AMPLIFY

Allergy and Anaphylaxis: Follow the Evidence

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Financial Disclosures

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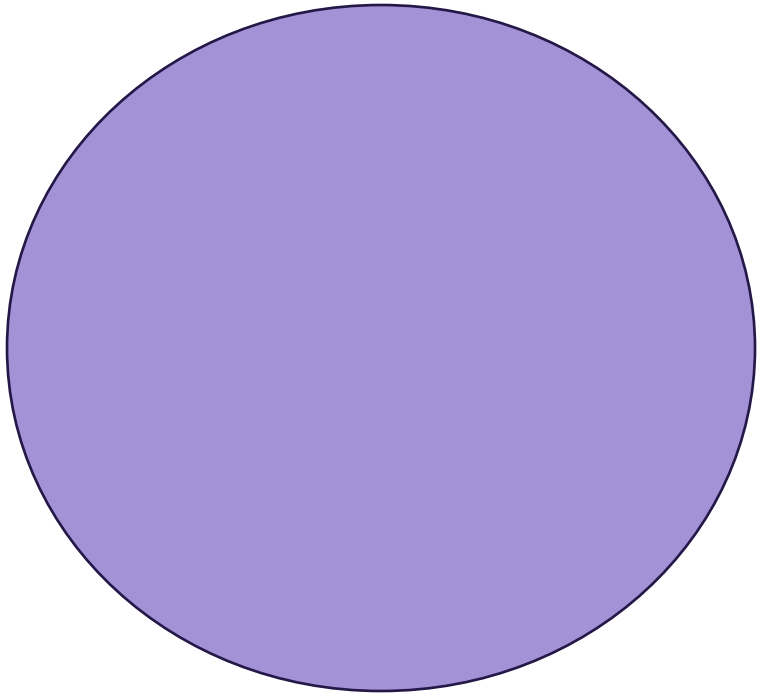
Objectives

- Describe the **range** of allergic reaction, from minor symptoms to anaphylaxis
- Discern the features of **anaphylaxis** among other allergic presentations
- Discuss **evidence-based treatments** for the range of allergic reactions which might be seen in urgent care
- Explain the newest knowledge regarding the risk and benefit of **corticosteroids** in the treatment of allergic reactions
- Determine the **safest dispositions** from urgent care for these patients
- **Strengthen the role of the urgent care clinician** in treating patients with allergic reactions

Just another day at the office……

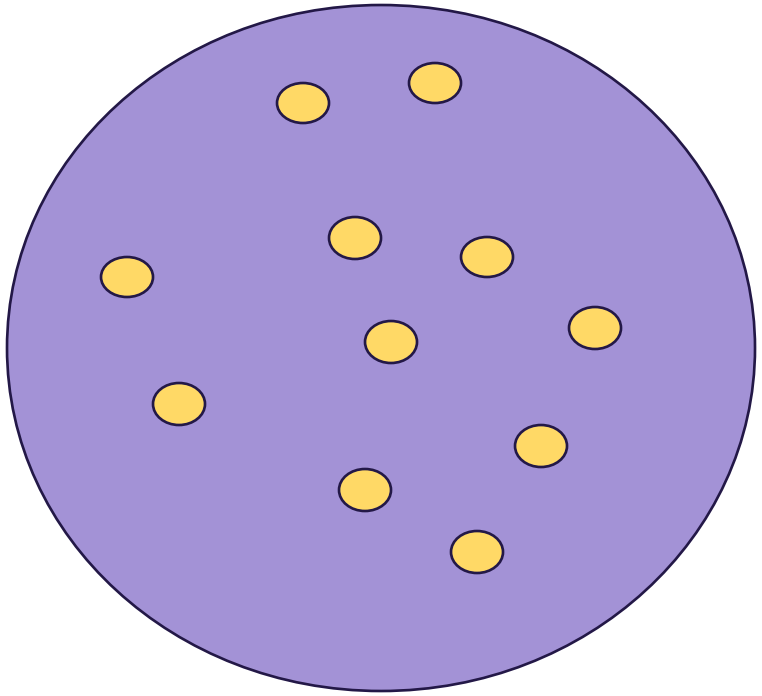
- A mom of 3 children (ages 11, 9, and 7) arrives with them after picking them up from school after being called about them not feeling well. They all have low grade fever, runny noses, cough and one of them has an itchy rash…..
- A 26 year old man with known peanut allergy accidentally took a bite of his girlfriend's PB cookie and has gotten some progressive lower lip swelling and feels some tightness in his throat……
- A 40 year old woman arrived with diffuse skin erythema, complaining of feeling lightheaded. You are called to triage because she just passed out…….

