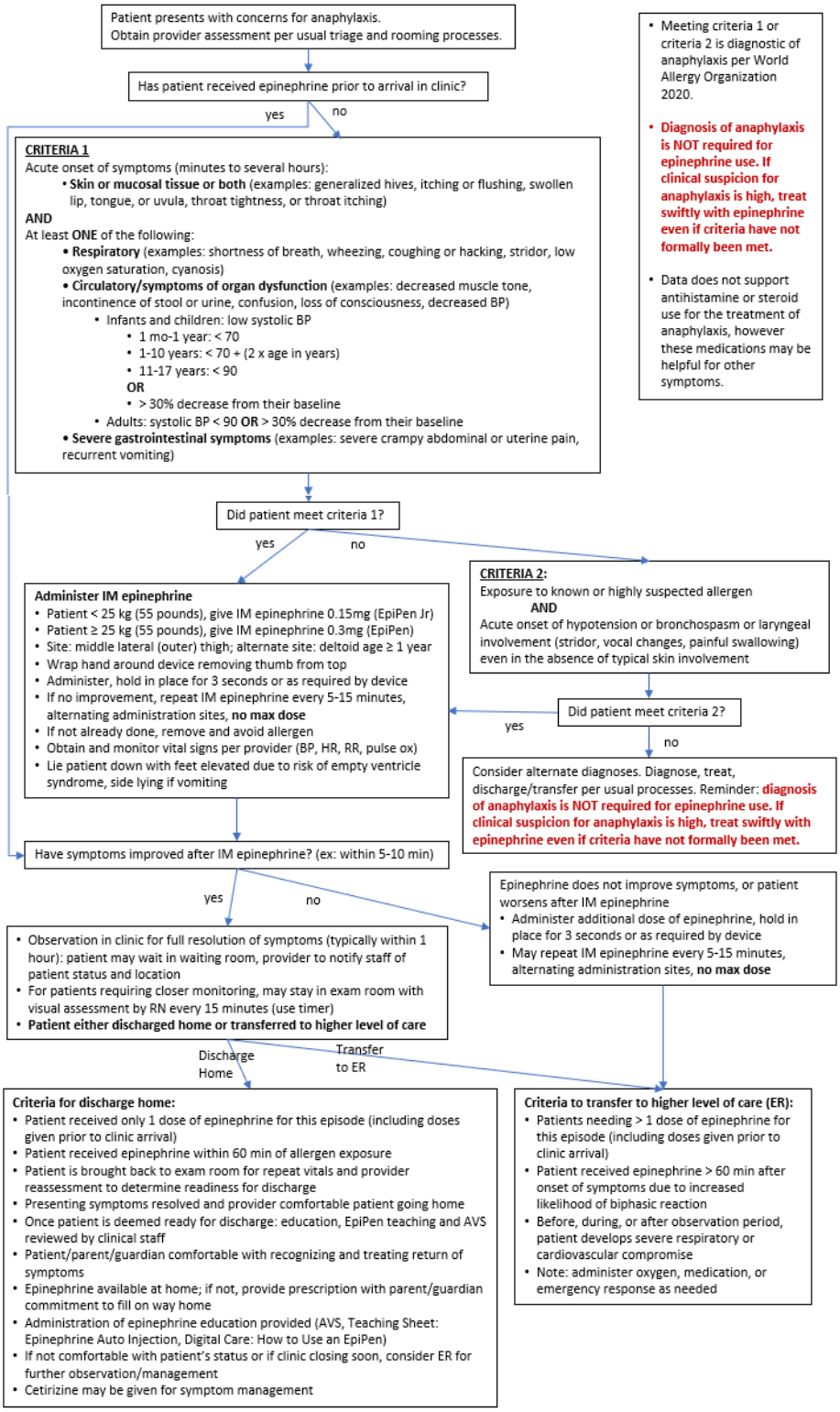
Children's Hospital and Health System
CW Urgent Care Evidence Based Guideline

Subject: Anaphylaxis



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Purpose: To recognize and initiate emergent treatment for signs and symptoms of anaphylaxis.

Definitions: Anaphylaxis is a severe, life threatening, multisystem allergic reaction which is rapid in onset, usually not anticipated, and may lead to death. Anaphylaxis is often under recognized and under treated, as it can present without obvious signs and symptoms, vary in its presentation, and can appear very similar to other conditions. However, it is extremely important to recognize and treat as severe anaphylaxis can lead to respiratory and cardiac arrest within minutes. Early recognition is vital to prompt epinephrine treatment for best treatment results. Patients are more responsive to epinephrine when treated early and it reduces risks for severe, biphasic or refractory anaphylaxis (Golden, 2024).

