
Anaphylaxis

Hossin I Mohamed Elsharif,* Abdulnabi A. Masoud,* Abdalsamed Altaher,* Mutwakil G. Ahmed,*

Background:

The first documented case of anaphylaxis was purportedly the death of the Pharaoh Menes in 2640 BC from a wasp sting.¹ Portier and Richet first coined the term *anaphylaxis* in 1902 when a second vaccinating dose of sea anemone toxin caused a dog's death. The term is derived from the Greek words *ana* - ("up, back, again") and *phylaxis* ("guarding, protection, immunity").²

At present, there is no universally agreed definition of anaphylaxis. The European Academy of Allergology and Clinical Immunology Nomenclature Committee proposed the following broad definition: Anaphylaxis is a severe, life-threatening, generalised or systemic hypersensitivity reaction.^{3,4} This is characterised by rapidly developing life-threatening airway and/or breathing and/or circulation problems usually associated with skin and mucosal changes.^{5,6}

The overall prognosis of anaphylaxis is good, with a case fatality ratio of less than 1% reported in most population-based studies.⁷⁻⁹

Risk of death is, however, increased in those with pre-existing asthma, particularly if the asthma is poorly controlled or in those asthmatics who fail to use, or delay treatment with, adrenaline.¹⁰ However, the risk of an individual suffering recurrent anaphylactic reaction appears to be quite substantial, being estimated at approximately 1 in 12 per year in the UK.¹¹

Triggers:

Anaphylaxis can be triggered by any of a very broad range of triggers, but those most commonly identified include food, drugs and venom¹¹⁻¹³ (Table 1). However, in many cases, no cause can be identified. A significant number of cases of anaphylaxis are idiopathic (non-IgE mediated).¹¹

Table 1. Common Triggers

Anaphylaxis: IgE-mediated mast cell degranulation
Foods • Peanuts • Tree nuts • Fish and shellfish • Milk • Eggs • Soy products
Insect stings • Bee venom • Wasp venom
Chemicals and drugs • Intravenous anaesthetic agents, e.g. suxamethonium, propofol • Penicillin and other antibiotics • Latex
Anaphylactoid: non-IgE-mediated mast cell degranulation
Drugs • Aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) • Opiates • Radiocontrast media
Physical • Exercise • Cold
Idiopathic • No cause is identified in 20% of patients with anaphylaxis

*) Department of Medicine, Sebha University, Sebha – Libya.

Clinical Presentation:

All individuals who have had a known or suspected anaphylactic episode require a careful and complete review of their clinical history. Initially, patients often describe a sense of impending doom, accompanied by pruritus and flushing. Other symptoms can evolve rapidly, such as the following¹⁵⁻¹⁸:

- Dermatologic/ocular: Flushing, urticaria, angioedema, cutaneous and/or conjunctival injection or pruritus, warmth, and swelling
- Respiratory: Nasal congestion, coryza, rhinorrhea, sneezing, throat tightness, wheezing, shortness of breath, cough, hoarseness, dyspnea
- Cardiovascular: Dizziness, weakness, syncope, chest pain, palpitations
- Gastrointestinal: Dysphagia, nausea, vomiting, diarrhea, bloating, cramps
- Neurologic: Headache, dizziness, blurred vision, and seizure (very rare and often associated with hypotension)
- Other: Metallic taste, feeling of impending doom.

Examination may reveal the following findings¹⁵⁻¹⁸:

- General appearance and vital signs: Vary according to the severity of the anaphylactic episode and the organ system(s) affected; patients are commonly restless and anxious
- Respiratory findings: Severe angioedema of the tongue and lips; tachypnea; stridor or severe air hunger; loss of voice, hoarseness, and/or dysphonia; wheezing
- Cardiovascular: Tachycardia, hypotension; cardiovascular collapse and shock can occur immediately, without any other findings
- Neurologic: Altered mentation; depressed level of consciousness or may be agitated and/or combative
- Dermatologic: Classic skin manifestation is urticaria (ie, hives) anywhere on the body; angioedema (soft-tissue swelling);

generalized (whole-body) erythema (or flushing) without urticaria or angioedema

- Gastrointestinal: Vomiting, diarrhea, and abdominal distention

Diagnosis of Anaphylaxis:

