Challenges in Identifying and Managing Anaphylaxis in Infants and Toddlers

Michael Pistiner MD, MMSc
Director of Food Allergy Advocacy, Education and Prevention,
Mass General Brigham for Children
Assistant Professor in Pediatrics, Harvard Medical School
Boston, MA

Mass General Brigham for Children

HARVARD MEDICAL SCHOOL

1

Mass General Brigham for Children

Faculty Disclosure Information

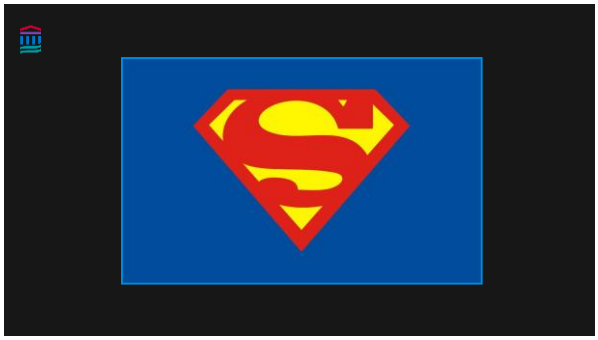
I have the following financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity:"

- Research support from: Kaleo, Egg Nutrition Center
- Consultant for: Asthma and Allergy Foundation of America, Allergy Asthma Network, and FARE
- Program support: National Peanut Board, Asthma and Allergy Foundation of America, Kaleo, Kenvue, Allergy and Asthma Network, ARS, Aquestive, Stallergenes Greer
- Advisory board: Novartis, Bryn, Kaleo, Food Graph and Anjo
- Co-Founder and content creator: AllergyHome and Allergy Certified Training

I will give a balanced presentation using the best available evidence to support my conclusions and recommendations.

I **do not** intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

2



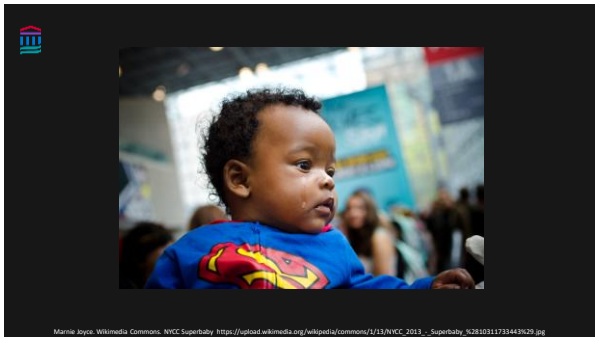
3

DC Action Comics Vol 1 #161 1951 https://ebonstorm.medium.com/is-kryptonite-made-from-the-element-krypton-4303d237208b

4

DC Adventure Comics 231 1956 Super-feats of Super Baby https://dc.fandom.com/wiki/Adventure_Comics_Vol_1_231

5



Marnie Joyce. Wikimedia Commons. NYCC Superbaby https://upload.wikimedia.org/wikipedia/commons/1/13/NYCC_2013_-_Superbaby_%2810311733443%29.jpg

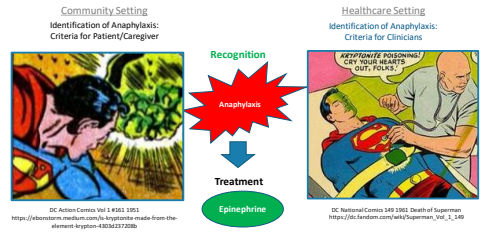
6

Mass General Brigham for Children

Learning Objectives:

1. Identify infant and toddler specific challenges in recognizing and managing anaphylaxis
2. Know the infant and toddler specific and relevant recommendations from the 2023 Anaphylaxis Practice Parameter Update

7



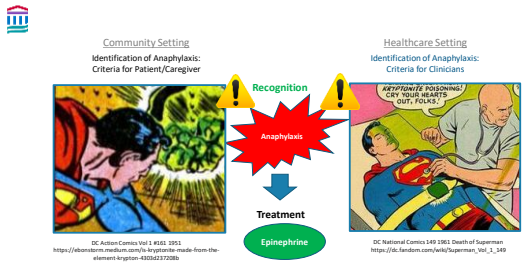
DC Action Comics Vol 1 #161 1951 https://ebonstorm.medium.com/is-kryptonite-made-from-the-element-krypton-4303d237208b

DC National Comics 149 1961 Death of Superman https://dc.fandom.com/wiki/Superman_Vol_1_149

Greenhawt M, Gupta R, Meadows A, MD; Pistiner M, Spergel J, Camargo C, Lieberman, P, Simons E. Guiding Principles for the Recognition, Diagnosis, and Management of Infants with Anaphylaxis: An Expert Panel Consensus. The Journal of Allergy and Clinical Immunology: In Practice. 2019 Feb 5.

Wang J, Lieberman JA, Camargo CA, Pistiner M. Diverse perspectives on recognition and management of anaphylaxis. Annals of Allergy, Asthma & Immunology. 2021 Jan 23.

8



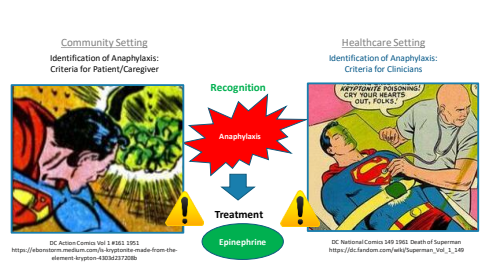
DC Action Comics Vol 1 #161 1951 https://ebonstorm.medium.com/is-kryptonite-made-from-the-element-krypton-4303d237208b

DC National Comics 149 1961 Death of Superman https://dc.fandom.com/wiki/Superman_Vol_1_149

Greenhawt M, Gupta R, Meadows A, MD; Pistiner M, Spergel J, Camargo C, Lieberman, P, Simons E. Guiding Principles for the Recognition, Diagnosis, and Management of Infants with Anaphylaxis: An Expert Panel Consensus. The Journal of Allergy and Clinical Immunology: In Practice. 2019 Feb 5.

Wang J, Lieberman JA, Camargo CA, Pistiner M. Diverse perspectives on recognition and management of anaphylaxis. Annals of Allergy, Asthma & Immunology. 2021 Jan 23.

9

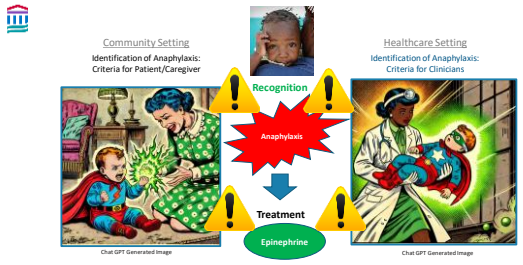


DC Action Comics Vol 1 #161 1951 https://ebonstorm.medium.com/is-kryptonite-made-from-the-element-krypton-4303d237208b

DC National Comics 149 1961 Death of Superman https://dc.fandom.com/wiki/Superman_Vol_1_149

Wang J, Lieberman JA, Camargo CA, Pistiner M. Diverse perspectives on recognition and management of anaphylaxis. Annals of Allergy, Asthma & Immunology. 2021 Jan 23.

10



Chat GPT Generated Image

Chat GPT Generated Image

Wang J, Lieberman JA, Camargo CA, Pistiner M. Diverse perspectives on recognition and management of anaphylaxis. Annals of Allergy, Asthma & Immunology. 2021 Jan 23.

11

Guiding Principles Expert Panel Recommendations

Chat GPT Generated Image

12

Guiding Principles for the Recognition, Diagnosis, and Management of Infants with Anaphylaxis: An Expert Panel Consensus

Expert panel tasked to provide guiding principles for infant anaphylaxis highlighted:

- Definition of Infant and Toddler:
  - An infant is a child under 12 months old
  - A toddler is a child between 12 and 36 months old
- Key Considerations for Anaphylaxis Management:
  - Appropriate and adequate epinephrine dosing
  - Proper EAI needle size selection
  - Accurate identification of symptoms indicating anaphylaxis
    - All are crucial for achieving good outcomes

Greenhawt M, Gupta R, Meadows A, MD; Pistiner M, Spergel J, Camargo C, Lieberman, P, Simons E. Guiding Principles for the Recognition, Diagnosis, and Management of Infants with Anaphylaxis: An Expert Panel Consensus. The Journal of Allergy and Clinical Immunology: In Practice. 2019 Feb 5.

13

Practice Parameters Joint Task Force Recommendations

Chat GPT

14

Anaphylaxis Practice Parameter 2023 Update

Practice Parameter Recommendations:

- Developed by JTFPP & Anaphylaxis Workgroup (AAAAI/ACAAI)
- A series of questions were formulated to create consensus-based recommendations to support clinicians and families
- Majority opinion reflected in final recommendations
- Strength and certainty assessed by the workgroup

Golden, David B.K. et al. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology, Volume 132, Issue 2, 124 – 176.

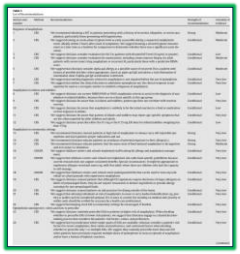
15

Anaphylaxis Practice Parameter 2023 Update

Practice Parameter Recommendations:

7 key areas, including infants/toddlers

- Infant and Toddler Recommendations:
  - Diagnosis and treatment of anaphylaxis in infants is complex
  - Infants may present with unique, age-specific symptoms
  - Reaction severity is not age-dependent
  - Anaphylaxis is rarely a first reaction to an allergen



Golden, David B.K. et al. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology, Volume 132, Issue 2, 124 – 176.

16

Anaphylaxis Practice Parameter 2023 Update: Infant/Toddler Specific Recommendations

#	Method	List of Recommendations: Anaphylaxis in Infants and Toddlers	Strength	Certainty of evidence
8	CBS	We suggest clinician s use current NIAID/FAAN or WAO anaphylaxis criteria to assist in the diagnosis of anaphylaxis in infants/toddlers, because there are no criteria specific to this age group.	conditional	low
9	CBS	We suggest clinicians be aware that, in infants and toddlers, patient age does not correlate with reaction severity.	conditional	Very low
10	CBS	We suggest clinicians be aware that anaphylaxis is unlikely to be the initial reaction to a food or medication on first exposure in infants.	conditional	low
11	CBS	We suggest clinicians be aware that parents of infants and toddlers may report age-specific symptoms that are less often reported by older children and adults.	conditional	Very low
12	CBS	We suggest clinicians prescribe either the 0.1mg or the 0.15mg EAI dose for infants/toddlers weighing less than15kg.	conditional	low

Golden, David B.K. et al. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology, Volume 132, Issue 2, 124 – 176.

17

Anaphylaxis Practice Parameter 2023 Update: Infant/Toddler Specific Recommendations

#	Method	List of Recommendations: Anaphylaxis in the Community Setting	Strength	Certainty of evidence
16	GRADE	We suggest childcare centers and schools implement staff training for allergy and anaphylaxis management.	Conditional	Very low
18	GRADE	We suggest that childcare centers and schools stock undesignated EAIs that can be used to treat any individual on school grounds who experiences anaphylaxis.	Conditional	Very low

Golden, David B.K. et al. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology, Volume 132, Issue 2, 124 – 176.

