



## Allergy and Anaphylaxis Question and Answer

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### Question 1: Please give a definition of anaphylaxis.

#### Answer

Traditionally, the term anaphylaxis has referred to a systemic, immediate hypersensitivity reaction caused by IgE-mediated immunologic release of mediators from mast cells and basophils. A change in terminology was suggested by the World Allergy Organization, which proposed that anaphylaxis refer to a 'severe, life threatening, generalized or systemic hypersensitivity reaction'. Anaphylaxis is defined by a number of signs and symptoms, alone or in combination, which occur within minutes, or up to a few hours, after exposure to a provoking agent. It can be mild, moderate or severe.

### Question 2: List common triggers for anaphylaxis.

#### Answer

##### 1. IgE-Mediated Reactions Foods

In theory, any food protein is capable of causing an anaphylactic reaction. Foods most frequently implicated in anaphylaxis are:

- Peanut (a legume)
- Tree nuts (walnut, hazel nut, cashew, pistachio nut, Brazil nut, pine nut, almond)
- Fish
- Shellfish (shrimp, crab, lobster, oyster, scallops)
- Milk
- Chicken eggs
- Seeds (cotton seed, sesame, mustard)
- Fruits, vegetables

Food sensitivity can be so severe that a systemic reaction can occur to particle inhalation, such as the odors of cooked fish or the opening of a package of peanuts. A severe allergy to pollen, for example, ragweed, grass or tree pollen, can indicate that an individual may be susceptible to anaphylaxis or to the oral allergy syndrome (manifested primarily by severe oropharyngeal itching, with or without facial angioedema) caused by eating certain plant-derived foods. This is due to homologous proteins found between pollens and foods. The main allergen of all grasses is profilin, which is a pan-allergen, found in many plants, pollens and fruits, and grass-sensitive individuals can sometimes react to many plant-derived foods.

Typical allergen cross-reactivity associations are:

- Birch pollen: apple, raw potato, carrot, celery and hazelnut
- Mugwort pollen: celery, apple, peanut and kiwifruit
- Ragweed pollen: melons (watermelon, cantaloupe, honeydew) and banana
- Latex: banana, avocado, kiwifruit, chestnut and papaya

Food-associated, exercise-induced anaphylaxis may occur when individuals exercise within 2-4 hours after ingesting a specific food. The individual is, however, able to exercise without symptoms, as long as the incriminated food is not consumed before exercise. The patient is likewise able to ingest the incriminated food with impunity as long as no exercise occurs for several hours after eating the food.

### **Antibiotics and other drugs**

Penicillin, cephalosporin, and sulphonamide antibiotics. Penicillin is the most common cause of anaphylaxis, not just drug-induced cases. Penicillin and other antibiotics are haptens, molecules that are too small to elicit immune responses, but which may bind to serum proteins and produce IgE antibodies. Serious reactions to penicillin occur about twice as frequently following intramuscular or intravenous administration versus oral administration, but oral penicillin administration may also induce anaphylaxis. Neither atopy, nor a genetic history of allergic rhinitis, asthma or eczema, are risk factors for the development of penicillin allergy.

### **Muscle relaxants**

Muscle relaxants, e.g., suxamethonium, alcuronium, vecuronium, pancuronium and atracurium, which are widely used in general anesthesia, account for 70-80% of all allergic reactions occurring during general anesthesia. Reactions are caused by an immediate IgE-mediated hypersensitivity reaction.

### **Insects**

Hymenoptera venoms (bee, wasp, yellow-jacket, hornet, fire ant) contain enzymes such as phospholipases and hyaluronidases and other proteins which can elicit an IgE antibody response.

### **Latex**

Latex is a milky sap produced by the rubber tree *Hevea brasiliensis*. Latex-related allergic reactions can complicate medical procedures, e.g., internal examinations, surgery, and catheterization. Medical staff may develop occupational allergy through use of latex gloves.

### **Foreign proteins**

Examples of foreign proteins which can cause anaphylaxis are insulin, seminal proteins, and horse-derived antitoxins, the latter of which is used to neutralize venom in snake-bites.