The history is the most important tool to determine whether a patient has had anaphylaxis and the cause of the episode. (C). The more rapidly anaphylaxis develops, the more likely the reaction is to be severe and potentially life-threatening. (C) A thorough differential diagnosis should be considered, and other conditions should be ruled out. (C) Laboratory tests can be helpful to confirm a diagnosis of anaphylaxis or rule out other causes (Box 1). Proper timing of such tests (e.g., serum tryptase) is essential (B).¹⁵⁻¹⁷

Box 1. Laboratory Studies

Histamine and tryptase assessment
Elevated eosinophil count
IgE assays
Skin prick tests
Intradermal (ID) tests
5-Hydroxyindoleacetic acid levels
Food skin tests
Skin testing for medication allergy
Nasal smear tests for eosinophils
Spirometry/pulmonary function tests
Nasal smear tests

A single set of criteria will not identify all anaphylactic reactions.^{15,16} There is a range of signs and symptoms, none of which are entirely specific for an anaphylactic reaction; however, certain combinations of signs make the diagnosis of an anaphylactic reaction more likely (tables 2-3).¹⁵⁻²⁰

Table 2. Diagnostic Criteria (UK Resuscitation Council 2008)¹⁵

Anaphylaxis is likely when all of the following 3 criteria are met:

- Sudden onset and rapid progression of symptoms
- Life-threatening Airway and/or Breathing and/or Circulation problems
- Skin and/or mucosal changes (flushing, urticaria, angioedema)

The following supports the diagnosis:

- Exposure to a known allergen for the patient

Table 3. Differential Diagnosis

Acute respiratory disorders Severe asthma; foreign body aspiration ; pulmonary embolism.
Cerebrovascular disease Seizure ; vasovagal attack; myocardial infarction; arrhythmia
Miscellaneous disorders Carcinoid syndrome, systemic mastocytosis, Chinese restaurant syndrome, scombroid fish ingestion, phaeochromocytoma, hereditary angioedema.
Nonorganic disease Hyperventilation syndrome, panic attacks, vocal cord dysfunction, Muchausen's syndrome and Muchausen's by proxy

Management of Anaphylaxis:

At present, there are no randomised controlled clinical trials in humans providing unequivocal evidence for the treatment of anaphylactic reactions.¹³⁻¹⁵ Nonetheless, there is a wealth of experience and systematic reviews of the limited evidence that can be used as illustrated by the UK Resuscitation (2008) and US National (2010) guidelines for management of anaphylaxis (Fig 1).¹⁴⁻¹⁶

1. Assess airway, breathing, circulation, and level of consciousness (altered mentation may suggest the presence of hypoxia).
2. Administer epinephrine. Aqueous epinephrine 1:1000 dilution (1 mg/mL), 0.2-0.5 mL (0.01 mg/kg in children, maximum 0.3 mg dosage) intramuscularly in the lateral aspect of the thigh or subcutaneously every 5 min, as necessary. (C)
3. Consider call for help.
4. Place the patient in a recumbent position and elevate the lower extremities.
5. Establish and maintain an airway. Ventilatory assistance via a one-way valve facemask with oxygen inlet port may be necessary.
6. Administer oxygen. Oxygen should be considered for patients with anaphylaxis who have prolonged reactions guided by continuous pulse oximetry and/or arterial blood gas determination.
7. Rapid IV fluid replacement should be started when the patient has failed to respond to the treatment as outlined above (B).
8. Consider diphenhydramine, 1-2 mg/kg or 25-50 mg/dose (parenterally).
9. Consider ranitidine, 50 mg in adults and 12.5-50 mg (1 mg/kg) in children.
10. Consider inhaled β -agonist (e.g., albuterol metered dose inhaler (MDI) 2-6 puffs or

nebulized, 2.5-5 mg in 3 mL saline and repeat as necessary) for bronchospasm resistant to adequate doses of epinephrine.