18

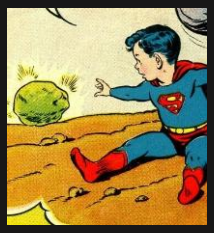
Anaphylaxis Practice Parameter 2023 Update: Infant/Toddler Specific Recommendations

#	Method	List of Recommendations: Epinephrine Auto-Injectors: When and How to prescribe	Strength	Certainty of evidence
26	CBS	We suggest that clinicians counsel patients that immediate activation of EMS may not be required if the patient experiences prompt, complete, and durable response to treatment with epinephrine, provided that additional epinephrine and medical care are readily available, if needed. We suggest that clinicians counsel patients to always activate EMS after epinephrine use if anaphylaxis is severe, fails to resolve promptly, fails to resolve completely or nearly completely, or returns or worsens after a first dose of epinephrine.	conditional	Very low
27	CBS	Serious adverse reactions to intramuscular epinephrine are very rare and should not pose a barrier to the prescription or early administration of EAIs when indicated. To manage the risk of adverse events, we recommend that clinicians counsel patients and caregivers on the proper use of EAIs, the common adverse effects, and the need for immediate evaluation and treatment when signs or symptoms of serious adverse events develop.	Strong	Low
28	CBS	We suggest that clinicians discuss the potential financial and psychosocial burdens of EAIs with patients while engaging in shared decision-making.	Conditional	Very low
29	CBS	When deciding which EAI to prescribe, we suggest that clinicians consider dosage, needle length, affordability, access, and patient treatment preferences.	Conditional	Very low
30	CBS	During visits with patients who have been prescribed EAIs, we recommend that clinicians routinely review the essentials of EAI carriage, storage, and use; encourage patients to regularly practice EAI administration with a trainer device; and discuss strategies to manage barriers to adherence that patients may have experienced.	Strong	Low

Golden, David B.K. et al. Anaphylaxis: A 2023 practice parameter update.
Annals of Allergy, Asthma & Immunology, Volume 132, Issue 2, 124 – 176.

19

"Do infants and toddlers present with different signs and symptoms of anaphylaxis compared with older children and adults?"



DC Adventure Comics 231 1956 Super-feats of Super Baby https://dc.fandom.com/wiki/Adventure_Comics_Vol_1_231

Wikimedia commons

20

2023 Anaphylaxis Practice Parameters Update: Recommendation # 11

Do infants and toddlers present with different signs and symptoms of anaphylaxis compared with older children and adults?

We suggest clinicians be aware that parents of infants and toddlers may report age-specific symptoms that are less often reported by older children and adults.

Strength of Recommendation: Conditional
Certainty of Evidence: Very Low

21

Anaphylaxis Recognition in Infants and Toddlers: Parent Report of Age Specific Symptoms

- **Age specific challenges:**
  - Infants cannot communicate subjective symptoms
  - Normal infant behavior and other issues can overlap with symptoms and signs of anaphylaxis
  - Current anaphylaxis criteria have not been validated for <2years of age and include language difficult to apply to this population

Wikimedia commons

Wang J, Lieberman JA, Camargo CA, Pistiner M. Diverse perspectives on recognition and management of anaphylaxis. Annals of Allergy, Asthma & Immunology. 2021 Jan 23.

22

Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers

Original Article

Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers

23

Mass General Brigham for Children

Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers

Study Overview

- National Survey of Primary Caregivers (Published in JACI: In Practice)
  - Survey conducted by Asthma and Allergy Foundation of America (AAFA)
  - 374 children under age 3:
    - 193 infants (<12 months)
    - 181 toddlers (12–35 months)
  - Caregivers reported symptoms observed during the most severe food-induced allergic reaction
  - Compared findings with Anaphylaxis in America survey instrument

Original Article

Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers

Pistiner M, Méndez-Reyes JE, Eftekhari S, Caneri M, Lieberman J, Wang J, Camargo J CA. Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2020 Nov 18.

24

Alternative Age-Specific Symptoms and Signs in Infants and Toddlers

TABLE IV. Alternative, age-specific symptoms/signs used in this study to help identify anaphylaxis in infants/toddlers

Language used in current diagnostic criteria*	Language used in AAFA Infant Toddler Anaphylaxis Study
Pruritis	Tongue thrusting, tongue pulling, repetitive lip licking, or licking of hands or objects. Throat itching. Ear pulling, scratching, or putting fingers in the ears. Eye rubbing, eye itching
Dyspnea	Belly breathing, fast breathing, nasal flaring, chest or neck "tugging"
Stridor	Hoarse voice, hoarse cry. Barky/croup-like cough
Reduced PEF	*(Currently no appropriate and practical way to get FEV$_1$ in this population in acute setting)*
Reduced BP (low systolic BP [age specific] or greater than 30% decrease in systolic BP)	*(Blood pressure in this population can be challenging to acquire and interpret. Hypotension is also a late phase cardiovascular symptom in this age group. Tachycardia may be an earlier vital sign change)* Wobbly appearance, lethargic, floppy, poor head control, difficult to wake up. Crankiness, withdrawn or clingy, inconsolable crying, subdued or less active, limp. Mottling of the skin or blue/gray skin (cyanosis) around mouth/lips or hands/feet
Hypotonia (collapse), syncope	Wobbly appearance, lethargic, floppy, poor head control, difficult to wake up. Crankiness, withdrawn or clingy, inconsolable crying, subdued or less active, limp
Incontinence	*(Can be challenging to differentiate in diaper wearing population)*
Persistent gastrointestinal symptoms	Abdominal pain, diarrhea, hiccups, spitting up, back arching, vomiting

AAFA, Asthma and Allergy Foundation of America; *BP*, blood pressure; *PEF*, peak expiratory flow.
*Clinical criteria for diagnosing anaphylaxis from Sampson et al.[1]

Pistiner M, Mendez-Reyes JE, Eftekhari S, Carver M, Lieberman J, Wang J, Camargo Jr CA. Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2020 Nov 18.

25

Mass General Brigham for Children

Asthma and Allergy Foundation of America | KIDS WITH FOOD ALLERGIES

Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers

Key Findings – Symptom Categories

- Symptom Frequency Reported by Caregivers
  - Skin reactions: 90% (itching, rashes, or hives)
  - Facial (eyes, lips, tongue, ears, nose) and extremity swelling: 59%
  - Gastrointestinal Issues: 51%
  - Coughing/wheezing: 45%
  - Eye rubbing, itching, redness: 44%
  - Sudden Behavioral Change: **34%**
  - Cardiovascular Symptoms: **17%**
- Unique Symptoms by Age Group:
  - Infants: Skin mottling, ear pulling/scratching, putting fingers in ears
  - Toddlers: Throat itching, coughing, wheezing

Pistiner M, Mendez-Reyes JE, Eftekhari S, Carver M, Lieberman J, Wang J, Camargo Jr CA. Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2020 Nov 18.

26

Mass General Brigham for Children

Asthma and Allergy Foundation of America | KIDS WITH FOOD ALLERGIES

Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers

Key Findings – Symptom Categories

- Symptom Frequency Reported by Caregivers
  - Skin reactions: 90% (itching, rashes, or hives)
  - Facial (eyes, lips, tongue, ears, nose) and extremity swelling: 59%
  - Gastrointestinal Issues: 51%
  - Coughing/wheezing: 45%
  - Eye rubbing, itching, redness: 44%
  - Sudden Behavioral Change: **34%**
  - Cardiovascular Symptoms: **17%**
- Unique Symptoms by Age Group:
  - Infants: Skin mottling, ear pulling/scratching, putting fingers in ears
  - Toddlers: Throat itching, coughing, wheezing

Pistiner M, Mendez-Reyes JE, Eftekhari S, Carver M, Lieberman J, Wang J, Camargo Jr CA. Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2020 Nov 18.

27

Mass General Brigham for Children

Asthma and Allergy Foundation of America | KIDS WITH FOOD ALLERGIES

Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers

Key Findings – Symptom Categories

- Symptom Frequency Reported by Caregivers
  - Skin reactions: 90% (itching, rashes, or hives)
  - Facial (eyes, lips, tongue, ears, nose) and extremity swelling: 59%
  - Gastrointestinal Issues: 51%
  - Coughing/wheezing: 45%
  - Eye rubbing, itching, redness: 44%
  - Sudden Behavioral Change: **34%**
  - Cardiovascular Symptoms: **17%**
- Unique Symptoms by Age Group:
  - Infants: Skin mottling, ear pulling/scratching, putting fingers in ears
  - Toddlers: Throat itching, coughing, wheezing

Pistiner M, Mendez-Reyes JE, Eftekhari S, Carver M, Lieberman J, Wang J, Camargo Jr CA. Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2020 Nov 18.

28

Mass General Brigham for Children

Asthma and Allergy Foundation of America | KIDS WITH FOOD ALLERGIES

Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers

Key Findings – Symptom Categories

- Symptom Frequency Reported by Caregivers
  - Skin reactions: 90% (itching, rashes, or hives)
  - Facial (eyes, lips, tongue, ears, nose) and extremity swelling: 59%
  - Gastrointestinal Issues: 51%
  - Coughing/wheezing: 45%
  - Eye rubbing, itching, redness: 44%
  - Sudden Behavioral Change: **34%**
  - Cardiovascular Symptoms: **17%**
- Unique Symptoms by Age Group:
  - Infants: Skin mottling, ear pulling/scratching, putting fingers in ears
  - Toddlers: Throat itching, coughing, wheezing

Pistiner M, Mendez-Reyes JE, Eftekhari S, Carver M, Lieberman J, Wang J, Camargo Jr CA. Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2020 Nov 18.

29

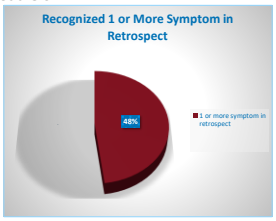
Mass General Brigham for Children

Asthma and Allergy Foundation of America | KIDS WITH FOOD ALLERGIES

Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers

Missed Symptoms

- Later-Recognized Signs of Anaphylaxis (48%)
  - Sudden behavioral change (15%)
  - Gastrointestinal symptoms (12%)
  - Skin reactions (12%)
  - Coughing or wheezing (11%)



Pistiner M, Mendez-Reyes JE, Eftekhari S, Carver M, Lieberman J, Wang J, Camargo Jr CA. Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2020 Nov 18.

30

"How should anaphylaxis be diagnosed in infants and toddlers?"

Images generated by Chat GPT

31

2023 Anaphylaxis Practice Parameters Update:
Recommendation # 8

How should anaphylaxis be diagnosed in infants and toddlers?

We suggest that clinicians use current NIAID/FAAN or WAO anaphylaxis criteria to assist in the diagnosis of anaphylaxis in infants/toddlers, because there are no criteria specific to this age group.

Strength of Recommendation: Conditional
Certainty of Evidence: Low

32

Current Anaphylaxis Criteria
(NIAID/FAAN 2006)

TABLE III. Symptoms/signs in current anaphylaxis diagnostic criteria* that can be difficult to evaluate in infants/toddlers

Anaphylaxis is highly likely when any 1 of the following 3 criteria 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 1 of the following:
   a. Respiratory compromise (eg, **dyspnea**, wheeze/bronchospasm, **stridor**, **reduced PEF**, 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**, **reduced PEF**, 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 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 mm Hg or greater than 30% decrease from that person's baseline

BP, Blood pressure; *PEF*, peak expiratory flow.
Bold text indicates symptoms/signs that can be difficult to evaluate in infants/toddlers.
*Clinical criteria for diagnosing anaphylaxis from 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; JACI 2006.

Pistiner M, Mendez-Reyes JE, Eftekhari S, Carver M, Lieberman J, Wang J, Camargo Jr CA. Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2020 Nov 18.

33

Current Anaphylaxis Criteria
(NIAID/FAAN 2006)

TABLE III. Symptoms/signs in current anaphylaxis diagnostic criteria* that can be difficult to evaluate in infants/toddlers

Anaphylaxis is highly likely when any 1 of the following 3 criteria 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 1 of the following:
   a. Respiratory compromise (eg, **dyspnea**, wheeze/bronchospasm, **stridor**, **reduced PEF**, 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**, **reduced PEF**, 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 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 mm Hg or greater than 30% decrease from that person's baseline

BP, Blood pressure; *PEF*, peak expiratory flow.
Bold text indicates symptoms/signs that can be difficult to evaluate in infants/toddlers.
*Clinical criteria for diagnosing anaphylaxis from 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; JACI 2006.

