

## Definition of anaphylaxis

There are many definitions of anaphylaxis in the literature and recently there has been considerable effort internationally to develop clear and consistent definitions and guidelines. The Australasian Society of Clinical Immunology and Allergy (ASCIA) define anaphylaxis as:

*“Anaphylaxis is a rapidly evolving generalized multi-system allergic reaction characterized by one or more symptoms or signs of respiratory and/or cardiovascular involvement and involvement of other systems such as the skin and/or the gastrointestinal tract.”<sup>1</sup>*

Anaphylaxis is set apart from simple allergic reactions such as urticaria and asthma by the simultaneous involvement of several organ systems. The combination of cardiorespiratory symptoms with mucosal and/or skin changes is most specific.

## Etiology

Anaphylaxis is triggered by the binding of allergen to specific immunoglobulin E (IgE). It implies previous exposure and sensitisation to the triggering substance or a cross reactive allergen. When an allergen binds to the IgE receptors on the surface of mast cells and basophils this results in cellular activation and degranulation. These cells release preformed mediators such as histamine and tryptase (an enzyme specific to mast cells) that elicit the signs and symptoms of anaphylaxis. This mechanism is also known as the Type 1 immediate hypersensitivity reaction.

“Anaphylactoid” reactions are clinically indistinguishable from anaphylaxis, but differ by their immune mechanism. As distinction between anaphylaxis and anaphylactoid reaction is impossible on the basis of clinical signs and symptoms alone, a clinical definition cannot differentiate between the two.

Treatment is the same.

## Signs and symptoms of anaphylaxis

Symptoms/signs of respiratory/cardiovascular involvement are:<sup>2</sup>

### Respiratory

- Difficulty/noisy breathing
- Swelling of the tongue
- Swelling/tightness of the throat
- Difficulty talking and/or hoarse voice
- Wheezing or persistent cough

### Cardiovascular

- Loss of consciousness
- Collapse
- Pale and floppy (in young children)
- Hypotension

## Differentiating between anaphylaxis and a faint

|                  | Faint   | Anaphylaxis  |
|------------------|---|--|
| Onset            | Usually at the time or soon after the injection           | Usually some delay between 5–30 minutes after injection              |
| <b>System</b>    |   |  |
| Skin             | Pale, sweaty, cold and clammy                             | Red, raised, and itchy rash; swollen eyes and face, generalised rash |
| Respiratory      | Normal to deep breaths                                    | Noisy breathing from airway obstruction (wheeze or stridor)          |
| Cardiovascular   | Bradycardia, transient hypotension                        | Tachycardia, hypotension   |
| Gastrointestinal | Nausea/vomiting   | Abdominal cramps   |
| Neurological     | Transient loss of consciousness, good response once prone | Loss of consciousness, little response once prone                    |

Patients often report a sense of doom in the early phase of an anaphylactic episode.

The presence of mucosal/cutaneous signs is key to differentiating anaphylaxis from similar clinical syndromes with different etiology such as fainting or hypotonic hyporesponsive episode (HHE). Evidence of skin involvement is therefore required at level one of diagnosis.<sup>3</sup>

## Anaphylaxis following immunisation

All vaccinations have the potential to produce an anaphylactic reaction, albeit very rarely. The incidence of anaphylaxis varies from less than one in a million to up to 3 per million. While this is a rare event, it is vital that it is recognised and managed well. The International Brighton Collaboration case definition and guidelines for anaphylaxis have provided the following diagnostic criteria.<sup>3</sup>

### Case definition of anaphylaxis following immunisation

Level 1 offers highly specific diagnosis while levels 2 and 3 are less specific but more sensitive so that all possible cases can be captured. Details about the severity should always be recorded.

For all levels of diagnostic certainty anaphylaxis is a clinical syndrome characterised by sudden onset AND

- rapid progression of signs and symptoms AND
- involving multiple (2) organ systems, as follows:

#### Level 3 – not specific

- 1 minor cardiovascular OR respiratory criterion AND
- 1 minor criterion from each of 2 different systems/categories.

