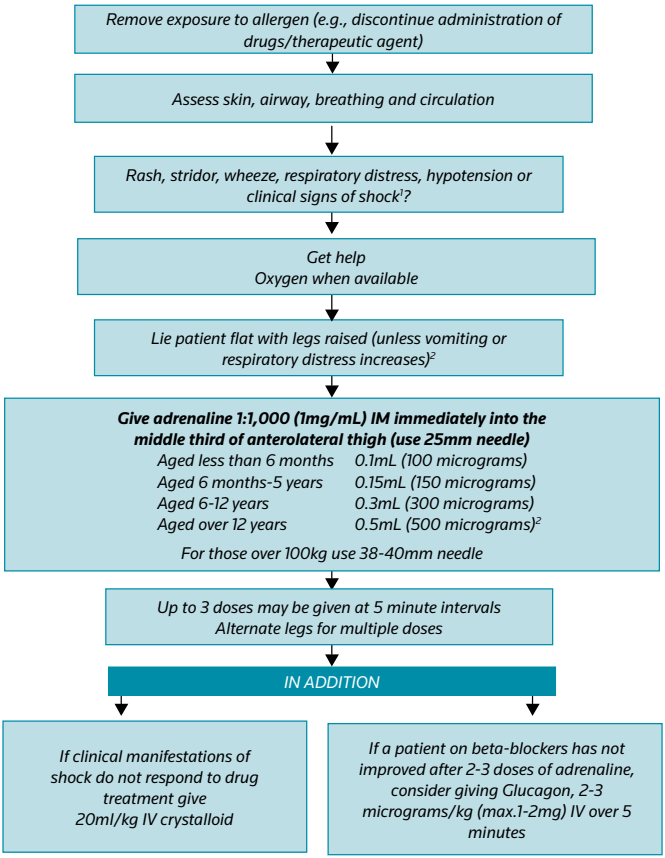
Anaphylaxis: Management by First Medical Responders (in GP surgery or hospital)



1. Give CPR/ALS if necessary. If severe hypotension, consider **slow** IV adrenaline 1:10,000 solution, dose 10 microgram/kg, maximum dose 500 micrograms, over several minutes. **This is hazardous and is recommended only in a hospital setting under supervision by an intensivist**. ***Note the different strength for IV use.***
2. Two 300 microgram doses may be used if neither 1mg/ml vial or 500 microgram auto-injector are available

NOTE: **There are no contraindications to adrenaline.** Immediate administration of adequate doses of adrenaline will decrease patient mortality and morbidity. All patients with signs of a systemic reaction, especially hypotension, airway swelling or difficulty breathing, should receive immediate intramuscular (IM) adrenaline in the anterolateral thigh.

Antihistamines or corticosteroids have no role in treating the respiratory or cardiovascular manifestations of anaphylaxis. An antihistamine may alleviate the cutaneous manifestations. A non-sedating oral antihistamine is preferred to chlorphenamine, which may sedate and which may cause hypotension when given IV.

Corticosteroids (preferably given orally) may be indicated if an acute asthma attack may have contributed to the severity of the anaphylaxis.

ANAPHYLAXIS

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

1. Acute onset of an illness (minutes to several hours) with involvement of the skin and/or mucosal tissue (e.g., generalised urticaria, pruritus or flushing, swollen lips-tongue-uvula)

and at least one of the following

   a. Airway/Breathing: Respiratory compromise (e.g., dyspnoea, wheeze-bronchospasm, stridor, reduced peak expiratory flow, hypoxaemia)

   b. Circulation: Reduced blood pressure (BP) or associated symptoms of end-organ dysfunction (e.g., hypotonia (collapse) syncope, incontinence)

   c. Other: Severe gastrointestinal symptoms (e.g., severe crampy abdominal pain, repetitive vomiting), especially after exposure to non-food allergens.

or

2. Onset within minutes to several hours of hypotension* or bronchospasm or laryngeal involvement** after exposure to a known or probable allergen even in the absence of skin involvement.

* Infants and children under 10 years: systolic BP less than 70 plus (twice age in years) mm Hg

Children aged 10 years and older and adults: systolic BP less than 90mm Hg

**Symptoms including stridor, vocal changes, painful swallowing

Anaphylaxis is an acute, potentially fatal, multiorgan system reaction caused by the release of chemical mediators from mast cells and basophils. This results in capillary leakage, mucosal oedema and ultimately shock and asphyxia. It is caused by foreign protein antigens such as food, drugs, vaccines and bee stings. The US Vaccine Safety Datalink studied the rate of anaphylaxis following vaccination, using the Brighton case definition. This showed a rate of 1.31 (95% Confidence Interval, 0.90-1.84) per million vaccine doses. Most episodes begin within 30 minutes of vaccination.

It can vary in severity and rate of progression with manifestations over a few minutes or may be delayed for hours, adding to diagnostic difficulty. Shorter intervals to onset generally indicate more severe reactions. Fatal outcome is extremely rare. It usually results from delayed administration of adrenaline

and from severe respiratory and/or cardiovascular complications. Other risk factors for fatal anaphylaxis include previous cardiovascular morbidity, older age, beta-lactam antibiotics, radiocontrast injections, and upright posture.

Vaccine recipients should be observed for at least 15 minutes after vaccination. If this is not practicable, vaccine recipients should wait in the vicinity for 15 minutes.

If there is a specific concern about a possible vaccine allergy e.g., previous anaphylaxis to a vaccine component or mastocytosis, vaccine recipients should be observed for 30 minutes.