> Biphasic Anaphylaxis: A recurrence of symptoms that develop following the resolution of the initial anaphylaxis episode with no additional exposure to the trigger. Biphasic anaphylaxis is highly likely when all four of the following criteria are fulfilled:
> 1) New or recurrent symptoms and/or examination findings that fulfill anaphylaxis criteria
> 2) Initial symptoms and examination findings have completely resolved before the onset of new or recurrent symptoms or examination findings
> 3) Absence of allergen or trigger re-exposure
> 4) New or recurrent symptoms or examination finding occur within 1 to 48 hours from complete resolution of the initial symptoms or examination findings.
>
> Biphasic anaphylaxis is associated with greater severity of an initial reaction, persistence of the reaction, and use of more than one dose of epinephrine. (Golden, 2024) This occurs in up to 21% of adults and 11% of children (Sicherer, 2017). It typically occurs within 1-72 hours of the resolution of the original anaphylaxis process. The only way to decrease the likelihood of a biphasic reaction is by giving IM epinephrine as soon as possible after onset of anaphylaxis signs/symptoms.

Etiology: Anaphylaxis is an IgE mediated hypersensitivity reaction that occurs when a sensitizing antigen elicits an IgE antibody response in a susceptible individual. The antigen-specific IgE antibodies then bind to mast cells and basophils. Subsequent exposure to the sensitizing antigen results in cross linking of the cell bound IgE, resulting in mast cell and basophil degranulation, which in turn releases histamine, tryptase, and newly generated leukotrienes, prostaglandins, and platelet activating factor. These are all responsible for the signs and symptoms of an IgE mediated anaphylaxis reaction. These signs and symptoms appear rapidly but can take up to 2 hours after the allergen exposure. The onset of symptoms will be more rapid if the allergen had been injected or administered by IV. Anaphylaxis may also be a non-IgE mediated reaction. This occurs when the sensitizing allergen triggers activation of the complement system, direct mast cell activation, or IgG mediated reaction (McLendon K, 2023).

Risk Factors for severe anaphylaxis (Yegit, 2023)**:**

- Venom allergy
- Proton pump inhibitor allergy
- Parental route of medication administration
- Medical history of mastocytosis

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Common Causes of Anaphylaxis:

- Foods (30% of all cases)
    - Peanuts, tree nuts, egg, seafood, fish, cow's milk, and wheat
- Insect venom (26% of all cases)
    - Bees and wasps
- Medications (13% of all cases)
    - NSAIDS and beta-lactam antibiotics most common medications (Atanaskovic-Markovic, 2019)
        - PCNs account for 14% of anaphylactic medication reactions however cause 75% of all fatal anaphylactic episodes
    - Radiocontrast and neuromuscular blockers
- Natural rubber latex

Less Common Causes of Anaphylaxis:

- Exercise
- Semen
- Food additives: Monosodium Glutamate and Metabiosulfate
- Hormone changes
- Topical medications
- Transfusions

Differential Diagnosis (Cardona, 2020)

- Acute asthma exacerbation
- Vasovagal syncope
- Panic/anxiety attack
- Foreign body aspiration
- Myocardial infarction
- Seizure disorders
- Acute generalized urticaria
- Food poisoning
- Caustic ingestion
- Hypoglycemia
- Pulmonary embolism
- Shock from other causes
- Mastocytosis/clonal mast cell disorders
- Basophilic Leukemia
- Vocal cord dysfunction
- Hyperventilation
- Psychosomatic episode
- Hereditary angioedema
- Angioedema from other causes
- Red Man Syndrome
- Systemic Capillary Leak Syndrome
- Pheochromocytoma

Guideline

Subjective Data/History

- **Assess for risk factors for fatal anaphylaxis:**
    - Failure to give IM epinephrine
    - Age:
        - Infants highest risk age group due to atypical presentation including persistent vomiting, drowsiness, fussiness, persistent crying
        - Adolescents
        - Geriatrics
        - Pregnancy
    - Comorbid Conditions:
        - Asthma
        - Chronic respiratory diseases
        - Cardiovascular diseases
        - Allergic Rhinitis
        - Eczema
        - Mastocytosis
        - Depression
    - Cognitive dysfunction
    - Medications: beta- and alpha-adrenergic blockers, ACE inhibitors, psychotropic medications, drugs of abuse, alcohol, NSAIDS, diuretics, angiotensin receptor blockers, and calcium channel blockers
    - Cofactors: exercise, acute infection, emotional stress, and premenstrual status

Objective Data / Physical Exam
Not everyone presents in the same way. Some signs and symptoms may have resolved prior to arrival, especially skin and mucosal changes. Always inquire about the presence of all possible symptoms that may be yet occurring or may have resolved prior to arrival.