#### Early Warning

#### Level 2 – not as specific however more sensitive

- 1 major cardiovascular AND
- 1 major respiratory criterion OR
- 1 major cardiovascular OR respiratory criterion AND
- 1 minor criterion involving 1 different system (other than cardiovascular or respiratory systems) OR
- 1 major dermatologic AND 1 minor cardiovascular AND/OR minor respiratory criterion.

#### Level 1 – highly Specific for Anaphylaxis

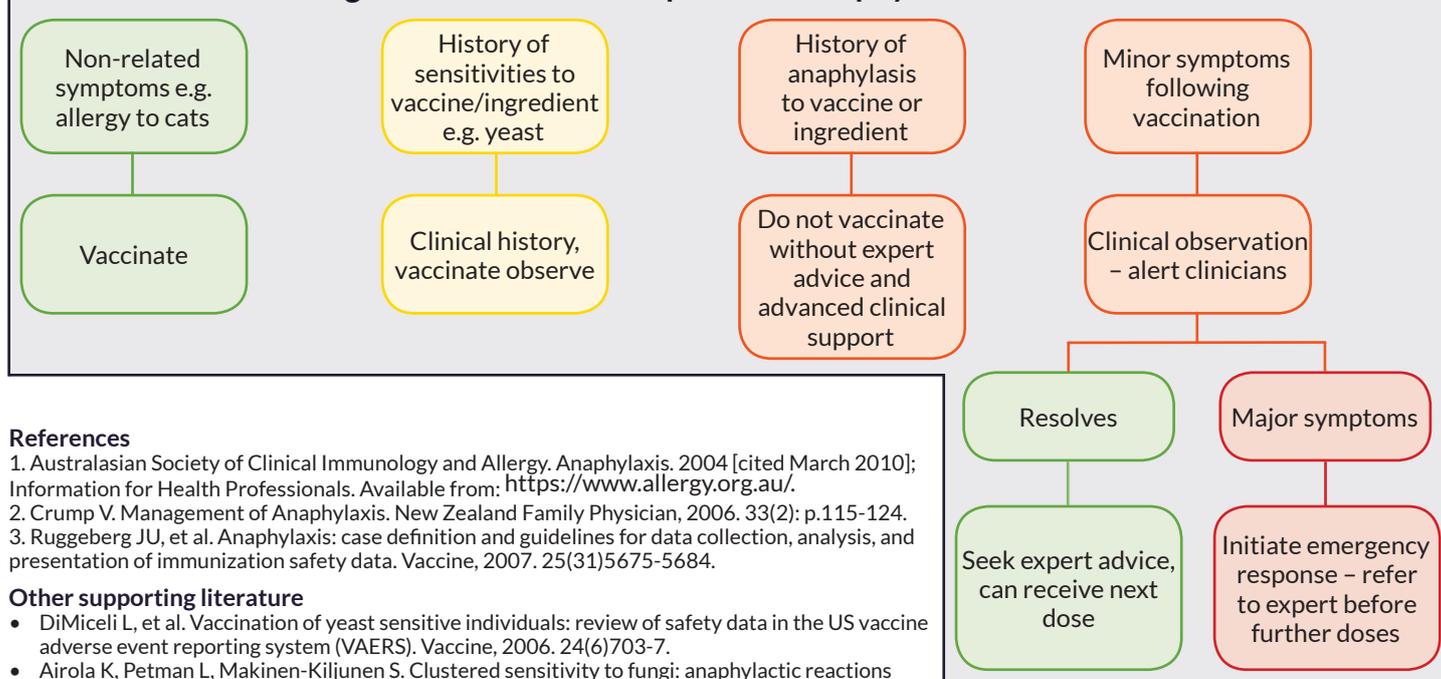
- 1 major dermatological AND
- 1 major cardiovascular AND/OR
- 1 major respiratory criterion.