### **Elective medical procedures**

Allergen immunotherapy

## **2. Cytotoxic and Immune Complex- Complement?Mediated Reactions**

### ***Whole blood, serum, plasma, fractionated serum products, immunoglobulins, dextran***

Anaphylactic responses have been observed after the administration of whole blood or its products, including serum, plasma, fractionated serum products and immunoglobulins. One of the mechanisms responsible for these reactions is the formation of antigen-antibody reactions on the red blood cell surface or from immune complexes resulting in the activation of complement. The active by-products generated by complement activation (anaphylatoxins C3a, C4a and C5a) cause mast cell (and basophil) degranulation, mediator release and generation, and anaphylaxis.

In addition, complement products may directly induce vascular permeability and contract smooth muscle. Individuals who have IgA deficiency may become sensitized to the IgA provided in blood products. Those selective IgA deficient subjects (1:500 of the general population) can develop anaphylaxis when given blood products, because of their anti- IgA antibodies (probably IgE-anti-IgA). Cytotoxic reactions can also cause anaphylaxis, via complement activation. Antibodies (IgG and IgM) against red blood cells, as occurs in a mismatched blood transfusion reaction, activate complement. This reaction causes agglutination and lysis of red blood cells and perturbation of mast cells resulting in anaphylaxis.

## **3. Non-Immunologic Mast Cell Activators**

### ***Radiocontrast media, low-molecular weight chemicals***

Mast cells may degranulate when exposed to low-molecular-weight chemicals. Hyperosmolar iodinated contrast media may cause mast cell degranulation by activation of the complement and coagulation systems. These reactions can also occur, but much less commonly, with the newer contrast media agents.

### **Narcotics**

Narcotics are mast cell activators capable of causing elevated plasma histamine levels and non-allergic anaphylaxis. They are most commonly observed by anesthesiologists.

## **4. Modulators of Arachidonic Acid Metabolism**

### ***Aspirin, ibuprofen, indomethacin and other non-steroidal anti-inflammatory agents (NSAIDs)***

IgE antibodies against aspirin and other NSAIDs have not been identified. Affected individuals tolerate choline or sodium salicylates, substances closely structurally related to aspirin but different in that they lack the acetyl group.

## 5. Sulfiting Agents

### **Sodium and potassium sulfites, bisulfites, metabisulfites, and gaseous sulfur dioxides**

These preservatives are added to foods and drinks to prevent discoloration and are also used as preservatives in some medications. Sulfites are converted in the acid environment of the stomach to SO<sub>2</sub> and H<sub>2</sub>SO<sub>3</sub>, which are then inhaled. They can produce asthma and non-allergic hypersensitivity reactions in susceptible individuals.

## 6. Idiopathic Causes

### **Exercise**

Exercise alone can cause anaphylaxis as can food-induced anaphylaxis, Exercise-induced anaphylaxis can occur during the pollinating season of plants to which the individual is allergic.

### **Catamenial Anaphylaxis**

Catamenial anaphylaxis is a syndrome of hypersensitivity induced by endogenous progesterone secretion. Patients may exhibit a cyclic pattern of attacks during the premenstrual part of the cycle.

### **Idiopathic Anaphylaxis**

Flushing, tachycardia, angioedema, upper airway obstruction, urticaria and other signs and symptoms of anaphylaxis can occur without a recognizable cause. Diagnosis is based primarily on the history and an exhaustive search for causative factors. Serum tryptase and urinary histamine levels may be useful.

### **Question 3: List the possible symptoms of a severe anaphylactic reaction.**

#### **Answer**

The symptoms and signs of anaphylaxis may be isolated to one organ system or involve a number of systems. The initial manifestation of anaphylaxis may be loss of consciousness. Overall, the most common manifestations are cutaneous, followed by respiratory, cardiovascular, and gastrointestinal manifestations.

**Cutaneous:** Diffuse erythema, flushing, urticaria, pruritus, angioedema.

**Respiratory:** Upper airway obstruction from angioedema of the tongue, oropharynx or larynx; bronchospasm, chest tightness, cough, wheezing; rhinitis, sneezing, congestion, rhinorrhea.  
**Cardiovascular:** Faintness, hypotension, arrhythmias, hypovolemic shock, syncope, chest pain.

