

ایمان



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SIGN, SYMPTOM AND DIAGNOSIS OF ANAPHYLAXIS

INTRODUCTION

- Anaphylaxis is an **acute**, potentially **life-threatening**, **multisystem** syndrome caused by the **sudden release of mast cell mediators** into the systemic circulation.
- It most often results from IgE-mediated reactions to foods, drugs, and insect stings, but any agent capable of inciting a sudden, systemic degranulation of mast cells can induce it.

PREVALENCE

- In industrialized countries, the estimated lifetime prevalence of anaphylaxis from all causes is between 0.05 and 2 percent in the general population, and the rate of occurrence is increasing.
- In the United States, the reported lifetime prevalence of anaphylaxis is at least 1.6 percent, based on strict clinical diagnostic criteria.

DIAGNOSTIC CRITERIA

- There are three diagnostic criteria for anaphylaxis, each reflecting a different clinical presentation.
- Anaphylaxis is highly likely when any one of the following three criteria is fulfilled:

CRITERION 1:

- Acute onset of an illness (minutes to several hours) involving the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula) and at least one of the following:
- Respiratory compromise (eg, dyspnea, wheeze/bronchospasm, stridor, reduced peak expiratory flow, hypoxemia)

OR

- Reduced blood pressure (BP) or associated symptoms and signs of end-organ malperfusion (eg, hypotonia [collapse], syncope, incontinence)
- Note that skin symptoms and signs are present in up to 90 percent of anaphylactic episodes. This criterion will therefore frequently be helpful in making the diagnosis.

CRITERION 2:

- Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):
- Involvement of the skin-mucosal tissue (eg, generalized hives, itch-flush, swollen lips-tongue-uvula).
- Respiratory compromise (eg, dyspnea, wheeze/bronchospasm, stridor, reduced peak expiratory flow, hypoxemia).
- Reduced BP or associated symptoms and signs of end-organ malperfusion (eg, hypotonia [collapse], syncope, incontinence).
- Persistent gastrointestinal symptoms and signs (eg, crampy abdominal pain, vomiting).

CRITERION 3:

- Reduced BP after exposure to a known allergen for that patient (minutes to several hours):
- Reduced BP in adults is defined as a systolic BP of less than 90 mmHg or greater than 30 percent decrease from that person's baseline.
- In infants and children, reduced BP is defined as low systolic BP (age-specific)* or greater than 30 percent decrease in systolic BP.

* Low systolic BP for children is defined as:

- Less than 70 mmHg from 1 month up to 1 year
- Less than $(70 \text{ mmHg} + [2 \times \text{age}])$ from 1 to 10 years
- Less than 90 mmHg from 11 to 17 years

- Note that criterion 3 is intended to detect anaphylactic episodes in which only one organ system is involved and is applied to patients who have been exposed to a substance to which they are known to be allergic (for example, hypotension or shock after an insect sting).

- There will be patients who do not fulfill any of these criteria but for whom the administration of epinephrine is appropriate. As an example, it would be appropriate to administer epinephrine to a patient with a history of severe anaphylaxis to peanut who presents with urticaria and flushing that developed within minutes of a known or suspected ingestion of peanut

Diagnostic criteria for anaphylaxis

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 tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula)

AND AT LEAST ONE OF THE FOLLOWING:

A. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, hypoxemia)

B. Reduced BP* or associated symptoms of end-organ dysfunction (eg, 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 (eg, generalized hives, itch-flush, swollen lips-tongue-uvula)

B. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, hypoxemia)

C. Reduced BP* or associated symptoms (eg, hypotonia, collapse, syncope, incontinence)

D. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)

3. Reduced BP* *after exposure to a 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 that person's baseline

BP: blood pressure.