11. Glucocorticosteroids should never be used in place of or prior to epinephrine and are not helpful acutely. However, they have the potential to prevent recurrent or protracted anaphylaxis.
12. When anaphylaxis is not responding to the above measures, the use of IV epinephrine, vasopressors and glucagon may need to be considered.
13. Cardiopulmonary resuscitation and advanced cardiac life support for cardiopulmonary arrest during anaphylaxis.
14. Atropine if asystole or pulseless electrical activity (PEA) is present.
15. Prolonged resuscitation is encouraged, if necessary, since a successful outcome is more likely in anaphylaxis.
16. Transport to emergency department or intensive care, as setting dictates.
17. Remove and/or treat the trigger if possible.
18. Observation and Subsequent Follow-Up.
19. Consider Consultation with Allergist-Immunologist.

Prevention of Anaphylaxis¹⁵⁻²⁰

1. Avoidance management should be individualized, taking into consideration factors such as age, activity, occupation, hobbies, residential conditions, access to medical care, and the patient's level of personal anxiety. (C)
2. Even in cases when the allergen is known, avoidance measures may not always be successful. Therefore, patients should be instructed in self-management of anaphylaxis. (C)
3. Venom immunotherapy (VIT) is successful in preventing anaphylaxis in up to 98% of

- patients who have previously experienced venom-induced anaphylaxis. (A)
4. Pharmacologic prophylaxis should be used in select situations, e.g. to prevent recurrent anaphylactic reactions to radiographic contrast material. (C)
 5. Desensitization to medications that are known to have caused anaphylaxis can be effective. (C).
 6. Patient education might be the most important preventive strategy. (B)
 7. Patient instruction to wear and/or carry identification denoting his or her condition (e.g., Medic Alert jewelry). (C)

