Anaphylaxis Guideline

Definition

Anaphylaxis is defined using the US NIAID criteria established. (Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium.AUSampson HA, Muñoz-Furlong A, Campbell RL, Adkinson NF Jr, Bock SA, Branum A, Brown SG, Camargo CA Jr, Cydulka R, Galli SJ, Gidudu J, Gruchalla RS, Harlor AD Jr, Hepner DL, Lewis LM, Lieberman PL, Metcalfe DD, O'Connor R, Muraro A, Rudman A, Schmitt C, Scherrer D, Simons FE, Thomas S, Wood JP, Decker WW). There are three separate diagnostic criteria with each reflecting a different clinical presentation.

Epidemiology

The overall incidence of anaphylaxis is estimated at 32-50 per 100,000 person-years (1,2,3). The lifetime prevalence is 0.05-2% (4,5). The largest number of incident cases is among children and adolescents (4), with children aged 0-4 having an almost 3 times higher incidence than that of other age groups (7). An increase in anaphylaxis, particularly food-related anaphylaxis, has been noted in recent years (2,6). One study estimated a nearly 10% increase of food-related anaphylaxis per year, most commonly affecting children (2).

Etiology

Food allergy is the most common trigger of anaphylaxis in the pediatric population, accounting for at least 50% of cases, with some studies (1, 5) reporting rates as high as 90%. The most common food triggers are peanut, tree nuts, cow's milk, egg, shellfish, and seeds (1, 6). Young children are more likely to present with anaphylaxis triggered by cow's milk and egg (8). Insect stings and medications, including antibiotics, NSAIDs, allergen immunotherapy, and monoclonal antibodies, are also important triggers. Other important though less common causes of anaphylaxis include exercise-induced and idiopathic cases (7).

Guideline Eligibility Criteria

Criteria 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)

Criteria 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).

Note that skin symptoms or signs are absent or unrecognized in up to 20 percent of anaphylactic episodes.

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

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

Guideline Exclusion Criteria

- Pregnancy
- History of severe airway abnormality, surgery, or tracheostomy
- Age < 6 months

Differential Diagnosis

- *Generalized urticaria*
- *Angioedema*
- *Asthma exacerbation*
- *Vasovagal syncope*
- *Anxiety or panic attack*
- *Mast cell activation syndrome (including Mastocytosis)*
- *Oral allergy syndrome (Pollen-food)*
- *Foreign body aspiration*
- *Food poisoning*
- *Cardiovascular events (myocardial infarction, pulmonary embolus)*
- *Neurologic events (seizure, stroke)*
- *Shock*
- *Caustic ingestion*
- *Red man syndrome (vancomycin)*

Methods

Evidence Found with Searches

Check Type of Evidence Found	Summary of Evidence – All Questions	Number of Articles Obtained
☒	Systematic Reviews	5
☒	Meta-analysis articles	
☐	Randomized Controlled Trials	
☐	Non-randomized studies	
☐	Review articles	
☐	Government/State agency regulations	
☐	Professional organization guidelines, white papers, etc.	
☒	Observational	5
☒	Other: Expert Opinion	2

Evaluating the Quality of the Evidence

The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. The table below defines how the quality of evidence is rated and how a strong versus a weak recommendation is established.

Recommendation	
Strong	Desirable effects clearly outweigh undesirable effects or vice versa
Weak	Desirable effects closely balanced with undesirable effects
Type of Evidence	
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Diagnostic Evaluation

While providers should focus on diagnostic criteria listed above to guide diagnosis and subsequent treatment, anaphylaxis can present with a variety of clinical signs and symptoms. History and Physical Exam should focus on the following categories specifically:

- Timing: Symptoms usually being with seconds to minutes after a potential exposure. The progression of anaphylaxis cannot be predicted at the onset of illness, thus the early administration of epinephrine is vital to prevent progression to life-threatening complications.
- Time course: In up to 15% of children there can be a biphasic anaphylaxis which is defined as a recurrence of symptoms that develops following apparent resolution with no additional exposure. They typically occur within 12 hours after the initial resolution. *(Epidemiology and clinical predictors of biphasic reactions in children with anaphylaxis.Alqurashi W, Stiell I, Chan K, Neto G, Alsadoon A, Wells G , Ann Allergy Asthma Immunol. 2015 Sep;115(3):217-223.e2. Epub 2015 Jun 22.)*
- Skin and mucosal symptoms: The most commonly affected system (up to 90% of episodes), and can include generalize hives, itching, swollen lips/tongue/uvula, periorbital swelling or conjunctival swelling (chemosis)
- Respiratory: Classic symptoms include stridor, shortness of breath, or wheezing. One should not overlook other respiratory symptoms such as nasal congestion, nasal discharge, change in voice, or the subjective feeling of choking or throat closure.
- Gastrointestinal symptoms: Often overlooked, especially in nonverbal children, these symptoms can include nausea, vomiting, diarrhea and crampy abdominal pain and occur in up to 45% of episodes.
- Cardiovascular symptoms: May be falsely attributed to other disease if a provider is not thinking of potential triggers or anaphylaxis; these symptoms include hypotonia, syncope, incontinence, dizziness and hypotension.

Clinical Management

- If there is clinical concern for anaphylaxis and the patient meets criteria, give IM Epinephrine first and immediately.
    - Consider another dose of IM epinephrine if no improvement or worsens (can repeat every 5-15 minutes, even sooner if clinically indicated)
- Epi medication table and dosing

Outside hospital = Prescribe EpiPEN	**ED/Inpatient** = Weight based dosing using 1mg/mL solution
< 25 kg: 0.15mg (EpiPen Jr.) IM PRN	0.01 mg/kg IM q 5-15 min PRN (Max 0.3mg if < 13 years, 0.5mg if ≥ 13 years)
≥ 25 kg: 0.3mg (EpiPen) IM PRN	

- Remove any affecting antigen or medication, while also performing ACLS/PALS
- If there is any upper airway obstruction, consider racemic epinephrine nebulizer treatment, steroids, and intubation.
- If there is any hypotension, consider IV fluids and pressors.
- If there is any bronchospasm, consider albuterol nebulizer treatment and steroids.
- Once the patient is stable, can give Benadryl for itching/hives
- Admission recommended for patients requiring more than 1 epinephrine dose, with risk factors for biphasic reaction, current asthma flare, or any hemodynamic/respiratory instability.
    - ICU for more severe cases
- Recommend a minimum 4-hour observation after the first epinephrine dose to meet discharge criteria.
- Provide a written Anaphylaxis Action Plan to every patient/family at discharge.
    - Specify allergic trigger if known/suspected
    - If unknown/unclear, state "unknown trigger, history of anaphylaxis/ED visit"
- Perform epinephrine auto-injector training prior to discharge.
    - Bedside nurse using auto-injector trainer. Patient/family return demonstration.
    - FARE (Food Allergy Research and Education) training video for patients and families:
        - https://www.foodallergy.org/life-with-food-allergies/anaphylaxis/recognizing-responding-to-anaphylaxis
    - Links to all epinephrine auto-injector device training videos:
        - https://www.foodallergy.org/life-with-food-allergies/epinephrine/epinephrine-options-and-training
- Prescribe epinephrine auto-injectors for home/school (2 twin-packs) prior to discharge.
- Follow-up instructions at the time of discharge.
    - PCP in 24 hours
    - Allergy referral
        - DCMC Allergy referral - 1 month

Anaphylaxis Pathway

EXCLUSION CRITERIA
- Pregnancy
- History of severe airway abnormality, surgery, or tracheostomy
- Age <6 months

Acute Allergic Reaction and Anaphylaxis (>6 months) – Dell Childrens

Yes

Clinical concern for anaphylactic reaction?