Common Signs and Symptoms of Anaphylaxis:

- Skin/mucosa: (≥ 90% of all anaphylaxis reactions)
    - Generalized urticaria
    - Itching or flushing
    - Swollen lips, tongue, uvula
    - Periorbital edema
    - Conjunctival swelling
    - Throat tightness/itching
    - Perioral tingling
- Respiratory: (≥ 40-60% anaphylaxis reactions)
    - Dyspnea/shortness of breath
    - Cough

    - Wheeze
    - Stridor
    - Profuse rhinorrhea
    - Nasal congestion
    - Voice changes
    - Cyanosis
    - Hypoxemia
- GI: (25-30% of anaphylaxis reactions)
    - Nausea
    - Vomiting
    - Diarrhea
    - Abdominal pain
- Cardiovascular: (30-35% of anaphylaxis reactions)
    - Hypotonia/collapse
    - Syncope
    - Confusion
    - Dizziness
    - Tachycardia
    - Hypotension
- Miscellaneous: (<10% anaphylaxis reactions)
    - Incontinence
    - Substernal pain
    - Headache
    - Seizure

Diagnostic Studies: See Treatment Algorithm at top of document

The diagnosis of anaphylaxis is a clinical diagnosis that does not need diagnostic tests to confirm the diagnosis. Tryptase levels are usually elevated compared to baseline level during an anaphylaxis reaction (Muraro A, 2022) (Golden, 2024). However, we do not obtain this level in Urgent Care as it takes several days for the result to return.

- Diagnostic criterion have been validated by the World Allergy Organization. Meeting any one of the criterion is diagnostic of anaphylaxis.
    - Sensitivity: 97%
    - Specificity: 82%
    - Negative Predictive Value: 98%
    - Positive Predictive Value: 67%

Treatment: See Treatment Algorithm at top of document (Cardona, 2020)

- **If anaphylaxis is suspected, the priority is rapid administration of IM epinephrine. Simultaneously remove the allergen and obtain full vitals if not yet performed.**
    - **Patient < 25 kg, give IM epinephrine 0.15mg (EpiPen Jr)**
    - **Patient ≥ 25 kg, give IM epinephrine 0.3mg (EpiPen)**

    - If no epinephrine auto injector is available for use, draw up epinephrine 1:1000 (1 mg/ml) concentration into a syringe 0.15mg (0.15ml) or 0.3mg (0.3ml) based on the dose desired.
- Anaphylaxis is a rapidly progressing process and is very unpredictable.
- It does have a potential to resolve quickly on its own, however it is much more likely to become biphasic and protracted or rapidly progress to respiratory and cardiovascular compromise and death if IM epinephrine is not given or is delayed.
- Keep in mind that the administration of epinephrine is at times appropriate even in cases that do not fully meet any of the 2 Criterion.
- There is no absolute contraindication to the use of epinephrine for the use of anaphylaxis.
- IM epinephrine may be administered every 5-15 minutes as needed for either no response or for an inadequate response. There is no maximum dosing.
- Epinephrine can be given through the clothes. Do not delay giving epinephrine in order to undress the patient.
- A possible complication from using an auto injector is a laceration at the injection site. This occurs when the auto injector is kept in the muscle longer than 3 seconds and/or the child moves during the injection process. Make sure the auto injector is not held in place for longer than 3 seconds. Make sure the limb that the injection is being given into is securely immobilized.
- Place the patient in Trendelenburg position to prevent the possibility of empty ventricle syndrome due to anaphylaxis.
- Antihistamines may be given for itch, hives, etc. but no direct benefit to anaphylaxis specifically.
- Steroids are not indicated for anaphylaxis.

Family Education

- Side effects of IM epinephrine: pallor, tremor, anxiety, palpitations, dizziness, or headache.
- Patients with severe anaphylaxis may be admitted to the hospital.
- All patients discharged home with the diagnosis of anaphylaxis should be given a prescription for an epinephrine autoinjector as well as a referral to CW Asthma/Allergy (and/or primary care provider at a minimum).

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Treatment information also provided by David Vyles, DO, Emergency Medicine, and Sara Lowe, Pediatric Nurse Practitioner, Asthma, Allergy and Immunology, Children's Wisconsin (personal communications, August 2020).

Treatment information also provided by Andrew MacGinnitie, MD. Asthma, Allergy and Immunology, Children's Wisconsin (personal communication, October 2024).