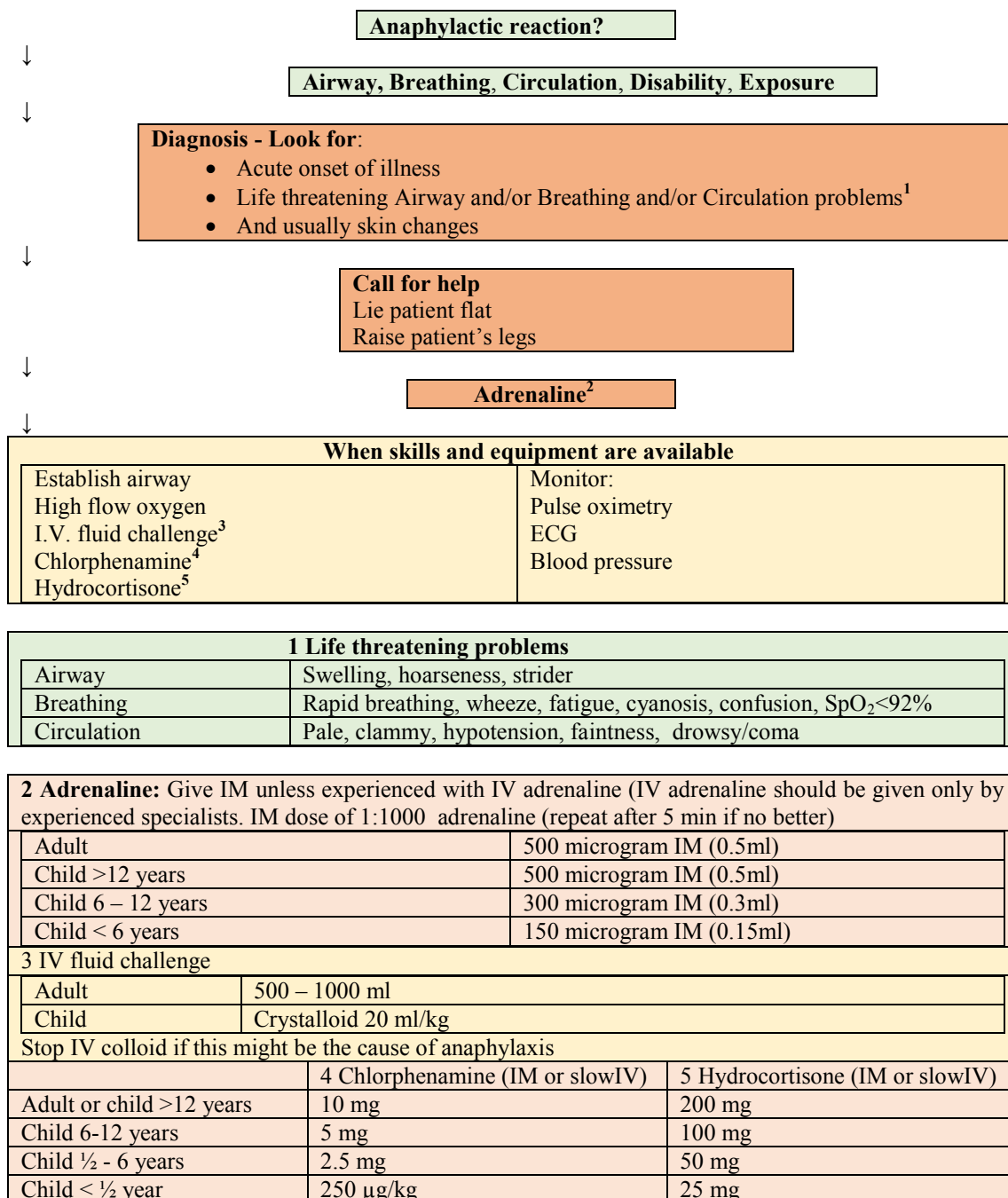


Fig. 1: Resuscitation Council UK (2008) – Anaphylaxis Alogarithm¹⁵

Definitions:

Category of Evidence¹⁶

- Ia** Evidence from meta-analysis of randomized controlled trials
- Ib** Evidence from at least one randomized controlled trial
- IIa** Evidence from at least one controlled study without randomization
- IIb** Evidence from at least one other type of quasiexperimental study
- III** Evidence from non-experimental descriptive studies, such as comparative studies
- IV** Evidence from expert committee reports or opinions or clinical experience of respected authorities or both

References:

