Exploring the Progression of Anaphylaxis: Stages and Treatment of Anaphylaxis: A Review Article

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***Abstract*—Anaphylaxis is an acute, life-threatening hypersensitivity disorder defined as a generalized, rapidly evolving, multi-systemic allergic reaction. Anaphylactic reactions were classified as IgE-mediated responses, while anaphylactic reactions were classified as IgE-independent events. Physical presentations of anaphylaxis range from mild skin flushing and pruritus to severe respiratory symptoms**

***Index Terms*—Skin Rash, Hives, tryptase, Adrenaline**

I. INTRODUCTION

Anaphylaxis is rare, but some people are more likely to have it than others. Most people recover from it. But it's important to tell doctor about any drug or latex allergies you have before any kind of medical treatment, including dental care. It's also a good idea to wear a medical alert bracelet or pendant or carry a card with information about allergy.

Anaphylaxis is a sudden and severe allergic reaction that occurs within minutes or hours of exposure. Immediate medical attention is needed for this condition. Without treatment, anaphylaxis can get worse very quickly and lead to death within 15 minutes.

Anaphylaxis is an acute, life-threatening hypersensitivity disorder defined as a generalized, rapidly evolving, multi-systemic allergic reaction. Anaphylactic reactions were classified as IgE-mediated responses, while anaphylactic reactions were classified as IgE-independent events. Physical presentations of anaphylaxis range from mild skin flushing and pruritus to severe respiratory symptoms. This activity describes the evaluation and treatment of anaphylaxis and explains the role of the interprofessional team in managing patients with this condition.

Anaphylaxis symptoms include skin reactions, breathing difficulties, and fall in blood pressure if not treated can lead to respiratory arrest and even death.

II. STAGES OF ANAPHYLAXIS

Anaphylaxis doesn't always follow distinct stages, but it can be described in four phases:

- Early stage: Itching, hives, anxiety.
- Progressive stage: Difficulty breathing, abdominal pain.
- Life-threatening stage: Low blood pressure, shock.
- Late phase reaction: Recurrence of symptoms after initial recovery.

Stage 1: Mild anaphylaxis	Stage 2: Moderate anaphylaxis	Stage 3: Severe anaphylaxis	Stage 4: Life-threatening anaphylaxis
Skin rash, redness, itching, or hives Runny nose	More widespread symptoms, including Hives that are spreading Mild swelling in the lips or tongue Difficulty swallowing	Signs of anaphylactic shock, including Difficulty breathing Extensive swelling Weak pulse Dizziness Dangerously low blood pressure	Symptoms include Losing consciousness Being unable to breathe Inadequate blood flow to vital organs Blood stops circulating

Stage 1: Sensitization And Initial Exposure

The early stages of anaphylaxis begin with sensitization, which occurs when the immune system is first exposed

to an allergen. During this stage, the immune system recognizes the allergen as harmful and produces the antibody immunoglobulin E (IgE). Immunoglobulin antibodies activate mast cells and basophils, which are responsible for releasing inflammatory chemicals. The immune system's response to allergen exposure initially does not cause symptoms but rather prepares the immune system for a potential reaction upon consecutive exposure.

Stage 2: Early Allergic Reaction

The second stage of an anaphylactic reaction occurs when someone is re-exposed to an allergen, whether it's a specific food, medication, or insect sting. Sensitized mast cells and basophils identify the allergen and release histamine and other inflammatory chemicals, such as tryptase, carboxypeptidase A, and proteoglycan, into the bloodstream.

This release of inflammatory chemicals triggers the early symptoms of anaphylaxis, which can appear within minutes to hours following exposure. The most common signs and symptoms of an allergic reaction in the early stages include:

- Hives
- Skin redness
- Itchy or watery eyes
- Sneezing
- Nasal congestion
- Mild wheezing
- Nausea, vomiting, or diarrhea

Anaphylaxis signs and symptoms typically manifest in skin reactions, respiratory symptoms, and gastrointestinal issues. While not life-threatening, they can rapidly progress if not immediately treated.