* Low systolic blood pressure for children is defined as:

- Less than 70 mmHg from 1 month to 1 year
- Less than (70 mmHg + [2 x age]) from 1 to 10 years
- Less than 90 mmHg from 11 to 17 years

SYMPTOMS AND SIGNS

- Anaphylaxis may present with various combinations of approximately 40 potential symptoms and signs
- Common symptoms and signs of anaphylaxis include the following:

SYMPTOMS AND SIGNS

- **Skin and mucosal** symptoms and signs, which occur in **up to 90 percent** of episodes, including generalized hives, itching or flushing, swollen lips-tongue-uvula, periorbital edema, or conjunctival swelling. However, urticaria, flushing and itching may have resolved by the time the patient reaches a medical facility, so it is important to ask about skin findings at the start of the reaction.
- **Respiratory** symptoms and signs, which occur in **up to 85 percent** of episodes, including nasal discharge, nasal congestion, sneezing, itching of the throat and ear canals, change in voice quality, sensation of throat closure or choking, stridor, shortness of breath, wheeze, or cough.

SYMPTOMS AND SIGNS

- **Gastrointestinal** symptoms and signs, which occur in **up to 45 percent** of episodes, including nausea, vomiting, diarrhea, and crampy abdominal pain.
- **Cardiovascular** symptoms and signs, which occur in **up to 45 percent** of episodes, including hypotonia (collapse), syncope, incontinence, dizziness, tachycardia, and hypotension.
- **Death** from anaphylaxis usually results from asphyxiation due to upper or lower airway obstruction or from cardiovascular collapse.

Symptoms and signs of anaphylaxis

Skin

Feeling of warmth, flushing (erythema), itching, urticaria, angioedema, and "hair standing on end" (piloerection)

Oral

Itching or tingling of lips, tongue, or palate

Edema of lips, tongue, uvula, metallic taste

Respiratory

Nose - Itching, congestion, rhinorrhea, and sneezing

Laryngeal - Itching and "tightness" in the throat, dysphonia, hoarseness, stridor

Lower airways - Shortness of breath (dyspnea), chest tightness, cough, wheezing, and cyanosis

Gastrointestinal

Nausea, abdominal pain, vomiting, diarrhea, and dysphagia (difficulty swallowing)

Cardiovascular

Feeling of faintness or dizziness; syncope, altered mental status, chest pain, palpitations, tachycardia, bradycardia or other dysrhythmia, hypotension, tunnel vision, difficulty hearing, urinary or fecal incontinence, and cardiac arrest

Neurologic

Anxiety, apprehension, sense of impending doom, seizures, headache and confusion; young children may have sudden behavioral changes (cling, cry, become irritable, cease to play)

Ocular

Periorbital itching, erythema and edema, tearing, and conjunctival erythema

Other

Uterine cramps in women and girls

TIME COURSE

- Anaphylaxis is usually characterized by a defined exposure to a potential cause, followed usually within **seconds to minutes** but **rarely up to hours later**, by rapid onset, evolution, and ultimate resolution of symptoms and signs.
- However, anaphylaxis is **unpredictable**. It may be **mild and resolve spontaneously** due to endogenous production of compensatory mediators (eg, epinephrine, angiotensin II, endothelin, and others) or it may be **severe** and progress within minutes to respiratory or cardiovascular compromise and death.
- At the onset of an anaphylactic episode, it is not possible to predict how severe it will become, how rapidly it will progress, and whether it will resolve promptly and completely or become biphasic or protracted, because the factors that determine the course of anaphylaxis in an individual patient are not fully understood. Thus, early administration of epinephrine is essential to prevent the progression to life-threatening manifestations.

BIPHASIC ANAPHYLAXIS

- Biphasic anaphylaxis is defined as a recurrence of symptoms that develops following the apparent resolution of the initial anaphylactic episode with no additional exposure to the causative agent.
- Rates of biphasic reactions in the contemporary literature range from as low as 0.4 percent in one study of adult ED patients to 14.7 percent in a study of pediatric anaphylaxis, with an estimated overall rate of 5 percent. They typically occur within 12 hours after resolution of the initial symptoms, although recurrences up to 72 hours later have been reported.