Pistiner M, Mendez-Reyes JE, Eftekhari S, Carver M, Lieberman J, Wang J, Camargo Jr CA. Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2020 Nov 18.

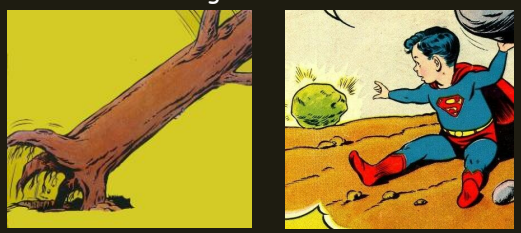
34

"If a tree falls in the forest and no-one is there to hear it, did it make a sound?"

Ramona Fradon, Dave Hunt. The Adventures of Superbaby. Random House 1980.
https://www.abebooks.com/first-edition/Adventures-Superbaby-Fradon-Ramona-Illustrator-Hunt/20273338896/bd#&gid=1&pid=1

35

"If an infant has anaphylaxis and no-one can recognize it……?"



Ramona Fradon, Dave Hunt. The Adventures of Superbaby. Random House 1980.
https://www.abebooks.com/first-edition/Adventures-Superbaby-Fradon-Ramona-Illustrator-Hunt/20273338896/bd#&gid=1&pid=1

36

Cardiovascular Symptoms/Signs in Infants and Toddlers with Anaphylaxis

- Hypotension is a late phase finding of shock and signifies **decompensated shock**

- Physiologically and developmentally appropriate symptoms/signs that signify **shock**
  - Tachycardia not related to crying
  - Poor perfusion (cyanosis or mottling, decreased capillary refill)
  - Tachypnea
  - Change in mental status (lethargy, inconsolability, or hypotonia)

Pistiner M, Handorf A, Camargo Jr C, Cohen A. Approaching Cardiovascular Symptoms/Signs in Infants and Toddlers with Anaphylaxis . The Journal of Allergy and Clinical Immunology: In Practice. 2021 Feb; 9(2):1044-1046. doi:10.1016/j.jaip.2020.11.058.

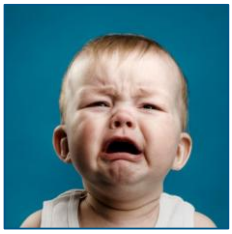
Kleinman ME, et. al. Part 14: pediatric advanced life support: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2010;122(18_suppl_3):S876-908.

Poor KM, Ducklow TB. Benefit of BP Measurement in Pediatric ED Patients. ISRN Nurs. 2012;2012:627354.

37

Address Infant and Toddler Behavior During Anaphylaxis Assessment

- Mental status changes can be secondary to cardiovascular involvement in anaphylaxis and range from inconsolability to hypotonia, lethargy, or loss of consciousness
- Less severe allergic etiologies of behavioral change can be secondary to discomfort caused by pruritis or abdominal pain
- Expected behaviors exhibited by this age group due to nonallergic causes can overlap with mental status change secondary to anaphylaxis
  - Hunger
  - Fear
  - Wet/dirty diaper
  - Hot/cold
  - Temper tantrum/frustration
  - Tired/overtired
  - Pain/injury

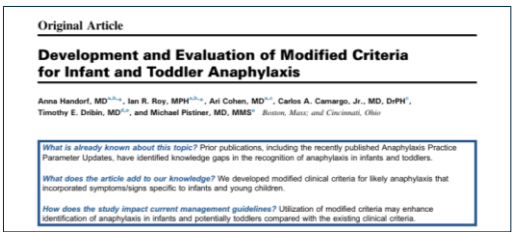


Pistiner M, Handorf A, Camargo Jr C, Cohen A. Approaching Cardiovascular Symptoms/Signs in Infants and Toddlers with Anaphylaxis . The Journal of Allergy and Clinical Immunology: In Practice. 2021 Feb; 9(2):1044-1046. doi:10.1016/j.jaip.2020.11.058.

Pistiner M. Address Infant and Toddler Behavior During Anaphylaxis Assessment. The Journal of Allergy and Clinical Immunology: In Practice. 2022 March; 10(3):885-887. doi:10.1016/j.jaip.2021.12.016.

38

Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis



Original Article

Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis

Anna Handorf, MD[a,b,*], Ian R. Roy, MPH[a,b,*], Ari Cohen, MD[c,d], Carlos A. Camargo, Jr., MD, DrPH[e], Timothy E. Dribin, MD[c,d], and Michael Pistiner, MD, MMS[c] *Boston, Mass; and Cincinnati, Ohio*

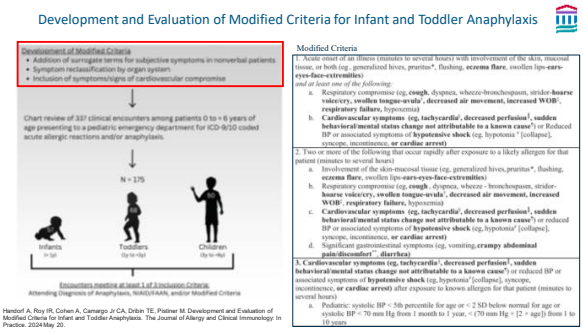
What is already known about this topic? Prior publications, including the recently published Anaphylaxis Practice Parameter Updates, have identified knowledge gaps in the recognition of anaphylaxis in infants and toddlers.

What does the article add to our knowledge? We developed modified clinical criteria for likely anaphylaxis that incorporated symptoms/signs specific to infants and young children.

How does the study impact current management guidelines? Utilization of modified criteria may enhance identification of anaphylaxis in infants and potentially toddlers compared with the existing clinical criteria.

39

Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis



Handorf A, Roy IR, Cohen A, Camargo Jr CA, Dribin TE, Pistiner M. Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis. The Journal of Allergy and Clinical Immunology: In Practice. 2024 May 20.

40

Proposed Modified Criteria for Infants and Toddlers

Figure 3. Proposed modified criteria for likely anaphylaxis in infants and toddlers

WOB, work of breathing, BP, blood pressure

Tachycardia: >160 bpm for infants, >150 bpm for 12-35 m.o., >135 bpm for > 36 m.o.

* pruritus of skin-tongue-eyes-ears (i.e., itchy skin, scratching; itchy mouth/tongue, tongue thrusting/pulling, licking lips/hands/objects; itchy eyes, conjunctival injection, rubbing eyes, chemosis, lacrimation; itchy ears, ear tugging, fingers-in-ears)

† swelling of tongue/uvula, drooling, difficulty swallowing)

‡ tachypnea, belly breathing, retractions, nasal flaring

§ decreased capillary refill, cool extremities, weak pulse, mottling, pallor, cyanosis

¶ irritable/crankiness; withdrawn/clingy, less activity without another explanation, obtunded, lethargic, difficult to arouse

wobbly, floppy, limp, poor head control

** knees to chest, back arching, nausea, gagging/retching, hiccups

Handorf A, Roy IR, Cohen A, Camargo Jr CA, Dribin TE, Pistiner M. Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis. The Journal of Allergy and Clinical Immunology: In Practice. 2024 May 20.

Modified Criteria

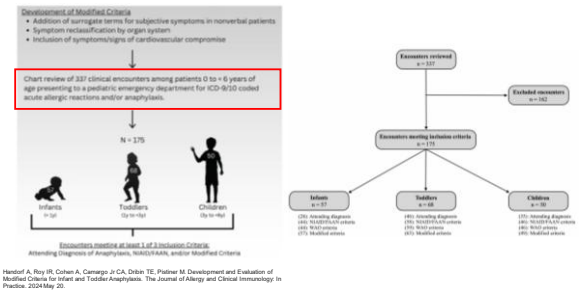
1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg , generalized hives, pruritus*, flushing, **eczema flare**, swollen lips-**ears-eyes-face-extremities**)
and at least one of the following:
a. Respiratory compromise (eg, **cough**, dyspnea, wheeze-bronchospasm, stridor-**hoarse voice/cry, swollen tongue-uvula†, decreased air movement, increased WOB‡, respiratory failure,** hypoxemia)
b. **Cardiovascular symptoms (eg, tachycardia‡, decreased perfusion§, sudden behavioral/mental status change not attributable to a known cause¶)** or Reduced BP or associated symptoms of **hypotensive shock** (eg, hypotonia ** [collapse], syncope, incontinence, **or cardiac arrest**)

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,pruritus*, flushing, **eczema flare**, swollen lips-**ears-eyes-face-extremities**)
b. Respiratory compromise (eg, **cough** , dyspnea, wheeze - bronchospasm, stridor-**hoarse voice/cry, swollen tongue-uvula†, decreased air movement, increased WOB‡, respiratory failure,** hypoxemia)
c. **Cardiovascular symptoms (eg, tachycardia‡, decreased perfusion§, sudden behavioral/mental status change not attributable to a known cause¶)** or reduced BP or associated symptoms of **hypotensive shock** (eg, hypotonia** [collapse], syncope, incontinence, **or cardiac arrest**)
d. Significant gastrointestinal symptoms (eg, vomiting,**crampy abdominal pain/discomfort††, diarrhea**)

3. Cardiovascular symptoms (eg, tachycardia‡, decreased perfusion§, sudden behavioral/mental status change not attributable to a known cause¶) or reduced BP or associated symptoms of **hypotensive shock** (eg, hypotonia** [collapse], syncope, incontinence, **or cardiac arrest**) after exposure to known allergen for that patient (minutes to several hours)
a. Pediatric: systolic BP < 5th percentile for age or < 2 SD below normal for age or systolic BP < 70 mm Hg from 1 month to 1 year, < (70 mm Hg + [2 × age]) from 1 to 10 years

41

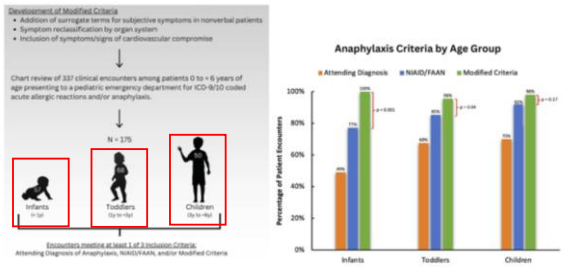
Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis



Handorf A, Roy IR, Cohen A, Camargo Jr CA, Dribin TE, Pistiner M. Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis. The Journal of Allergy and Clinical Immunology: In Practice. 2024 May 20.

42

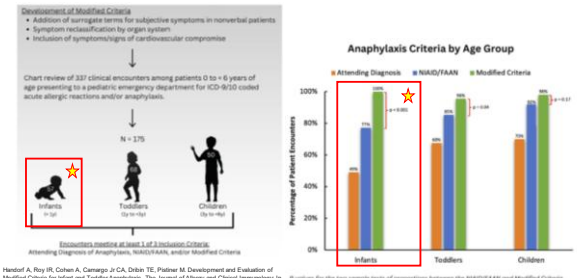
Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis



Handorf A, Roy IR, Cohen A, Camargo Jr CA, Dribin TE, Pistiner M. Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis. The Journal of Allergy and Clinical Immunology: In Practice. 2024 May 20.

43

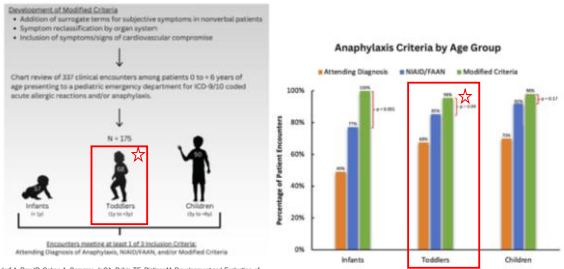
Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis



Handorf A, Roy IR, Cohen A, Camargo Jr CA, Dribin TE, Pistiner M. Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis. The Journal of Allergy and Clinical Immunology: In Practice. 2024 May 20.