#### Emergency action!

## Brighton Collaboration minor and major criteria used in the case definition of anaphylaxis<sup>3</sup>

| Minor Criteria   | Major Criteria  |
|--|---|
| <b>Dermatologic or mucosal</b> <ul style="list-style-type: none"> <li>generalised pruritus without skin rash</li> <li>generalised prickle sensation</li> <li>localised injection site urticaria</li> <li>red and itchy eyes</li> </ul>   | <b>Dermatologic or mucosal</b> <ul style="list-style-type: none"> <li>generalised urticaria (hives) or generalised erythema</li> <li>angioedema (non hereditary), localised or generalised</li> <li>generalised pruritus with skin rash</li> </ul>  |
| <b>Cardiovascular</b> <ul style="list-style-type: none"> <li>reduced peripheral circulation as indicated by the combination of at least 2 of                             <ul style="list-style-type: none"> <li>tachycardia and</li> <li>a capillary refill time of &gt;3 seconds without hypotension</li> <li>a decreased level of consciousness</li> </ul> </li> </ul> | <b>Cardiovascular</b> <ul style="list-style-type: none"> <li>measured hypotension</li> <li>clinical diagnosis of uncompensated shock, indicated by the combination of at least 3 of the following:                             <ul style="list-style-type: none"> <li>tachycardia</li> <li>capillary refill time &gt;3 seconds</li> <li>reduced central pulse volume</li> <li>decreased level of consciousness or loss of consciousness</li> </ul> </li> </ul>  |
| <b>Respiratory</b> <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> <li>sneezing, rhinorrhea</li> </ul>   | <b>Respiratory</b> <ul style="list-style-type: none"> <li>bilateral wheeze (bronchospasm)</li> <li>stridor</li> <li>upper airway swelling (lip, tongue, throat, uvula, or larynx)</li> <li>respiratory distress—2 or more of the following:                             <ul style="list-style-type: none"> <li>tachypnoea</li> <li>increased use of accessory respiratory muscles (sternocleidomastoid, intercostals, etc.)</li> <li>recession</li> <li>cyanosis</li> <li>grunting</li> </ul> </li> </ul> |
| <b>Gastrointestinal</b> <ul style="list-style-type: none"> <li>diarrhoea</li> <li>abdominal pain</li> <li>nausea</li> <li>vomiting</li> </ul>  |   |
| <b>Laboratory</b> <ul style="list-style-type: none"> <li>Mast cell tryptase elevation &gt; upper normal limit</li> </ul>   |   |

## Clinical decision making around vaccines and potential anaphylaxis



### References

1. Australasian Society of Clinical Immunology and Allergy. Anaphylaxis. 2004 [cited March 2010]; Information for Health Professionals. Available from: <https://www.allergy.org.au/>.
2. Crump V. Management of Anaphylaxis. New Zealand Family Physician, 2006. 33(2): p.115-124.
3. Ruggeberg JU, et al. Anaphylaxis: case definition and guidelines for data collection, analysis, and presentation of immunization safety data. Vaccine, 2007. 25(31):5675-5684.

### Other supporting literature

- DiMiceli L, et al. Vaccination of yeast sensitive individuals: review of safety data in the US vaccine adverse event reporting system (VAERS). Vaccine, 2006. 24(6):703-7.
- Airola K, Petman L, Makinen-Kiljunen S. Clustered sensitivity to fungi: anaphylactic reactions caused by ingestive allergy to yeasts. Annals of Allergy, Asthma, & Immunology, 2006. 97(3):294-7.
- Viswanath PK, Horng-Der S, and Hari V. Immunobiology of fungal allergens. International Archives of Allergy and Immunology, 2002. 129(3):181.
- Grotto I, et al. Major adverse reactions to yeast-derived hepatitis B vaccines—a review. Vaccine, 1998. 16(4):29-334.
- Bohilke K, et al. Risk of anaphylaxis after vaccination of children and adolescents. Pediatrics, 2003. 112(4):815-20.
- Gold M, et al. Re-vaccination of 421 children with a past history of an adverse vaccine reaction in a special immunisation service. Archives of Disease in Childhood, 2000. 83(2):128-31.
- Patja A, et al. Allergic reactions to measles-mumps-rubella vaccination. Pediatrics, 2001. 107(2):E27.