Basic pathophysiology



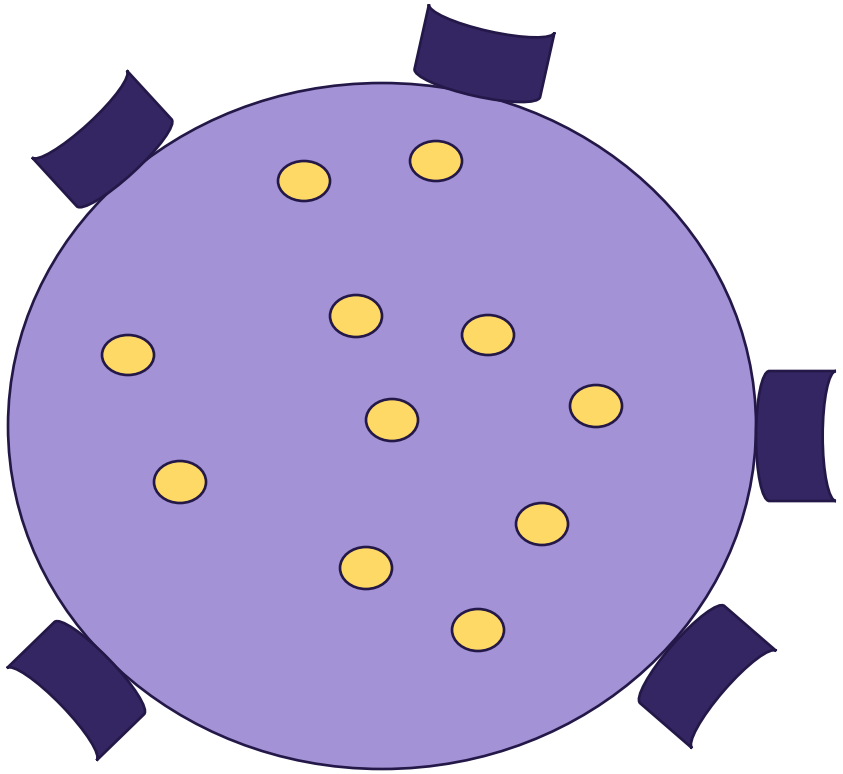
Mast Cell

Basic pathophysiology