Stage 3: Systemic Reaction and Escalation

The systemic effects often come into play as the anaphylactic reaction progresses and inflammatory chemicals circulate throughout the body. The third stage of anaphylaxis is marked by a more severe and widespread allergic reaction, with symptoms that affect multiple organ systems.

Anaphylaxis causes vasodilation, which leads to a drop in blood pressure from blood vessels widening. The histamine increases vascular permeability, which causes fluid to leak from blood vessels into surrounding tissues. This reaction further lowers blood pressure and causes swelling. Bronchoconstriction causes the airways to narrow, making it difficult to breathe during an anaphylactic reaction.

The symptoms experienced during this stage may include:

- Swelling of the face, lips, and throat (angioedema)
- Difficulty breathing
- Coughing or wheezing
- Rapid or weak pulse
- Dizziness or fainting
- Severe abdominal pain and cramps

This stage is a critical point in anaphylaxis, which requires immediate intervention and treatment to prevent progression to anaphylactic shock and organ failure.

Stage 4: Anaphylactic Shock and Organ Failure

The final stage of anaphylaxis is anaphylactic shock, which is a life-threatening condition that calls for emergency treatment. Anaphylactic shock is when the body's circulatory system fails to maintain sufficient blood flow and oxygen delivery to vital organs, leading to organ dysfunction and potential failure.

Critical features of anaphylactic shock include:

- Severe hypotension
- Respiratory failure
- Loss of consciousness
- Potential organ failure

Hypotension is critically low blood pressure that causes the body to go into shock. Severe airway obstruction and bronchospasm caused by food allergen exposure can lead to respiratory failure.

Some individuals experiencing anaphylaxis may lose consciousness from a lack of oxygen to the brain. As the allergic reaction progresses, organ failure can happen in the heart, lungs, liver, and kidneys. Without prompt administration of epinephrine and medical attention, anaphylaxis can be fatal.

Clinical features

System	Features of anaphylaxis
Respiratory (most common in children)	Persistent cough Wheeze, stridor, hoarse voice, difficulty talking or change in

	character of cry Tongue swelling Chest pain or dyspnoea Subjective feeling of swelling, tightness or tingling the throat or mouth
Cardiovascular	Pale and floppy (infant) Palpitations, tachycardia, bradycardia Hypotension, pallor Collapse with or without unconsciousness Cardiac arrest
Neurological	Dizziness Altered consciousness, confusion, sudden behaviour change
Gastrointestinal	Nausea, vomiting, dysphagia Diarrhoea Abdominal or pelvic pain
Dermatological	Urticarial rash Erythema, flushing, tearing Angioedema Pruritus (skin, eyes, nose, throat, mouth)

Investigations

- Anaphylaxis is a clinical diagnosis**.** A serum tryptase has no role in acute management of anaphylaxis. It should only be ordered after consultation with a paediatric allergy specialist in special circumstances.

Treatment

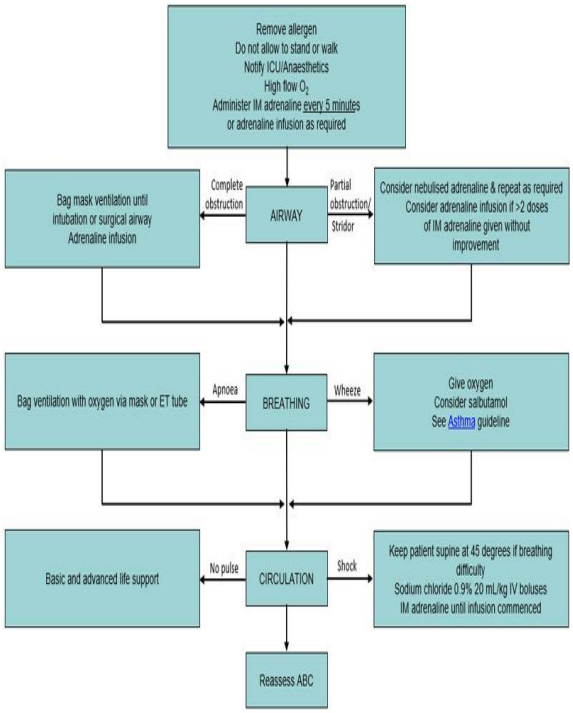
- Remove allergen if still present (eg insect stinger, food debris in mouth)
- Lay patient flat. Do not allow the child to stand or walk. Fatality can occur within seconds if the child stands or sits suddenly. Treat the child in the supine position or lying on their side. If a vomiting child is sat upright, monitor for hypotension
- Intramuscular adrenaline 10 microgram/kg or 0.01 mL/kg of 1:1000 (maximum 0.5 mL), into lateral thigh which should be repeated after 5 minutes if the child is not improving
- Do not use subcut adrenaline, as absorption is less reliable than the IM route
- Do not use IV bolus adrenaline unless cardiac arrest is imminent
- Use an adrenaline autoinjector if unable to calculate exact dose or to avoid delay, including in children <1 year old