44

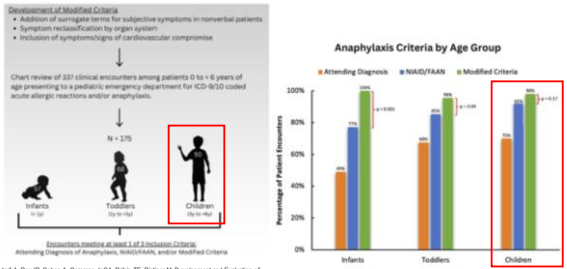
Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis



Handorf A, Roy IR, Cohen A, Camargo Jr CA, Dribin TE, Pistiner M. Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis. The Journal of Allergy and Clinical Immunology: In Practice. 2024 May 20.

45

Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis



Handorf A, Roy IR, Cohen A, Camargo Jr CA, Dribin TE, Pistiner M. Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis. The Journal of Allergy and Clinical Immunology: In Practice. 2024 May 20.

46

Mass General Brigham for Children

- **43% increase in the number of patients of all ages that experienced cardiovascular impairment as defined by modified criteria against NIAID/FAAN (*P* < .001)**
  - **When disaggregated by age group, the difference in respiratory symptoms remained statistically significant for infants, toddlers, and children**
- 32% increase in the number of patients of all ages that experienced respiratory symptoms as defined by modified criteria against NIAID/FAAN (*P* < .001)
  - When disaggregated by age group, the difference in respiratory symptoms remained statistically significant for infants, toddlers, and children

Organ system involvement (n, %)	NIAID/FAAN criteria organ system definitions	Modified criteria organ system definitions	*P* value
Infants (n = 57)	n (%)	n (%)	
Mucocutaneous	51 (89.5)	51 (89.5)	.999
Respiratory	14 (24.6)	31 (54.4)	.001
Gastrointestinal	30 (52.6)	36 (63.2)	.25
Cardiovascular/end organ dysfunction	3 (5.3)	29 (50.9)	<.001
Toddlers (n = 65)			
Mucocutaneous	60 (92.3)	62 (95.4)	.42
Respiratory	20 (30.8)	42 (64.6)	<.001
Gastrointestinal	30 (46.2)	32 (49.2)	.73
Cardiovascular/end organ dysfunction	0 (0.0)	32 (49.2)	<.001
Children (n = 49)			
Mucocutaneous	45 (91.8)	47 (95.9)	.40
Respiratory	25 (51.0)	40 (81.6)	.001
Gastrointestinal	26 (53.1)	28 (57.1)	.69
Cardiovascular/end organ dysfunction	2 (4.1)	17 (34.7)	<.001

Handorf A, Roy IR, Cohen A, Camargo Jr CA, Dribin TE, Pistiner M. Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis. The Journal of Allergy and Clinical Immunology: In Practice. 2024 May 20.

47

Mass General Brigham for Children

- 43% increase in the number of patients of all ages that experienced cardiovascular impairment as defined by modified criteria against NIAID/FAAN (*P* < .001)
  - When disaggregated by age group, the difference in respiratory symptoms remained statistically significant for infants, toddlers, and children
- **32% increase in the number of patients of all ages that experienced respiratory symptoms as defined by modified criteria against NIAID/FAAN (*P* < .001)**
  - **When disaggregated by age group, the difference in respiratory symptoms remained statistically significant for infants, toddlers, and children**

Organ system involvement (n, %)	NIAID/FAAN criteria organ system definitions	Modified criteria organ system definitions	*P* value
Infants (n = 57)	n (%)	n (%)	
Mucocutaneous	51 (89.5)	51 (89.5)	.999
Respiratory	14 (24.6)	31 (54.4)	.001
Gastrointestinal	30 (52.6)	36 (63.2)	.25
Cardiovascular/end organ dysfunction	3 (5.3)	29 (50.9)	<.001
Toddlers (n = 65)			
Mucocutaneous	60 (92.3)	62 (95.4)	.42
Respiratory	20 (30.8)	42 (64.6)	<.001
Gastrointestinal	30 (46.2)	32 (49.2)	.73
Cardiovascular/end organ dysfunction	0 (0.0)	32 (49.2)	<.001
Children (n = 49)			
Mucocutaneous	45 (91.8)	47 (95.9)	.40
Respiratory	25 (51.0)	40 (81.6)	.001
Gastrointestinal	26 (53.1)	28 (57.1)	.69
Cardiovascular/end organ dysfunction	2 (4.1)	17 (34.7)	<.001

Handorf A, Roy IR, Cohen A, Camargo Jr CA, Dribin TE, Pistiner M. Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis. The Journal of Allergy and Clinical Immunology: In Practice. 2024 May 20.

48

Mass General Brigham for Children

TABLE IV. Modified criteria organ system symptom breakdown by age group among patients meeting the modified criteria (n = 171)

Signs and symptoms, n (%)	NF	WAO	M	Infants (n = 57)	Toddlers (n = 65)	Children (n = 49)	All patients (n = 171)
Cardiovascular/end-organ dysfunction							
Altered mental status‡			x	22 38.6	18 (27.7)	10 (20.4)	50 (29.2)
Tachycardia			x	14 24.6	22 (33.8)	10 (20.4)	46 (26.9)
Pallor			x	3 (5.3)	1 (1.5)	3 (6.1)	7 (4.1)
Obtunded/lethargy			x	3 (5.3)	1 (1.5)	3 (6.1)	7 (4.1)
Cardiovascular cyanosis			x	5 8.8	0 (0.0)	1 (2.0)	6 (3.5)
Hypotonia	x	x	x	3 (5.3)	0 (0.0)	1 (2.0)	4 (2.4)
Incontinence	x	x	x	0 (0.0)	0 (0.0)	1 (2.0)	1 (1.2)
Hypotension	x	x	x	0 (0.0)	0 (0.0)	2 (4.1)	2 (1.2)
Mottling			x	1 (1.8)	0 (0.0)	0 (0.0)	1 (0.6)
Syncope	x	x	x	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

NF, NIAID/FAAN criteria; *M*, modified criteria; *W*, WAO criteria.

NF, NIAID/FAAN criteria; *M*, modified criteria; *W*, WAO criteria.
*Dyspnea, shortness of breath, chest tightness.
†Tachypnea, belly breathing, retractions, nasal flaring.
‡Mental status change (ie, crankiness, withdrawn/clingy, inconsolable, subdued, less active with no other explanation).

Handorf A, Roy IR, Cohen A, Camargo Jr CA, Dribin TE, Pistiner M. Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis. The Journal of Allergy and Clinical Immunology: In Practice. 2024 May 20.

49

Mass General Brigham for Children

TABLE IV. Modified criteria organ system symptom breakdown by age group among patients meeting the modified criteria (n = 171)

Signs and symptoms, n (%)	NF	WAO	M	Infants (n = 57)	Toddlers (n = 65)	Children (n = 49)	All patients (n = 171)
Cardiovascular/end-organ dysfunction							
Altered mental status‡			x	22 (38.6)	18 (27.7)	10 (20.4)	50 (29.2)
Tachycardia			x	14 (24.6)	22 (33.8)	10 (20.4)	46 (26.9)
Pallor			x	3 (5.3)	1 (1.5)	3 (6.1)	7 (4.1)
Obtunded/lethargy			x	3 (5.3)	1 (1.5)	3 (6.1)	7 (4.1)
Cardiovascular cyanosis			x	5 (8.8)	0 (0.0)	1 (2.0)	6 (3.5)
Hypotonia	x	x	x	3 (5.3)	0 (0.0)	1 (2.0)	4 (2.4)
Incontinence	x	x	x	0 (0.0)	0 (0.0)	1 (2.0)	1 (1.2)
Hypotension	x	x	x	0 (0.0)	0 (0.0)	2 (4.1)	2 (1.2)
Mottling			x	1 (1.8)	0 (0.0)	0 (0.0)	1 (0.6)
Syncope	x	x	x	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

NF, NIAID/FAAN criteria; *M*, modified criteria; *W*, WAO criteria.
*Dyspnea, shortness of breath, chest tightness.
†Tachypnea, belly breathing, retractions, nasal flaring.
‡Mental status change (ie, crankiness, withdrawn/clingy, inconsolable, subdued, less active with no other explanation).

Handorf A, Roy IR, Cohen A, Camargo Jr CA, Dribin TE, Pistiner M. Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis. The Journal of Allergy and Clinical Immunology: In Practice. 2024 May 20.

50

Mass General Brigham for Children

TABLE IV. Modified criteria organ system symptom breakdown by age group among patients meeting the modified criteria (n = 171)

Signs and symptoms, n (%)	NF	WAO	M	Infants (n = 57)	Toddlers (n = 65)	Children (n = 49)	All patients (n = 171)
Cough			x	7 (12.3)	17 (26.2)	17 (34.7)	41 (24.0)
Wheeze-bronchospasm	x	x	x	8 (14.0)	10 (15.4)	15 (30.6)	33 (19.3)
dyspnea*	x	x	x	6 (10.5)	9 (13.8)	18 (36.7)	33 (19.3)
Tachypnea			x	11 (19.3)	6 (9.2)	3 (6.1)	20 (11.7)
Hoarse voice/cry		x	x	1 (1.8)	11 (16.9)	6 (12.2)	18 (10.5)
Drooling			x	6 (10.5)	5 (7.7)	5 (10.2)	16 (9.4)
Swollen uvula/soft palate	x	x	x	2 (3.5)	5 (7.7)	6 (12.2)	13 (7.6)
Increased work of breathing†			x	8 (14.0)	5 (7.7)	5 (10.2)	18 (6.4)
Swollen tongue	x	x	x	3 (5.3)	0 (0.0)	5 (10.2)	8 (4.7)
Stridor	x	x	x	2 (3.5)	4 (6.2)	2 (4.1)	8 (4.7)
Hypoxemia	x	x	x	2 (3.5)	2 (3.1)	2 (4.1)	6 (3.5)
Respiratory cyanosis			x	3 (5.3)	1 (1.5)	0 (0.0)	4 (2.4)

NF, NIAID/FAAN criteria; *M*, modified criteria; *W*, WAO criteria.
*Dyspnea, shortness of breath, chest tightness.
†Tachypnea, belly breathing, retractions, nasal flaring.
‡Mental status change (ie, crankiness, withdrawn/clingy, inconsolable, subdued, less active with no other explanation).