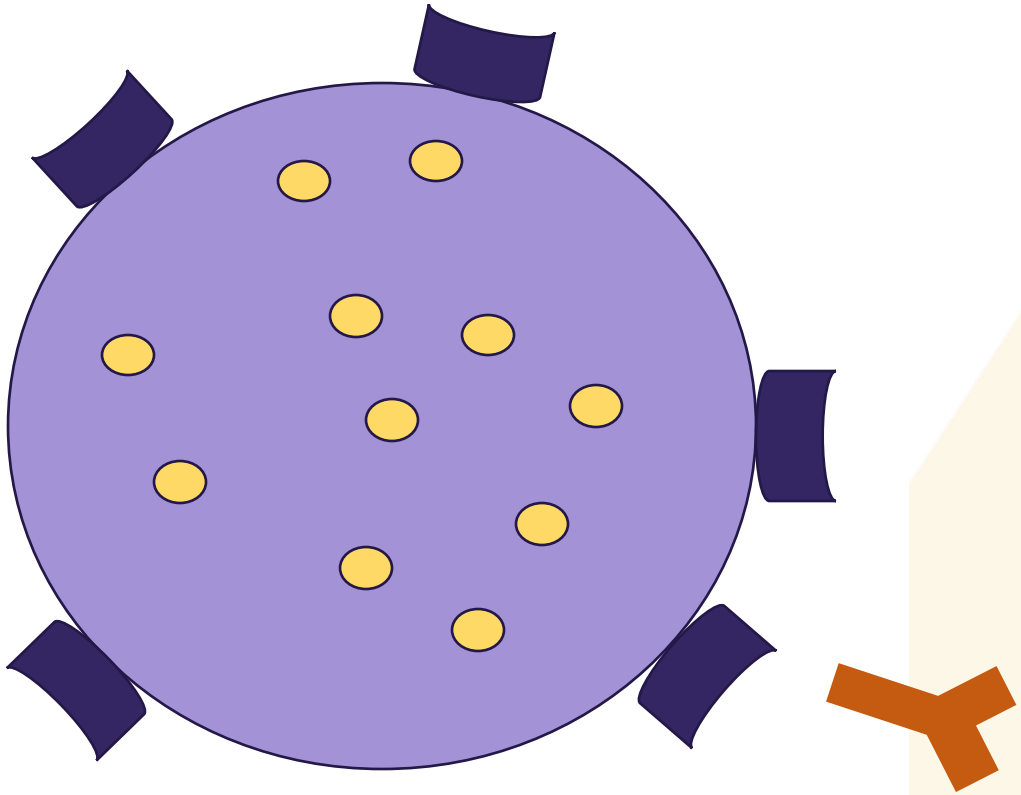
Histamine-containing Lysosomes

Basic pathophysiology