1. Cohen SG. The Pharaoh and the wasp. *Allergy Proc* 1989; 10:149-51. (Historical Article)
2. Cohen SG. Portier, Richet and the discovery of anaphylaxis. A centennial. *J Allergy Clin Immunol* 2002; 110: 331-6. (Historical Article)
3. Johansson SG, Bieber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, et al. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization. October 2003. *J Allergy Clin Immunol* 2004;113(5):832-6.
4. Yocum MW, Buuerfield JH, Klein JS et al. Epidemiology of anaphylaxis in Olmsted County: A population-based study. *J Allergy Clin Immunol* 1999;104(2 Pt 1): 452-6.
5. Sampson HA, MunozFurlong A, Bock SA, et al. Symposium on the definition and management of anaphylaxis: summary report. [http:// www. ncbi. nlm. nih. gov/ pubmed/15753908](http://www.ncbi.nlm.nih.gov/pubmed/15753908). 2006.
6. Allergy Clinic Online. Epidemiology, immune-pathogenesis and management of anaphylaxis. <http://allergycliniconline.com/2012/02/26/allergy-pediatric-reference-epidemiology-immunop>. 2012.
7. Lecture Notes in Dentistry. Anaphylactic Shock Clinical Features and Management. <http://dentallectnotes.blogspot.com/2011/08/anaphylactic-shock-clinical-feature-and.html>. 2011.
8. Brown AF, McKinnon D, DeStefano F et al. Epidemiology of anaphylaxis among children and adolescents enrolled in a health maintenance organization. *J Allergy Clin Immunol* 2001;108(5):861-6.
9. Bohlke K, Davis RL, DeStefano F et al. epidemiology of anaphylaxis among children and adolescents in a health maintenance organization. *J Allergy Clin Immunol* 2004;113(3):536-42.
10. Pumphrey RS, Sheikh A, Strachan DP et al. Burden of allergic disease in the UK: secondary analyses of national databases. *Clin Exp Allergy* 2004;34(4):520-6.
11. Gupta R, Sheikh A, Strachan DP et al. Burden of allergic disease in the UK: Secondary analysis of analyses of national databases. *Clin Exp Allergy* 2004; 34 (4): 520-6.
12. Simon FE, Arduoso LR, Ebisawa M et al. World Allergy Organization. Anaphylaxis Guidelines: 2013 update of the evidence base. *Arch Allergy Immunol*. 2013;162(3): 193-204 .
13. Mustafa M. Anaphylaxis: Treatment and Management. <http://emedicine.medscape.com/article/135065-treatment>. 2013.
14. Anand MK. Immediate Hypersensitivity Reactions Workup. <http://emedicine.medscape.com/article/136217-workup#a0719>. 2012.
15. National Institute for Health and Care Excellence (NICE). Anaphylaxis (CG123). <http://guidance.nice.org.uk/CG134>. 2011.
16. National Guideline Clearinghouse. The diagnosis and management of anaphylaxis practice parameter: 2010 update. [http://www. guideline.gov/content.aspx ?id =38449](http://www.guideline.gov/content.aspx?id=38449). 2010.
17. Haymore BR, Carr WW and Frank WT. Anaphylaxis and epinephrine prescribing in a military hospital: underutilization of the intramuscular route. *Allergy Asthma Proc* 2005;26(5):361-5.

Strength of Recommendation

- A** Directly based on category I evidence
- B** Directly based on category II evidence or extrapolated recommendation from category I evidence
- C** Directly based on category III evidence or extrapolated recommendation from category I or II evidence
- D** Directly based on category IV evidence or extrapolated recommendation from category I, II, or III evidence
- LB** (Lab Based)

18. Pediatric Emergency Practice. Allergic Emergencies in Children: The Pivotal Role of Epinephrine. www.ebmedicine.net/topics.php?action=showTopic&topic_id=150. 2007.
 19. Brown SG. Clinical features and severity grading of anaphylaxis. J Allergy Clin Immunol 2004;114(2):371-6.
 20. Johnston SL, Unsworth J, Gomples MM. Adrenaline given outside the context of life threatening allergic reactions. BMJ 2003;33(921):589-90.
- Further Reading**
- I. PDF Resuscitation Council (UK) www.resus.org.uk/pages/alsFacts.pdf
File format: Adobe PDF
 - II. Anaphylaxis - NICE
guidance.nice.org.uk/CG134
 - III. National Guideline Clearinghouse | The diagnosis and...www.guideline.gov/content.aspx?id=38449 Cached
The diagnosis and management of anaphylaxis practice parameter: 2010 update
 - IV. ERC European Resuscitation Council
www.erc.edu Cached
 - V. [PDF] Guideline 9.2.7 - Australian Resuscitation Council Website
resus.org.au/policy/guidelines/section_9/guideline-9-2-7...File format: Adobe PDF
 - VI. Guidelines & Policies » New Zealand Resuscitation Council
www.nzrc.org.nz/policies-and-guidelines Cached
 - VII. Allergy Prevention in Children | Australasian Society of ...
www.allergy.org.au/patients/allergy-prevention/allergy... Cached
 - VIII. Anaphylaxis - NHS Choices
www.nhs.uk/conditions/Anaphylaxis/Pages/Introduction.aspx Cached
 - IX. Anaphylaxis - MayoClinic.com - Mayo Clinic
www.mayoclinic.com/health/anaphylaxis/DS00009 Cached
 - X. World Allergy Organization Guidelines for Anaphylaxis Management
www.medscape.com/viewarticle/767159 Cached