51

Mass General Brigham for Children

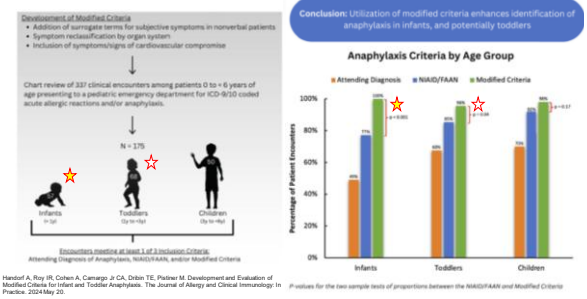
TABLE IV. Modified criteria organ system symptom breakdown by age group among patients meeting the modified criteria (n = 171)

Signs and symptoms, n (%)	NF	WAO	M	Infants (n = 57)	Toddlers (n = 65)	Children (n = 49)	All patients (n = 171)
Cough			x	7 (12.3)	17 (26.2)	17 (34.7)	41 (24.0)
Wheeze-bronchospasm	x	x	x	8 (14.0)	10 (15.4)	15 (30.6)	33 (19.3)
dyspnea*	x	x	x	6 (10.5)	9 (13.8)	18 (36.7)	33 (19.3)
Tachypnea			x	11 (19.3)	6 (9.2)	3 (6.1)	20 (11.7)
Hoarse voice/cry		x	x	1 (1.8)	11 (16.9)	6 (12.2)	18 (10.5)
Drooling			x	6 (10.5)	5 (7.7)	5 (10.2)	16 (9.4)
Swollen uvula/soft palate	x	x	x	2 (3.5)	5 (7.7)	6 (12.2)	13 (7.6)
Increased work of breathing†			x	8 (14.0)	5 (7.7)	5 (10.2)	18 (6.4)
Swollen tongue	x	x	x	3 (5.3)	0 (0.0)	5 (10.2)	8 (4.7)
Stridor	x	x	x	2 (3.5)	4 (6.2)	2 (4.1)	8 (4.7)
Hypoxemia	x	x	x	2 (3.5)	2 (3.1)	2 (4.1)	6 (3.5)
Respiratory cyanosis			x	3 (5.3)	1 (1.5)	0 (0.0)	4 (2.4)

NF, NIAID/FAAN criteria; *M*, modified criteria; *W*, WAO criteria.
*Dyspnea, shortness of breath, chest tightness.
†Tachypnea, belly breathing, retractions, nasal flaring.
‡Mental status change (ie, crankiness, withdrawn/clingy, inconsolable, subdued, less active with no other explanation).

52

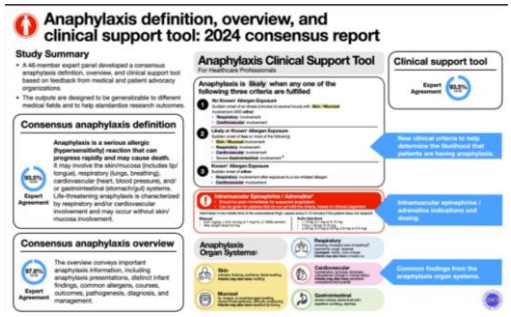
Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis



Handorf A, Roy IR, Cohen A, Camargo Jr CA, Dribin TE, Pistiner M. Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis. The Journal of Allergy and Clinical Immunology: In Practice. 2024 May 20.

P values for the two sample tests of proportions between the NIAID/FAAN and Modified Criteria

53



Dribin TE, Muraro A, Camargo Jr CA, Turner PJ, Wang J, Roberts G, Anagnostou A, Hallen S, Liebermann J, Worm M, Zuberbier T. Anaphylaxis definition, overview, and clinical support tool: 2024 consensus report. Journal of Allergy and Clinical Immunology. 2025 Jan 27.

54

"Should age of the infant/toddler experiencing anaphylaxis be used as a predictor of reaction severity?"

Images generated by Chat GPT

55

2023 Anaphylaxis Practice Parameters Update:
Recommendation # 9

Should age of the infant/toddler experiencing anaphylaxis be used as a predictor of reaction severity?

We suggest clinicians be aware that, in infants and toddlers, patient age does not correlate with reaction severity.

Strength of Recommendation: Conditional
Certainty of Evidence: Very Low

56

Mass General Brigham for Children

Reaction Severity in ED Setting

- Korean ED registry showed that 9.7% of 558 children < 2 yrs of age with anaphylaxis had severe reactions
- Nationwide Emergency Department Sample (trends of presentation to US EDs 2006-2015)
  - Proportion of visits for anaphylaxis in infants increased from approximately 20 per 100,000 visits to 50 over this time
  - Overall hospitalizations for anaphylaxis in infants presenting to the ED fell from 19% to 6%

Robinson LB, Arroyo AC, Faridi MK, Rudders S, Camargo Jr CA. Trends in US emergency department visits for anaphylaxis among infants and toddlers: 2006-2015. The Journal of Allergy and Clinical Immunology: In Practice. 2021 May 1;9(5):1931-8.

Soriano VX, Peters RL, Ponsonby AL, Dharmage SC, Perrett KP, Field MJ, Knox A, Tey D, Odoi S, Gell G, Perez BC. Earlier ingestion of peanut after changes to infant feeding guidelines: the EarlyNuts study. Journal of Allergy and Clinical Immunology. 2019 Nov 1;144(5):1327-35.

Jeong K, Ye YM, Kim SH, Kim KW, Kim JH, Kwon JW, Yang SI, Lee SY, Chung EH, Kim MA, Kim YH. A multicenter anaphylaxis registry in Korea: clinical characteristics and acute treatment details from infants to older adults. World Allergy Organization Journal. 2020 Aug 1;13(8):100449.

Golden DB, Wang J, Waserman S, Akin C, Campbell RL, Ellis AK, Greenhawt M, Lang DM, Ledford DK, Lieberman J, Oppenheimer J. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology. 2023 Dec 18.

57

Mass General Brigham for Children

Reaction severity in OFC Setting

- HealthNuts study of 916 infant OFC
  - Anaphylaxis in 2.1% positive challenges (14 cases)
  - Serum sIgE >=15ku/l for peanut/egg associated with mod/severe
  - Of 535 positive infant OFC (egg, peanut, or sesame) no biphasic, late or prolonged anaphylactic reactions occurring at the study clinic or home.
- Multicenter clinical challenge cohort (CHOP/VUMC): of OFC reactions in infants and toddlers < 24 mo,
  - 10% of reactions were cardiovascular, neurological, lower respiratory, or laryngeal symptoms

- Kennedy K, Alfaro MK, Spergel ZC, Dorris SL, Spergel JM, Capucilli P. Differences in oral food challenge reaction severity based on increasing age in a pediatric population. Annals of Allergy, Asthma & Immunology. 2021 Nov 1;127(5):562-7.
- Chan JC, Peters RL, Koplin JJ, Dharmage SC, Gurrin LC, Wake M, Tang ML, Prescott S, Allen KJ, Ponsonby AL, Matheson M. Food challenge and community-reported reaction profiles in food-allergic children aged 1 and 4 years: a population-based study. The Journal of Allergy and Clinical Immunology: In Practice. 2017 Mar 1;5(2):398-409.
- Koplin JJ, Tang ML, Martin PE, Osborne NJ, Lowe AJ, Ponsonby AL, Robinson MN, Tey D, Thiele L, Hill DJ, Gurrin LC. Predetermined challenge eligibility and cessation criteria for oral food challenges in the HealthNuts population-based study of infants. Journal of allergy and clinical immunology. 2012 Apr 1;129(4):1145-7.
- Tsuang A, Chan ES, Wang J. Food-induced anaphylaxis in infants: can new evidence assist with implementation of food allergy prevention and treatment?. The Journal of Allergy and Clinical Immunology: In Practice. 2021 Jan 1;9(1):57-69.

58

Mass General Brigham for Children

Reaction severity in OFC Setting

Prospective study of oral food challenge outcomes (age <36 mo)

- 530 clinically indicated OFCs (Nov 2019 – July 2022)
- 14 (2.6%) systemic and thus treated with epinephrine
- No reaction resulted in hospitalization/rapid response, transfer to the ED, IV fluid bolus, or O2

Total	N = 530
Pass	350 (66.0 %)
Indeterminate	26 (4.9 %)
Conditional Pass	60 (11.3 %)
Positive Systemic Reaction	92 (17.4 %) 14 (2.6 %)

Ramirez L, Roy I, Taneja I, Yap S, Mendez-Reyes J, Andre M, Hazi A, Esteban C, Ongaro Z, Pan L, Shreffler W, Pistiner M. Systemic Reactions in Infants and Toddlers: A Prospective Study of OFC Outcomes. Scheduled for oral presentation at AAAAI National Conference 2023. San Antonio, Texas.

59

Mass General Brigham for Children

Reaction severity in OFC Setting

Frequency and predictors of multisystem reactions to peanut in infant oral food challenges

- Analysis of 52 positive OFCs to peanut
  - Median age was 8 months (interquartile range 6.9–9.4)
  - 12 (23%) treated with epinephrine
  - 19 (37%) multisystem reactions
    - 1 child had circulatory symptoms (tachycardia) and treated with epinephrine x 2
  - No reaction resulted in hospitalization, referral to the emergency department or refractory symptoms
  - Although reassuring, this study supports that infants can have significant reactions that require medical intervention

Keet CA, Wood RA, Dantzer J, Plesa M, Taneja I, Andre M, Shreffler W, Togias A, Pistiner M. Frequency and predictors of multisystem reactions to peanut in infant oral food challenges. The Journal of Allergy and Clinical Immunology: In Practice. 2024 Jan 1;12(1):252-4.

60

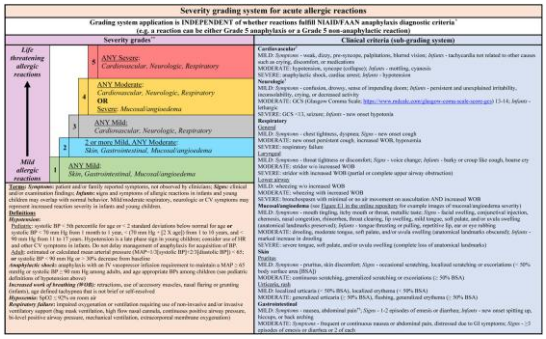
Severity grading system for acute allergic reactions: A multidisciplinary Delphi study

Timothy E. Dribin, MD,[a,b] David Schnadower, MD, MPH,[a,b] Jonathan M. Spergel, MD, PhD,[c] Ronna L. Campbell, MD, PhD,[d] Marcus Shaker, MD, MSc,[e,f] Mark I. Neuman, MD, MPH,[a,b] Kenneth A. Michelson, MD, MPH,[a,b] Peter S. Capucilli, MD,[f] Carlos A. Camargo, Jr, MD, DrPH,[f] David C. Brousseau, MD, MS,[g] Susan A. Rudders, MD, MS,[a,b] Amal H. Assa'ad, MD,[h,m] Kimberly A. Risma, MD, PhD,[h,m] Mariana Castells, MD, PhD,[a] Lynda C. Schneider, MD,[a,i] Julie Wang, MD,[a] Juhee Lee, MD,[c] Rakesh D. Mistry, MD, MS,[j] David Vyles, DO, MS,[k] Michael Pistiner, MD, MMSc,[a] John K. Witry, MS,[a] Yin Zhang, MS,[l] and Hugh A. Sampson, MD[c]
Cincinnati, Ohio; Philadelphia, Pa; Rochester, Minn; Hanover, NH; Boston, Mass; and Rochester and New York, NY

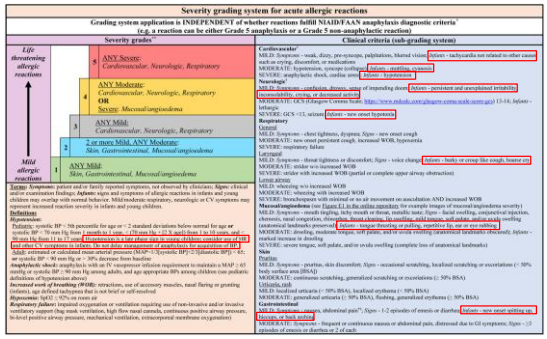
- Panel of 21 experts in Emergency Medicine, Pediatrics and Allergy Immunology developed a consensus severity grading system for acute allergic reactions, including anaphylactic and non-anaphylactic reactions.
- Nine members formed a writing group to critically appraise and assess the strengths and limitations of prior severity grading systems and develop the structure and content for an optimal severity grading system.
- The entire study panel then revised the grading system and sought consensus utilizing Delphi methodology.

Dribin, Timothy E., et al. "Severity grading system for acute allergic reactions: A multidisciplinary Delphi study." Journal of Allergy and Clinical Immunology 148.1 (2021): 173-181.