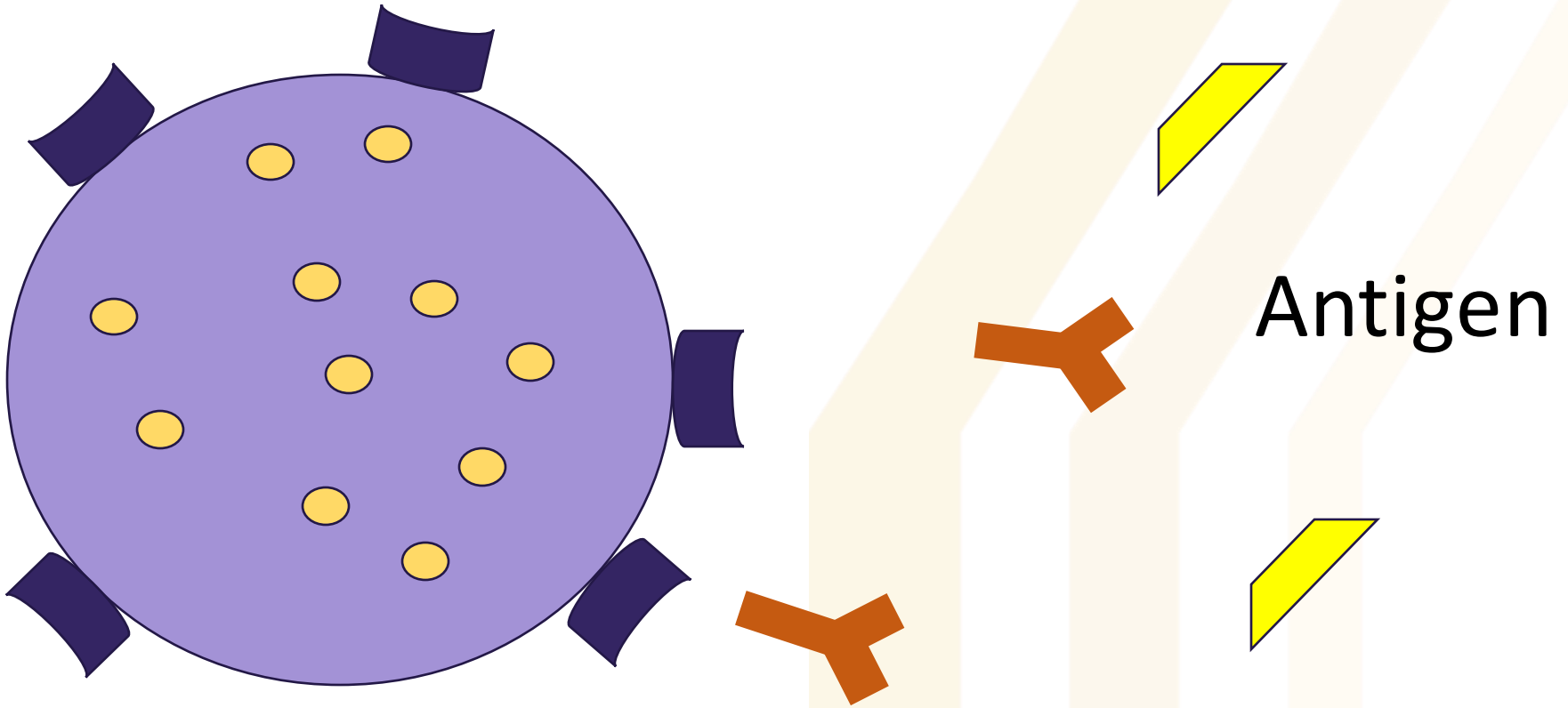
Ig E Receptors

Basic pathophysiology

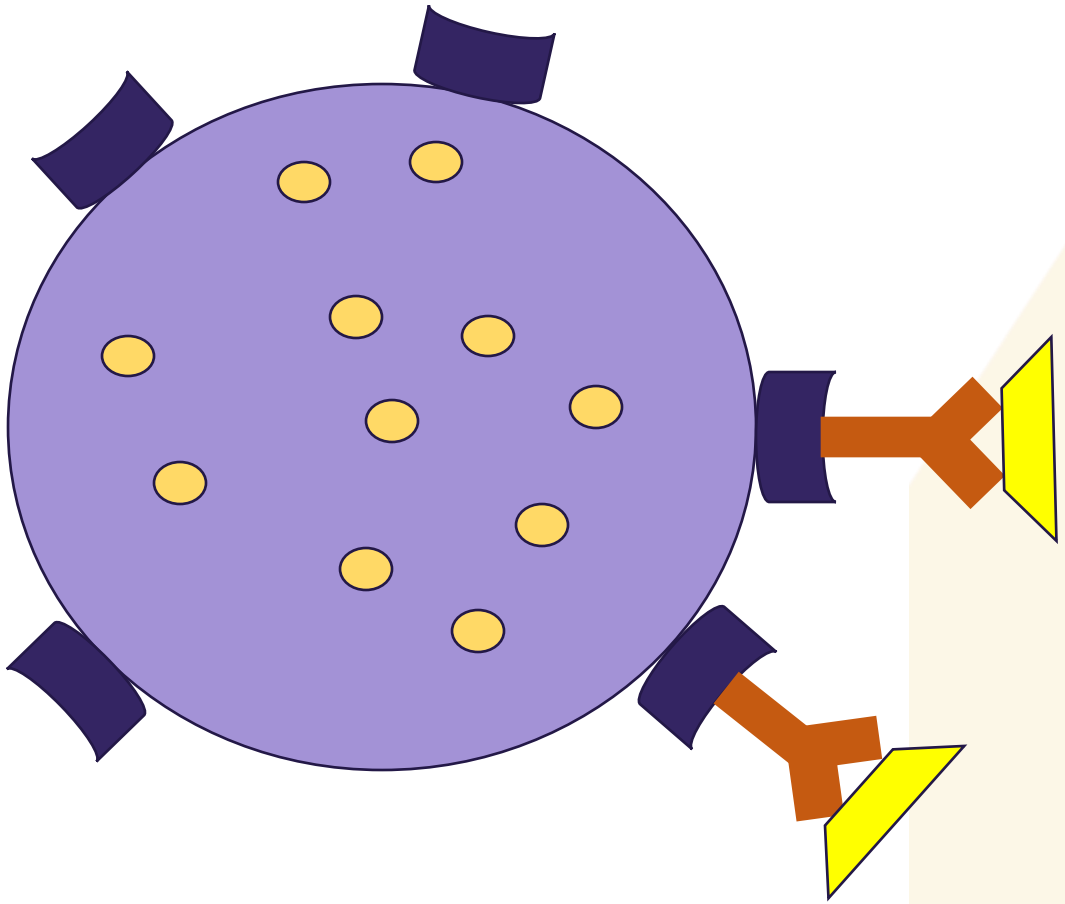