**Gastro-intestinal:** Abdominal pain, hyperperistalsis with faecal urgency or incontinence, nausea, vomiting, diarrhea.

**Oral:** Pruritus of lips, tongue and palate, edema of lips and tongue.

**Ocular:** Periorbital edema, erythema, conjunctival erythema, tearing.  
**Genito-urinary:** Uterine cramps, urinary urgency or incontinence.

Severe initial symptoms develop rapidly, reaching peak severity within 3-30 minutes. There may occasionally be a quiescent period of 1-8 hours before the development of a second reaction (a biphasic response).

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

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissues, or both (e.g., generalized hives, pruritus or flushing, swollen lips-tongue-uvula)

AND AT LEAST ONE OF THE FOLLOWING:

a. Respiratory compromise (e.g., dyspnea, wheeze-bronchospasm, stridor, reduced Peak Expiratory Flow [PEF], hypoxemia)

b. Reduced BP or associated symptoms of end-organ dysfunction (e.g., hypotonia [collapse], syncope, incontinence)

2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):

- a. Involvement of the skin-mucosal tissue (e.g., generalized hives, itch-flush, swollen lips-tongue-uvula)
- b. Respiratory compromise (e.g., dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
- c. Reduced blood pressure (BP) or associated symptoms of end-organ dysfunction (e.g., hypotonia [collapse], syncope, incontinence)
- d. Persistent gastrointestinal symptoms (e.g., crampy abdominal pain, vomiting)

3. Reduced BP after exposure to known allergen for that patient (minutes to several hours):

- a. Infants and children: low systolic BP (age specific) or greater than 30% decrease in systolic BP
- b. Adults: systolic BP of less than 90 mmHg or greater than 30% decrease from their baseline

From Sampson HA et al. Second symposium on the definition and management of anaphylaxis. J Allergy Clin Immunol 2006; 117:391 - 397.

**Question 4: Which drug must be given if there is evidence of a severe systemic allergic reaction?**

**Answer**

Adrenaline is the drug of choice in the emergency treatment of acute severe anaphylactic reactions due to insect bites, drugs and other allergens.

Adrenaline is a sympathomimetic drug (mimicks action of the sympathetic division of the autonomic nervous system). Major effects are increased systolic blood pressure, reduced diastolic pressure, tachycardia, hyperglycaemia and hypokalaemia. It is a powerful cardiac stimulant. It has vaso-pressor properties, an antihistaminergic action and is a bronchodilator. The onset of action is rapid and of short duration. After intravenous infusion the half-life is approximately five to ten minutes. Adrenaline is rapidly distributed to the heart, spleen, several glandular tissues and adrenergic nerves.

Antihistamine therapy can be useful as adjunctive treatment with adrenalin. Although this therapy is not life-saving, it can at times offer dramatic relief of itching and urticaria. The exact role of corticosteroids in the management of anaphylaxis has not been established. Perhaps the most likely rationale for the use of corticosteroids relates to their effects on the late-phase reaction. Because anaphylaxis can be biphasic, a role for corticosteroids in preventing such a recurrence has been postulated. However, based on a review of available studies, as of yet no clear-cut benefit of corticosteroids can be demonstrated in this regard even though some studies do show potential efficacy.

**Question 5: Jack Jumper Ant stings are an important cause of anaphylaxis in Australia. Only one laboratory (in Australia) performs Specific IgE to Jack Jumper Ant. Where do we refer requests for Jack Jumper Ant specific IgE?**

**Answer**

Jack Jumper Ants are members of the "Hymenoptera" order and are therefore related to other stinging insects such as bees and wasps. They do not bite, but rather grasp with their jaws and bend around and sting the victim. Deaths have been recorded.

SA Pathology, Flinders Medical Centre (ph 08 8222 3000) perform Specific IgE for Jack Jumper Ant on the Immunocap 250. Phadia have produced this allergen cap from known positive patients attending Flinders Medical Centre Immunology Clinic. Studies indicate that the assay has a very high specificity, but a limited sensitivity.