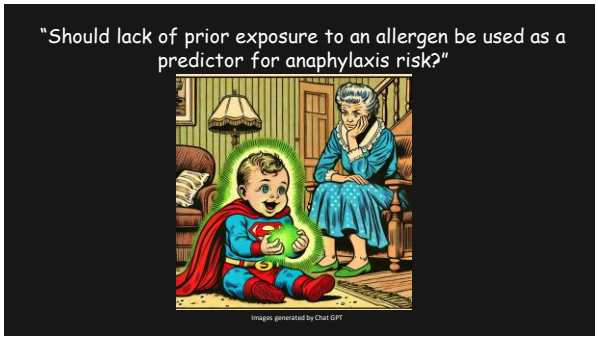
61



62



63



64

2023 Anaphylaxis Practice Parameters Update:

Recommendation # 10

Should lack of prior exposure to an allergen be used as a predictor for anaphylaxis risk?

We suggest clinicians be aware that anaphylaxis is unlikely to be the initial reaction to a food or medication on first exposure in infants.

Strength of Recommendation: Conditional
Certainty of Evidence: Low

65

Mass General Brigham for Children

Clinical trial data for early introduction

- Data has suggested that for initial reactions, anaphylaxis is less common than mild to moderate and cutaneous, but does occur

- Du Toit G, Roberts G, Sayre PH, Bahnson HT, Radulovic S, Santos AF, Brough HA, Phippard D, Basting M, Feeney M, Turcanu V. Randomized trial of peanut consumption in infants at risk for peanut allergy. New England Journal of Medicine. 2015 Feb 26;372(9):803-13.
- Perkin MR, Logan K, Tseng A, Raji B, Ayis S, Peacock J, Brough H, Marrs T, Radulovic S, Craven J, Flohr C. Randomized trial of introduction of allergenic foods in breast-fed infants. New England Journal of Medicine. 2016 May 5;374(18):1733-43.
- Palmer DJ, Sullivan TR, Gold MS, Prescott SL, Makrides M. Randomized controlled trial of early regular egg intake to prevent egg allergy. Journal of Allergy and Clinical Immunology. 2017 May 1;139(5):1600-7.
- Golden DB, Wang J, Waserman S, Akin C, Campbell RL, Ellis AK, Greenhawt M, Lang DM, Ledford DK, Lieberman J, Oppenheimer J. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology. 2023 Dec 18.

66

Anaphylaxis Management in Infants and Toddlers

Chat GPT

67

"Should infants/toddlers be prescribed the 0.1 mg or 0.15 mg EAI?"

Images generated by Chat GPT

68

2023 Anaphylaxis Practice Parameters Update: Recommendation # 12

Should infants/toddlers be prescribed the 0.1 mg or 0.15 mg EAI?

We suggest clinicians prescribe either the 0.1 mg or the 0.15 mg EAI dose for infants/toddlers weighing less than 15 kg.

Strength of Recommendation: Conditional
Certainty of Evidence: Low

69

Mass General Brigham for Children

Epinephrine Auto-Injectors

- EAIs are available in a limited number of premeasured doses
  - FDA has approved 0.15 mg EAIs for 15–30 kg, and a 0.1 mg EAI (Auvi-Q) for 7.5–15 kg
  - AAP and JTFPP support use of 0.15 mg EAIs for young children less than 15 kg as the 0.1mg EAI is not universally available

Golden DB, Wang J, Waserman S, Akin C, Campbell RL, Ellis AK, Greenhawt M, Lang DM, Ledford DK, Lieberman J, Oppenheimer J. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology. 2023 Dec 18.

70

Mass General Brigham for Children

Epinephrine dose

- IM epinephrine 0.01 mg/kg, up to a maximum of 0.3 mg for children

Golden DB, Wang J, Waserman S, Akin C, Campbell RL, Ellis AK, Greenhawt M, Lang DM, Ledford DK, Lieberman J, Oppenheimer J. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology. 2023 Dec 18.

71

"What autoinjector characteristics should clinicians consider when prescribing EAIs?"

Images generated by Chat GPT

72

2023 Anaphylaxis Practice Parameters Update: Recommendation # 29

What autoinjector characteristics should clinicians consider when prescribing EAIs?

When deciding which EAI to prescribe, we suggest that clinicians consider dosage, needle length, affordability, access, and patient treatment preferences.

Strength of Recommendation: Conditional
Certainty of Evidence: Very Low

73

Mass General Brigham for Children

Epinephrine Auto-Injector Needle Length

- Based on ultrasound imaging measurements of skin-to-bone and skin-to-muscle
- Children <15 kg, risk of IO injection lower with Auvi-Q® 0.1 mg, compared with EpiPen® Jr. 0.15mg
- Risk of IO injection was low in children weighing >=15 kg
- Auvi-Q® 0.1 mg posed higher predicted risk of SC injection than other devices

- Brown JC, Tuuri RE, Akhter S, Guerra LD, Goodman IS, Myers SR, Nozicka C, Manzi S, Long K, Turner T, Conners GP. Lacerations and embedded needles caused by epinephrine autoinjector use in children. Annals of emergency medicine. 2016 Mar 1;67(3):307-15.
- Dreborg S, Kim L, Tsai G, Kim H. Epinephrine auto-injector needle lengths: can both subcutaneous and periosteal/intraosseous injection be avoided?. Annals of Allergy, Asthma & Immunology. 2018 Jun 1;120(6):648-53.
- Kim H, Dinakar C, McInnis P, Rudin D, Benain X, Daley W, Platz E. Inadequacy of current pediatric epinephrine autoinjector needle length for use in infants and toddlers. Annals of Allergy, Asthma & Immunology. 2017 Jun 1;118(6):719-25.
- Golden DB, Wang J, Waserman S, Akin C, Campbell RL, Ellis AK, Greenhawt M, Lang DM, Ledford DK, Lieberman J, Oppenheimer J. Anaphylaxis: A 2023 practice parameter update. Annals of Allerov. Asthma & Immunolov. 2023 Dec 18.

74

"What are the adverse events associated with EAI use? Are certain populations at increased risk of adverse events? How should this inform EAI prescription and patient education?"

Chat GPT Generated

75

2023 Anaphylaxis Practice Parameters Update: Recommendation # 27

What are the adverse events associated with EAI use? Are certain populations at increased risk of adverse events? How should this inform EAI prescription and patient education?

Serious adverse reactions to intramuscular epinephrine are very rare and should not pose a barrier to the prescription or early administration of EAIs when indicated. To manage the risk of adverse events, we recommend that clinicians counsel patients and caregivers on the proper use of EAIs, the common adverse effects, and the need for immediate evaluation and treatment when signs or symptoms of serious adverse events develop.

Strength of Recommendation: Strong
Certainty of Evidence: Low

76

Mass General Brigham for Children

Potential adverse events following EAI administration:

- Lacerations or embedded needles may occur if child moves or grabs the device during administration, the device discharges off center due to malfunction, or the needle bends when hitting bone
- "Swing and jab" motion rather than a "place and press" technique may result in more leg movement and increased risk of laceration
- More research is needed to evaluate strategies to reduce the risk of EAI-related laceration and other injuries

Brown JC, Tuuri RE, Akhter S, Guerra LD, Goodman IS, Myers SR, et al. Lacerations and embedded needles caused by epinephrine autoinjector use in children. Ann Emerg Medicine 2016;67:307-315.e8

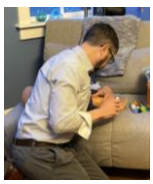
Golden DB, Wang J, Waserman S, Akin C, Campbell RL, Ellis AK, Greenhawt M, Lang DM, Ledford DK, Lieberman J, Oppenheimer J. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology. 2023 Dec 18.

77

Mass General Brigham for Children

Strategies to reduce the risk of EAI-related injury

1. Restrain the patient and firmly immobilize their leg before administering the EAI
2. Control the action of administration as much as possible, using a place and press motion rather than a swing and jab motion
3. Hold the EAI in place for the shortest time recommended by the manufacturer
4. Avoid reinserting the needle if it dislodges before the recommended hold time passes



Brown JC, Tuuri RE, Akhter S, Guerra LD, Goodman IS, Myers SR, et al. Lacerations and embedded needles caused by epinephrine autoinjector use in children. Ann Emerg Medicine 2016;67:307-315.e8

Golden DB, Wang J, Waserman S, Akin C, Campbell RL, Ellis AK, Greenhawt M, Lang DM, Ledford DK, Lieberman J, Oppenheimer J. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology. 2023 Dec 18.

78

Parental experience administering epinephrine for systemic reactions during infant and toddler oral food challenges

Mixed methods sub study examining parental experience administering epinephrine for systemic reactions during OFCs

- Parents were pre-trained in holding their child and using the auto-injector
  - 9 systemic reactions out of 343 total challenges
    - All 9 of these were administered by a trained caregiver
    - Post reaction structured survey & post reaction (48-72 hr) qualitative interview with child psychologist (one-phase, concurrent triangulation design)

Theodorakakis M, Machado S, Andre M, Hazi A, Ongaro Z, Pan L, Yap S, Shreffler W, Fleitner M. Parental experience administering epinephrine for systemic reactions during infant and toddler oral food challenges. The Journal of Allergy and Clinical Immunology: In Practice. 2024 Oct 1;12(10):2838-41.

79

Parental experience administering epinephrine for systemic reactions during infant and toddler oral food challenges

Main Insights

- Confidence Building – Parents reported increased confidence in recognizing anaphylaxis symptoms and using an EAI
- Positive Experience – Despite the reaction, parents found the experience helpful and reassuring
- Clinical Implication – OFCs that require epinephrine can serve as valuable training for families

Conclusion

Even when an OFC leads to a reaction requiring epinephrine, the experience can be **empowering and educational** for caregivers

Theodorakakis M, Machado S, Andre M, Hazi A, Ongaro Z, Pan L, Yap S, Shreffler W, Fleitner M. Parental experience administering epinephrine for systemic reactions during infant and toddler oral food challenges. The Journal of Allergy and Clinical Immunology: In Practice. 2024 Oct 1;12(10):2838-41.

80

"Should childcare centers and schools stock undesignated EAIs that can be used to treat any individual on school grounds who experiences anaphylaxis?"

Generated by Chat GPT

81

2023 Anaphylaxis Practice Parameters Update:

Recommendation # 18

Should childcare centers and schools stock undesignated EAIs that can be used to treat any individual on school grounds who experiences anaphylaxis?

We suggest that childcare centers and schools stock undesignated EAIs that can be used to treat any individual on school grounds who experiences anaphylaxis.

Strength of Recommendation: Conditional
Certainty of Evidence: Very Low

82

"Should childcare centers and schools implement training for personnel in the management of food allergy, rather than not implementing such training?"

Generated by Chat GPT

83

2023 Anaphylaxis Practice Parameters Update:

Recommendation # 16

Should childcare centers and schools implement training for personnel in the management of food allergy, rather than not implementing such training?

We suggest childcare centers and schools implement staff training for allergy and anaphylaxis management.

Strength of Recommendation: Conditional
Certainty of Evidence: Very Low

84

"What counseling, education, and/or training on epinephrine should clinicians provide to patients and caregivers?"

Images generated by Chat GPT

85

2023 Anaphylaxis Practice Parameters Update:
Recommendation # 30

What counseling, education, and/or training on epinephrine should clinicians provide to patients and caregivers?

During visits with patients who have been prescribed EAIs, we recommend that clinicians routinely review the essentials of EAI carriage, storage, and use; encourage patients to regularly practice EAI administration with a trainer device; and discuss strategies to manage barriers to adherence that patients may have experienced.