Use of adrenaline by health professionals for the immediate management of anaphylaxis or suspected anaphylaxis following vaccination

Anaphylaxis is a medical emergency that requires rapid identification and treatment. Adrenaline is the most important drug for the treatment of anaphylaxis. Adrenaline maintains blood pressure, restores adequate tissue oxygenation and causes bronchodilation. Adrenaline works best when given early after the onset of anaphylaxis symptoms. Delayed administration is associated with protracted reactions, hypotension and fatal outcome.

There are no contraindications to adrenaline.

Adrenaline should be given intramuscularly (IM) in the anterolateral thigh. This rapidly achieves peak plasma and tissue concentrations, and absorption is more rapid than from the deltoid muscle. Absorption from the subcutaneous (SC) layer is significantly slowed compared to IM injection and is biphasic. This is likely to lead to lower plasma levels in the first 10 minutes after injection.

If it is not feasible to expose the skin, the needle may be inserted through clothing, avoiding seams and pockets. Although there is a slightly increased risk of infection, timely administration of adrenaline is the priority. The risk of infection can be addressed once the person has stabilised.

The recommended needle length for IM injections in the anterolateral thigh is 25mm (38-40mm for those weighing more than 100kg and 16mm in infants weighing 2.5 - 3 kg). Needles which are 16mm or shorter may enter the SC layer and not the muscle in children and adults.

Adrenaline auto-injectors

Adrenaline auto-injectors are not recommended as first line treatment by health professionals for the immediate management of anaphylaxis or suspected anaphylaxis following vaccination, unless they are the only source of adrenaline available.

Four adrenaline auto-injectors are authorised in Ireland (not all may be marketed):

- Anapen 150, 300 and 500 micrograms
- Emerade 150, 300 and 500 micrograms
- Epipen 150 and 300 micrograms
- Jext 150 and 300 micrograms

All have needle lengths of 16mm or less, and are unlikely to reach the IM layer. All are designed to be injected through clothing or directly through the skin. If injecting through clothing, avoid seams or pockets. Although there is a slightly increased risk of infection, timely administration of adrenaline is the priority. The risk of infection can be addressed once the person has stabilised.

If a 500 microgram dose is not available, two 300 microgram doses should be given.

Auto-injectors are an appropriate rescue medication for use by patients or their carers in the community for the management of anaphylaxis.

Most patients respond to a single dose of IM adrenaline, particularly if it is given promptly after the onset of symptoms. When additional doses are required, typically only one or rarely two further doses are needed (e.g., in those with severe anaphylaxis). A second dose is necessary in up to 36% of cases.

Biphasic or late phase reactions, in which patients have a recurrence of symptoms and signs several hours after the initial episode, have been described in up to 20% of cases. They often occur after symptoms of anaphylaxis have resolved, can be more difficult to treat than the initial episode, and may require intubation. Patients should therefore be observed in hospital for at least 12 hours after severe episodes of anaphylaxis.
Fatal outcome is extremely rare. Death usually results from delayed administration of adrenaline and from severe respiratory and/or cardiovascular complications. Other risk factors for fatal anaphylaxis include previous cardiovascular morbidity, older age, beta-lactam antibiotics, radiocontrast injections, and upright posture.

Differential diagnosis

Anaphylaxis must be distinguished from fainting (vasovagal episode), anxiety, breath-holding episodes and idiopathic urticaria or angioedema, which are more common.

Table 1 shows features which may assist differentiating fainting from anaphylaxis.

Table 1: Differentiating Vasovagal episode and Anaphylaxis

		Vasovagal episode	Anaphylaxis
Onset		Immediate	Usually within 5 minutes, but can be delayed for hours
Symptoms/signs	**Skin**	Generalised pallor; cold, clammy skin	Itch, generalised erythema, urticaria or angioedema (localised swelling of face, mouth, etc.)
	Respiratory	Normal or shallow, not laboured	Cough, wheeze, stridor, tachypnoea, recession, cyanosis
	Cardiovascular	Bradycardia but strong carotid pulse Hypotension corrected when lying	Tachycardia, weak/absent pulse. Sustained hypotension unless specific treatment
	Neurological	Light-headed, possible loss of consciousness, improves on lying down	Severe anxiety and distress. Loss of consciousness

Those experiencing **anxiety** may appear fearful, pale and sweaty, and complain of light-headedness, dizziness and numbness or tingling of their hands or feet. Hyperventilation is usually present.

During a **breath-holding episode** the child is suddenly silent and may be agitated. Facial flushing or pallor can occur as breath-holding continues. Some episodes end with resumption of crying, but others can be followed by a brief period of unconsciousness during which breathing resumes.
Urticaria or angioedema may appear at or away from the injection site but are not always caused by an allergic reaction and may disappear without additional treatment.

If any other symptoms occur, even if considered mild (sneezing, nasal congestion, coughing, etc.), adrenaline should be given. There is little risk to the use of adrenaline, especially in children, whereas delay in its administration in anaphylaxis may result in death. The features of anaphylaxis include obstructive swelling of the upper airway, marked bronchospasm and hypotension.

Beta blockers

Beta blockers may interfere with the action of adrenaline or with the compensatory mechanisms which occur in anaphylaxis.

If a patient on beta-blockers has not improved after 2-3 doses of adrenaline, consider giving Glucagon, 2-3 micrograms/ kg (max. 1-2mgs) IV over five minutes, IV salbutamol, and/or IV atropine. These should only be used in hospital, preferably under the supervision of an intensivist.

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