No → Consider Allergy Consult

Yes

1.Remove affecting antigen or medication immediately
2. Perform ALS/PALS

Meets Anaphylactic Criteria? 1

No → **History of Severe Anaphylaxis?**

No → Manage Off Pathway

Yes → Epinephrine IM Injection

Unclear → Serum ß-tryptase within 15 min to 3 hours after presentation, consider treating as anaphylaxis, consider allergy/ immunology consult

Yes → Epinephrine IM Injection 2

Epinephrine IM Injection 2

Reevaluate after 5 minutes

Not Improving → **2nd EPI IM**
To be Given prior to any adjuncts or if persistent symptoms after 5mins from 1st EPI

Symptoms Resolving → Benadryl for Itching and Hives

Consider IV access

Upper airway Obstruction?

Yes → 1. Upper Airway Obstruction Treatment
2. Consider Steroids

No → **Hypotension?**

Yes → Hypotension Treatment in Anaphylaxis

No → **Bronchospasm?**

Yes → 1. Inhaled Bronchodilator
2. Consider Steroids

Resolution of Symptoms?

No → Consider Additional EPI IM → Use Adjuncts as needed → Admit to appropriate level

Yes

Floor Criteria
Refer to Box 3

Meets Criteria → Admit to Floor

No

ICU Criteria
1.) Frequent Airway assessment or management
2.) Requires support of ongoing hypotension
3.) Requires any Drips
4.)Ongoing severe Anaphylaxis Symptoms

Meets Criteria → Admit to ICU

No or Resolved

Discharge Criteria
1.) Min 4 hour obs after 1st epinephrine given
2.) 100% receive plan to receive EPI Pen
3.) All patients receive standard hospital discharge instructions and epinephrine auto-injector training (See "DCMC Anaphylaxis Discharge Instructions for Families")
4.)Assess risk factors for biphasic or prolonged anaphylaxis (refer to box 3)

→ Discharge

Anaphylaxis Diagnosis Criteria 1

Criteria 1
- Acute onset of an illness (minutes to hours) with involvement of the skin, mucosa, or both (eg. generalized hives, pruritus or flushing, swollen lips-tongue-uvula)
- AND AT LEAST 1 OF THE FOLLOWING
  - Respiratory compromise (dyspnea, wheezing, stridor, hypoxia)
  - Reduced BP or associated symptoms of end-organ dysfunction (hypotonia, syncope, incontinence)

Criteria 2
- 2 or more of the following that occur rapidly (minutes to hours) after exposure to a LIKELY allergen
  - Involvement of the skin-mucosa (generalized hives, itch-flush, swollen lips-tongue-uvula)
  - Respiratory compromise (dyspnea, wheezing, stridor, hypoxia)
  - Reduced BP or associated symptoms (hypotonia, syncope, incontinence)
  - Persistent gastrointestinal symptoms (abdominal pain, vomiting)

Criteria 3
- Reduced BP after exposure to a patient's KNOWN allergen

Epinephrine IM Injection Dosage 2

Outside hospital = Prescribe EpiPEN	**ED/Inpatient** = Weight based dosing using 1mg/mL solution
< 25 kg: 0.15mg (EpiPen Jr.) IM PRN	0.01 mg/kg IM q 5-15 min PRN (Max 0.3mg if < 13 years, 0.5mg if ≥ 13 years)
≥ 25 kg: 0.3mg (EpiPen) IM PRN	

Red Flags 3
- History of biphasic or severe reactions
- Progression of / or persistent symptoms
- History of severe asthma
- Patient with 1 ICU admission and/or 3 IP admissions per year
- Current asthma flare
- Hypotension during ED stay
- Requires >1 Epinephrine dose
- Requires fluid bolus
- Upper airway obstruction i.e. stridor

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Executive Summary

Approved by the Pediatric Evidence-Based Outcomes Center Team

Revision History
Original Date Approved: 10/9/2019
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Next Review Date: October 2022

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Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible.

Approval Process

EBOC guidelines are reviewed by DCMC content experts, the EBOC committee, and are subject to a hospital wide review prior to implementation. Recommendations are reviewed and adjusted based on local expertise.

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