Strength of Recommendation: Strong
Certainty of Evidence: Low

86

Mass General Brigham for Children

Asthma and Allergy Foundation of America | KIDS WITH FOOD ALLERGIES

Factors Associated With Epinephrine Use in the Treatment of Anaphylaxis in Infants and Toddlers

- Objective: Examine factors influencing epinephrine use for food-induced anaphylaxis in children under 36 months
- Methods:
  - National online survey of primary caregivers.
  - 264 cases of probable anaphylaxis identified using the AAFA Infant and Toddler Anaphylaxis Study Criteria

Pizzner M, Mendez-Reyes JE, Elfenbein S, Carver M, Lieberman J, Wang J, Camargo Jr CA. Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2020 Nov 14.

87

Mass General Brigham for Children

Asthma and Allergy Foundation of America | KIDS WITH FOOD ALLERGIES

Factors Associated With Epinephrine Use in the Treatment of Anaphylaxis in Infants and Toddlers

Epinephrine Use:

- 39% of infants (<12 months) vs. 61% of toddlers (12-35 months) received epinephrine at any time (p=.001)
- Role of Food Allergy Diagnosis:
  - 62% of cases with a prior diagnosis of food allergy received epinephrine at any time vs. 26% without a diagnosis (p <.001)
- Anaphylaxis Action Plan (AAP):
  - In those with a prior diagnosis of food allergy, epinephrine use increased from 50% to 89% with an AAP in place (p=.001)
  - Adjusted* odds ratio for epinephrine use in cases with an AAP = 5.39 (95% CI, 2.18-13.30) *(for age and PDFA)

Pizzner M, Mendez-Reyes JE, Elfenbein S, Carver M, Lieberman J, Wang J, Camargo Jr CA. Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2020 Nov 14.

88

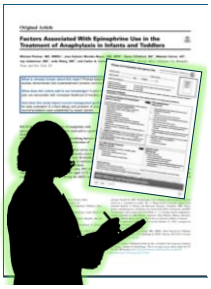
Mass General Brigham for Children

Asthma and Allergy Foundation of America | KIDS WITH FOOD ALLERGIES

Factors Associated With Epinephrine Use in the Treatment of Anaphylaxis in Infants and Toddlers

Conclusions and Impact

- Prior diagnosis of food allergy and provision of an anaphylaxis action plan are associated with increased likelihood of treating anaphylaxis with epinephrine among infants and toddlers
- These findings support current recommendations for early food allergy evaluation and the provision of anaphylaxis action plans
  - Until now, these recommendations were established by expert opinion only



Pizzner M, Mendez-Reyes JE, Elfenbein S, Carver M, Lieberman J, Wang J, Camargo Jr CA. Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2020 Nov 14.

89

Calling 911: Home vs Hospital Monitoring

https://estatesales.org/online-auctions/price-1978-dc-comics-original-21627725

90

2023 Anaphylaxis Practice Parameters Update: Recommendation # 26

When should EMS be activated after EAI use?

We suggest that clinicians counsel patients that immediate activation of EMS may not be required if the patient experiences prompt, complete, and durable response to treatment with epinephrine, provided that additional epinephrine and medical care are readily available, if needed. We suggest that clinicians counsel patients to always activate EMS after epinephrine use if anaphylaxis is severe, fails to resolve promptly, fails to resolve completely or nearly completely, or returns or worsens after a first dose of epinephrine.

Strength of Recommendation: Conditional
Certainty of Evidence: Very Low

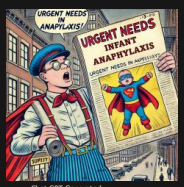
91

What Knowledge Infant and Toddler Specific Gaps Require Additional Research?

DC Adventure Comics 231 1956 Super-feats of Super Baby https://dc.fandom.com/wiki/Adventure_Comics_Vol_1_231

92

"Lack of data on symptom presentation from well-defined infant anaphylaxis cohorts to better determine whether infants need separate clinical criteria to define anaphylaxis as compared with older children, adolescents, and adults."



Chat GPT Generated

https://davidhayes.ca/2018/10/supermans-super-riter/

93

Mass General Brigham for Children

Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers

- Challenges in Recognizing and Documenting Allergic Reactions
  - Variability in Clinical Presentation:
    - Differences in interpretation among healthcare providers complicate the diagnostic process.
  - Unique Considerations for Infants and Toddlers:
    - Nonverbal population with distinctive signs and symptoms during allergic reactions and anaphylaxis.
    - Diagnosis is often more complex.

Pyle D, Mendez-Reyes JE, Esteban C, Hazi A, André M, Yap S, Shreffler W, Pistiner M. Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2024 Aug 1;12(8):2221-2.

94

Mass General Brigham for Children

Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers

- Standardized Assessment Template: A Practical Solution for Documentation:
  - Tailored templates provide structured documentation of signs and symptoms, especially when verbal communication of subjective symptoms is not possible.
  - Clinical and Operational Impact
  - Research Applications

Pyle D, Mendez-Reyes JE, Esteban C, Hazi A, André M, Yap S, Shreffler W, Pistiner M. Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2024 Aug 1;12(8):2221-2.

95

Mass General Brigham for Children

Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers

Development of the Assessment Template

- Age-specific literature on severe allergic reactions in infants and toddlers.
- Pediatric Advanced Life Support (PALS) criteria (e.g., signs of compensated shock: cyanosis, mottling, lethargy, hypotonia).
- PRACTALL scoring system for older patients.

Pyle D, Mendez-Reyes JE, Esteban C, Hazi A, André M, Yap S, Shreffler W, Pistiner M. Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2024 Aug 1;12(8):2221-2.

96

Mass General Brigham for Children

Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers

Template Design and Structure

- Comprehensive List of Signs and Symptoms:
  - Organized, categorized, and standardized for easy documentation.
  - Branch Logic Integration:
    - Guides documentation from simple cases to complex multisystem reactions.
  - Structured for Consistency:
    - Ensures accurate assessment and communication across providers.

Pyle D, Mendez-Reyes JE, Esteban C, Hazi A, André M, Yap S, Shreffler W, Pistiner M. Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2024 Aug 1;12(8):222 1-2.

97

Mass General Brigham for Children

Flowsheet Template

Infant / Toddler Food Challenge Symptoms

Reaction Trigger (if known): 1/16th tsp PB2

Time of Assessment: 11:05 — Baseline Assessment? ☐ Yes ☑ No

Symptoms:

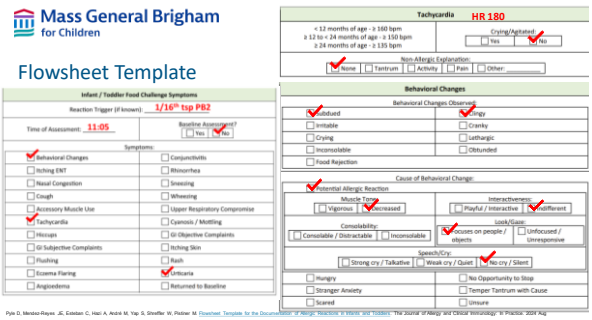
☑ Behavioral Changes	☐ Conjunctivitis
☐ Itching ENT	☐ Rhinorrhea
☐ Nasal Congestion	☐ Sneezing
☐ Cough	☐ Wheezing
☐ Accessory Muscle Use	☐ Upper Respiratory Compromise
☑ Tachycardia	☐ Cyanosis / Mottling
☐ Hiccups	☐ GI Objective Complaints
☐ GI Subjective Complaints	☐ Itching Skin
☐ Flushing	☐ Rash
☐ Eczema Flaring	☑ Urticaria
☐ Angioedema	☐ Returned to Baseline

Pyle D, Mendez-Reyes JE, Esteban C, Hazi A, André M, Yap S, Shreffler W, Pistiner M. Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2024 Aug 1;12(8):2221-2.

98

Mass General Brigham for Children

Flowsheet Template



Infant / Toddler Food Challenge Symptoms

Reaction Trigger (if known): 1/16th tsp PB2

Time of Assessment: 11:05 — Baseline Assessment? ☐ Yes ☑ No

Symptoms:

☑ Behavioral Changes	☐ Conjunctivitis
☐ Itching ENT	☐ Rhinorrhea
☐ Nasal Congestion	☐ Sneezing
☐ Cough	☐ Wheezing
☐ Accessory Muscle Use	☐ Upper Respiratory Compromise
☑ Tachycardia	☐ Cyanosis / Mottling
☐ Hiccups	☐ GI Objective Complaints
☐ GI Subjective Complaints	☐ Itching Skin
☐ Flushing	☐ Rash
☐ Eczema Flaring	☑ Urticaria
☐ Angioedema	☐ Returned to Baseline

Tachycardia HR 180

< 12 months of age - ≥ 160 bpm
≥ 12 to < 24 months of age - ≥ 150 bpm
≥ 24 months of age - ≥ 135 bpm

Crying/Agitated: ☐ Yes ☑ No

Non-Allergic Explanation: ☑ None ☐ Tantrum ☐ Activity ☐ Pain ☐ Other:

Behavioral Changes

Behavioral Changes Observed:

☑ Subdued	☑ Clingy
☐ Irritable	☐ Cranky
☐ Crying	☐ Lethargic
☐ Inconsolable	☐ Obtunded
☐ Food Rejection	

Cause of Behavioral Change:

☑ Potential Allergic Reaction

Muscle Tone: ☐ Vigorous ☑ Decreased

Interactiveness: ☐ Playful / Interactive ☑ Indifferent

Consolability: ☐ Consolable / Distractable ☐ Inconsolable

Look/Gaze: ☑ Focuses on people / objects ☐ Unfocused / Unresponsive

Speech/Cry: ☐ Strong cry / Talkative ☐ Weak cry / Quiet ☑ No cry / Silent

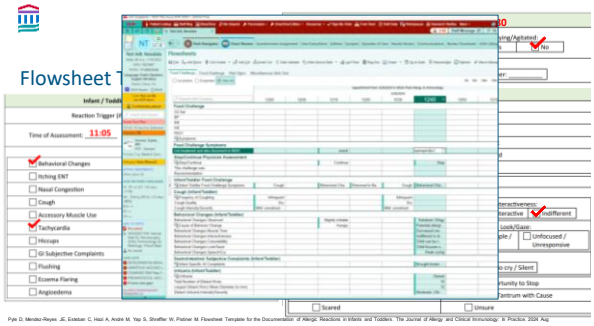
☐ Hungry	☐ No Opportunity to Stop
☐ Stranger Anxiety	☐ Temper Tantrum with Cause
☐ Scared	☐ Unsure

Pyle D, Mendez-Reyes JE, Esteban C, Hazi A, André M, Yap S, Shreffler W, Pistiner M. Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2024 Aug

99

Mass General Brigham for Children

Flowsheet

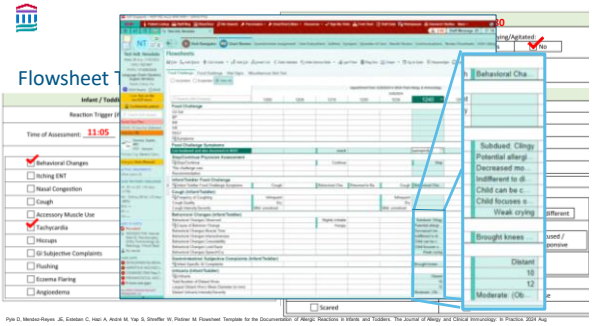


Pyle D, Mendez-Reyes JE, Esteban C, Hazi A, André M, Yap S, Shreffler W, Pistiner M. Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2024 Aug

100

Mass General Brigham for Children

Flowsheet



Pyle D, Mendez-Reyes JE, Esteban C, Hazi A, André M, Yap S, Shreffler W, Pistiner M. Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2024 Aug

101

Mass General Brigham for Children

Flowsheet Template

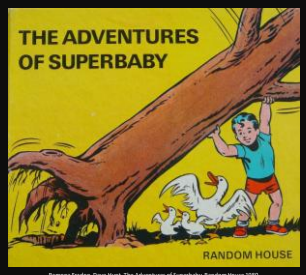
- Symptom Flowsheet Recipe for EMR/Database Builds

https://template.famp-it.org

Pyle D, Mendez-Reyes JE, Esteban C, Hazi A, André M, Yap S, Shreffler W, Pistiner M. Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2024 Aug

102

Thank You!