The following doses of adrenaline may be used

Adrenaline doses			
Age (years)	Weight (kg)	Volume of 1:1000 adrenaline (mL)	Adrenaline autoinjectors
<1	<7.5 kg	0.1 mL	Not available
<1 - 2	7.5 – 10	0.1 mL	150 microg device
2 – 3	15	0.15 mL	
4 – 5	18	0.18 mL	
5 – 6	20	0.2 mL	300 microg device
7 – 10	30	0.3 mL	
10 – 12	40	0.4 mL	
>12 and adults	>50	0.5 mL	300 microg or 500 microg device

- Give oxygen
- If not improving, give a second dose of adrenaline, consult senior staff and consider adrenaline infusion (0.05 - 0.5 microgram/kg/min)
- Continue giving IM adrenaline every 5 minutes until IV access is obtained

III. GUIDELINES FOR TREATMENT OF ANAPHYLAXIS



Other treatments to consider

repeated doses of IM adrenaline together with

- Nebulised or MDI salbutamol is recommended if the child has respiratory distress with wheezing. Also consider other anti-asthma medications. See Asthma
- Antihistamines may be given for symptomatic relief of pruritus. Second generation antihistamines are preferred (eg cetirizine). **Avoid promethazine as it can cause hypotension**
- Corticosteroids and leukotriene antagonists have no proven benefit in anaphylaxis
- Avoid NSAIDs

Observation and admission

- All patients with anaphylaxis should be observed for at least 4 hours in a supervised setting with facilities to manage deterioration Admission for a minimum 12-hour period of observation is recommended if:
- Further treatment is required within 4 hours of last adrenaline administration (biphasic or prolonged reaction)
- Previous history of biphasic reaction
- Poorly controlled asthma
- The child lives in an isolated location with delay to emergency services
- Anaphylaxis to monoclonal antibody

Peripheral IV adrenaline infusion

This should only be done in consultation with a senior staff member. Avoid high infusion rates for more than two hours as it may cause fluid overload Check local health service adrenaline infusion guidelines. Below is an example guideline:

- Mix 1 mL of **1:1000** adrenaline in 1000 mL of fluid
- Suitable fluids are glucose 5%, glucose 10%, sodium chloride 0.9% saline and glucose with sodium chloride combinations
- Start infusion at 0.1 microgram/kg/minute (6 mL/kg/hr)
- A dedicated line, infusion pump and anti-reflux valves should be used when possible
- Titrate dose according to response and side-effects
- Monitor continuously (all vitals, 12-lead ECG and conscious state)
- If possible, insert a second IV as fluid boluses may be needed
- If hypotensive, resuscitate with fluid; use boluses of 20 mL/kg of sodium chloride 0.9% for shock
- Nebulised adrenaline is not recommended as first-line therapy, but may be a useful adjunct after IM adrenaline if upper airway obstruction or bronchospasm is present
- If airway oedema is not responding to parenteral (IM, IV) and nebulised adrenaline**,** early intubation is indicated

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