PROTRACTED ANAPHYLAXIS

- Protracted anaphylaxis is defined as an anaphylactic reaction that lasts for hours, days, or even weeks in extreme cases

DELAYED ANAPHYLAXIS

- Rarely, the onset of anaphylaxis will be delayed (ie, beginning hours rather than minutes after exposure to the causative agent)

DIAGNOSTIC PITFALLS

- Anaphylaxis **is not always easy to recognize clinically**. The patterns of target organ involvement are variable and may differ among individuals, as well as among episodes in the same individual. Anaphylaxis is likely **underdiagnosed and under-reported** for a variety of reasons

DIAGNOSTIC PITFALLS

- Hypotension may go undetected when **measured very early** in the course of the episode (when compensated by reflex tachycardia), when the initial BP measurement is obtained **after epinephrine administration**, or when an inappropriately **small BP cuff** is used.

DIAGNOSTIC PITFALLS

- Age-appropriate standards for normal BP must be used for children and infants.
- Many of the dramatic physical signs associated with hypoxia and hypotension in anaphylaxis are nonspecific, such as dyspnea, stridor, wheeze, confusion, collapse, unconsciousness, and incontinence.
- Skin symptoms and signs (such as hives, itching, flushing, and angioedema), which are helpful in making the diagnosis, are **absent or unrecognized** in up to **10 percent of all episodes**. Skin symptoms and signs may be absent if a patient has taken an **H1 antihistamine**. They may also be missed if an individual **cannot describe itching** or is not undressed and fully examined during the episode.

DIAGNOSTIC PITFALLS

- Anaphylaxis in a patient with **asthma** may be mistaken for an asthma exacerbation if accompanying skin symptoms and signs, such as itching or hives, mucosal, tongue, or lip edema, or dizziness suggestive of impending shock, are overlooked.
- **Patients experiencing their first episode** may not recognize the symptoms as anaphylaxis. As a result, they may not report symptoms fully or may focus on one prominent symptom (eg, unless specifically asked, a patient presenting with vomiting may not report that the episode was preceded by diffuse itching).
- The above factors are further compounded in patients with **neurologic, psychiatric, or psychologic problems** or those who take **medications or substances**, such as a sedating **H1 antihistamine, ethanol**, or recreational drugs that potentially impair cognition and judgment, making anaphylaxis symptoms difficult to recognize

LABORATORY TESTS

- Anaphylaxis is a clinical diagnosis, and treatment **cannot await** laboratory confirmation. When the cause of the observed symptoms is in doubt, treatment for anaphylaxis is initiated.
- The clinical diagnosis can sometimes be **retrospectively supported** by documentation of elevated concentrations of serum or plasma total tryptase or plasma histamine, although the results of these tests are not immediately available to the treating clinician.
- It is critical to obtain blood samples for measurement of these mast cell and basophil mediators **soon after the onset of symptoms** because elevations are transient.

SERUM OR PLASMA TOTAL TRYPTASE

- The standardized assay for measurement of total serum or plasma tryptase is widely available in clinical laboratories (normal range 1 to 11.4 ng/mL).
- In infants under age 6 months, normal baseline total tryptase concentrations are higher than they are in older infants, children, and adults.
- Optimally, the blood sample for tryptase measurement needs to be obtained within 15 minutes to 3 hours of symptom onset. However, tryptase may remain elevated for 6 or more hours after the onset and therefore may still be informative if obtained after 3 hours.

SERUM OR PLASMA TOTAL TRYPTASE

- Tryptase elevations are more likely to be detected in anaphylaxis from **stinging insect venoms** or **medications** and during reactions that involve **hypotension**.
- A tryptase level that is within normal limits cannot be used to refute the clinical diagnosis of anaphylaxis. The **history is more important** than the test results. As an example, in individuals with food-induced anaphylaxis or in patients who are normotensive, tryptase levels are seldom elevated, even in optimally timed blood samples obtained within 15 minutes to 3 hours of symptom onset

PLASMA HISTAMINE

- Plasma histamine levels typically **peak within 5 to 15 minutes** of the onset of anaphylaxis symptoms and then **decline to baseline by 60 minutes** due to rapid metabolism by N-methyltransferase and diamine oxidase.

PLASMA HISTAMINE

- Measurement of this mediator may be useful in cases of anaphylaxis occurring in a hospital setting in which blood samples can be collected **soon** after the onset of symptoms.
- Histamine and histamine metabolites can sometimes be detected in the **urine** following anaphylaxis, and elevations are less fleeting than elevations in plasma histamine.

THANK
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