Ramona Fradon, Dave Hunt. The Adventures of Superbaby. Random House 1980.
https://www.abebooks.com/first-edition/Adventures-Superbaby-Fradon-Ramona-Illustrator-Hunt/20273338696/bd#&gid=1&pid=1

103

Mass General Brigham for Children

Handouts for:
Challenges in Identifying and Managing Anaphylaxis in Infants and Toddlers

Michael Pistiner MD, MMSc
Director of Food Allergy Advocacy, Education and Prevention,
Mass General for Children
Assistant Professor in Pediatrics, Harvard Medical School
Boston, MA

104

Anaphylaxis Practice Parameter 2023 Update: Infant/Toddler Specific Recommendations

#	Method	List of Recommendations: Anaphylaxis in Infants and Toddlers	Strength	Certainty of evidence
8	CBS	We suggest clinician s use current NIAID/FAAN or WAO anaphylaxis criteria to assist in the diagnosis of anaphylaxis in infants/toddlers, because there are no criteria specific to this age group.	conditional	low
9	CBS	We suggest clinicians be aware that, in infants and toddlers, patient age does not correlate with reaction severity.	conditional	Very low
10	CBS	We suggest clinicians be aware that anaphylaxis is unlikely to be the initial reaction to a food or medication on first exposure in infants.	conditional	low
11	CBS	We suggest clinicians be aware that parents of infants and toddlers may report age-specific symptoms that are less often reported by older children and adults.	conditional	Very low
12	CBS	We suggest clinicians prescribe either the 0.1mg or the 0.15mg EAI dose for infants/toddlers weighing less than15kg.	conditional	low

Golden, David B.K. et al. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology. Volume 132, Issue 2, 124 – 176.

105

Anaphylaxis Practice Parameter 2023 Update: Infant/Toddler Relevant Recommendations

#	Method	List of Recommendations: Anaphylaxis in the Community Setting	Strength	Certainty of evidence
16	GRADE	We suggest childcare centers and schools implement staff training for allergy and anaphylaxis management.	Conditional	Very low
18	GRADE	We suggest that childcare centers and schools stock undesignated EAIs that can be used to treat any individual on school grounds who experiences anaphylaxis.	Conditional	Very low

Golden, David B.K. et al. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology. Volume 132, Issue 2, 124 – 176.

106

Anaphylaxis Practice Parameter 2023 Update: Infant/Toddler Relevant Recommendations

#	Method	List of Recommendations: Epinephrine Auto-Injectors: When and How to prescribe	Strength	Certainty of evidence
26	CBS	We suggest that clinicians counsel patients that immediate activation of EMS may not be required if the patient experiences prompt, complete, and durable response to treatment with epinephrine, provided that additional epinephrine and medical care are readily available, if needed. We suggest that clinicians counsel patients to always activate EMS after epinephrine use if anaphylaxis is severe, fails to resolve promptly, fails to resolve completely or nearly completely, or returns or worsens after a first dose of epinephrine.	conditional	Very low
27	CBS	Serious adverse reactions to intramuscular epinephrine are very rare and should not pose a barrier to the prescription or early administration of EAIs when indicated. To manage the risk of adverse events, we recommend that clinicians counsel patients and caregivers on the proper use of EAIs, the common adverse effects, and the need for immediate evaluation and treatment when signs or symptoms of serious adverse events develop.	Strong	Low
28	CBS	We suggest that clinicians discuss the potential financial and psychosocial burdens of EAIs with patients while engaging in shared decision-making.	Conditional	Very low
29	CBS	When deciding which EAI to prescribe, we suggest that clinicians consider dosage, needle length, affordability, access, and patient treatment preferences.	Conditional	Very low
30	CBS	During visits with patients who have been prescribed EAIs, we recommend that clinicians routinely review the essentials of EAI carriage, storage, and use; encourage patients to regularly practice EAI administration with a trainer device; and discuss strategies to manage barriers to adherence that patients may have experienced.	Strong	Low

Golden, David B.K. et al. Anaphylaxis: A 2023 practice parameter update. Annals of Allergy, Asthma & Immunology. Volume 132, Issue 2, 124 – 176.

107

Mass General Brigham for Children

Asthma and Allergy Foundation of America

KIDS WITH FOOD ALLERGIES

TABLE IV. Alternative, age-specific symptoms/signs used in this study to help identify anaphylaxis in infants/toddlers

Language used in current diagnostic criteria*	Language used in AAFA Infant Toddler Anaphylaxis Study
Pruritis	Tongue thrusting, tongue pulling, repetitive lip licking, or licking of hands or objects. Throat itching. Ear pulling, scratching, or putting fingers in the ears. Eye rubbing, eye itching.
Dyspnea	Belly breathing, fast breathing, nasal flaring, chest or neck "tugging"
Stridor	Hoarse voice, hoarse cry. Barky/croup-like cough
Reduced PEF	*(Currently no appropriate and practical way to get FEV1 in this population in acute setting)*
Reduced BP (low systolic BP [age specific] or greater than 30% decrease in systolic BP)	*(Blood pressure in this population can be challenging to acquire and interpret. Hypotension is also a late phase cardiovascular symptom in this age group. Tachycardia may be an earlier vital sign change)* Wobbly appearance, lethargic, floppy, poor head control, difficult to wake up. Crankiness, withdrawn or clingy, inconsolable crying, subdued or less active, limp. Mottling of the skin or blue/grey skin (cyanosis) around mouth/lips or hands/feet
Hypotonia (collapse), syncope	Wobbly appearance, lethargic, floppy, poor head control, difficult to wake up. Crankiness, withdrawn or clingy, inconsolable crying, subdued or less active, limp
Incontinence	*(Can be challenging to differentiate in diaper wearing population)*
Persistent gastrointestinal symptoms	Abdominal pain, diarrhea, hiccups, spitting up, back arching, vomiting

AAFA, Asthma and Allergy Foundation of America; *BP*, blood pressure; *PEF*, peak expiratory flow.
*Clinical criteria for diagnosing anaphylaxis from Sampson et al.

Pistiner M, Mendez-Reyes JE, Iliraki S, Carver M, Lieberman J, Wang J, Camargo Jr CA. Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2020 Nov 18.

https://community.kidswithfoodallergies.org/blog/new-aafa-research-aims-to-improve-diagnosis-and-treatment-of-severe-allergic-reactions-in-infants-and-toddlers

Adapted from Pistiner, Michael, et al. "Caregiver-Reported Presentation of Severe Food-Induced Allergic Reactions in Infants and Toddlers." The Journal of Allergy and Clinical Immunology: In Practice, vol. 9, no. 1, 2021, pp. 311-321.e2.

108

Food Allergy Management and Prevention Support Platform for Infants and Toddlers

FAMP-IT

A free, practical tool for pediatricians and primary care providers to support the prevention and management of food allergies in infants and toddlers.

FAMP-IT.org

FEATURING...

- Up-to-date, evidence-based clinical guidance
- EMR-friendly templates for documentation
- Family-friendly patient education materials
- Infant Food Allergy Prevention Office Hours
- "Test Your Knowledge" quizzes

fampitfamily.org

109

Mass General Brigham for Children

Infant Anaphylaxis: Causes, Symptoms, and Treatment Guide

Free Infant Anaphylaxis Resources from Allergy & Asthma Network

Our new webpage and infographic detail the unique signs and symptoms to watch for in infants and toddlers with anaphylaxis.

VISIT AllergyAsthmaNetwork.org/Anaphylaxis/Infant-Anaphylaxis/

110

Proposed Modified Criteria for Infants and Toddlers

Figure 3. Proposed modified criteria for likely anaphylaxis in infants and toddlers

WOB, work of breathing, BP, blood pressure

Tachycardia: >160 bpm for infants, >150 bpm for 12-35 m.o., >135 bpm for > 36 m.o.

* pruritus of skin-tongue-eyes-ears (i.e., itchy skin, scratching; itchy mouth/tongue, tongue thrusting/pulling, licking lips/hands/objects; itchy eyes, conjunctival injection, rubbing eyes, chemosis, lacrimation; itchy ears, ear tugging, fingers-in-ears)

† swelling of tongue/uvula, drooling, difficulty swallowing)

‡ tachypnea, belly breathing, retractions, nasal flaring

§ decreased capillary refill, cool extremities, weak pulse, mottling, pallor, cyanosis

¶ irritable/crankiness; withdrawn/clingy, less activity without another explanation, obtunded, lethargic, difficult to arouse

wobbly, floppy, limp, poor head control

** knees to chest, back arching, nausea, gagging/retching, hiccups

Handoff A, Roy IR, Cohen A, Camargo Jr CA, Dribin TE, Pistiner M. Development and Evaluation of Modified Criteria for Infant and Toddler Anaphylaxis. The Journal of Allergy and Clinical Immunology: In Practice. 2024 May 20.

Modified Criteria

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg , generalized hives, pruritus*, flushing, **eczema flare**, swollen lips-**ears-eyes-face-extremities**)
and at least one of the following:
   a. Respiratory compromise (eg, **cough**, dyspnea, wheeze-bronchospasm, stridor-**hoarse voice/cry, swollen tongue-uvula**†, **decreased air movement, increased WOB**‡, **respiratory failure,** hypoxemia)
   b. **Cardiovascular symptoms (eg, tachycardia**‡, **decreased perfusion**§, **sudden behavioral/mental status change not attributable to a known cause**¶) or Reduced BP or associated symptoms of **hypotensive shock** (eg. hypotonia # [collapse], syncope, incontinence, **or cardiac arrest)**

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,pruritus*, flushing, **eczema flare**, swollen lips-**ears-eyes-face-extremities)**
   b. Respiratory compromise (eg, **cough** , dyspnea, wheeze - bronchospasm, stridor-**hoarse voice/cry, swollen tongue-uvula**†, **decreased air movement, increased WOB**‡, **respiratory failure,** hypoxemia)
   c. **Cardiovascular symptoms (eg, tachycardia**‡, **decreased perfusion**§, **sudden behavioral/mental status change not attributable to a known cause**¶) or reduced BP or associated symptoms of **hypotensive shock** (eg, hypotonia# [collapse], syncope, incontinence, **or cardiac arrest)**
   d. Significant gastrointestinal symptoms (eg, vomiting,**crampy abdominal pain/discomfort****, **diarrhea)**

3. **Cardiovascular symptoms (eg, tachycardia**‡, **decreased perfusion**§, **sudden behavioral/mental status change not attributable to a known cause**¶) or reduced BP or associated symptoms of **hypotensive shock** (eg, hypotonia# [collapse], syncope, incontinence, **or cardiac arrest)** after exposure to known allergen for that patient (minutes to several hours)
   a. Pediatric: systolic BP < 5th percentile for age or < 2 SD below normal for age or systolic BP < 70 mm Hg from 1 month to 1 year, < (70 mm Hg + [2 × age]) from 1 to 10 years

111

Mass General Brigham for Children

Infant and Toddler Flowsheet Template

- Symptom Flowsheet Recipe for EMR/Database Builds

https://template.famp-it.org

Pyle D, Mendez-Reyes JE, Esteban C, Hazi A, André M, Yep S, Sheffler W, Pistiner M. Flowsheet Template for the Documentation of Allergic Reactions in Infants and Toddlers. The Journal of Allergy and Clinical Immunology: In Practice. 2024 Aug

112