IgE

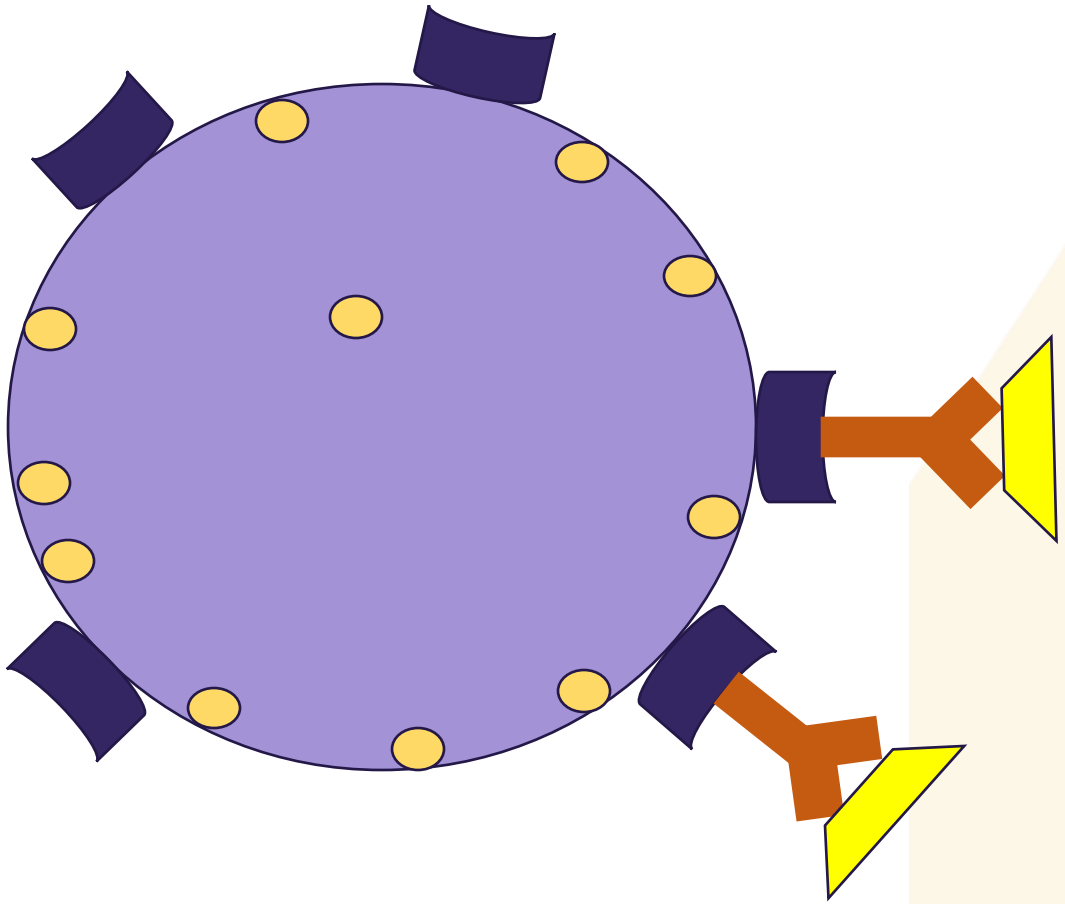
Basic pathophysiology



Basic pathophysiology

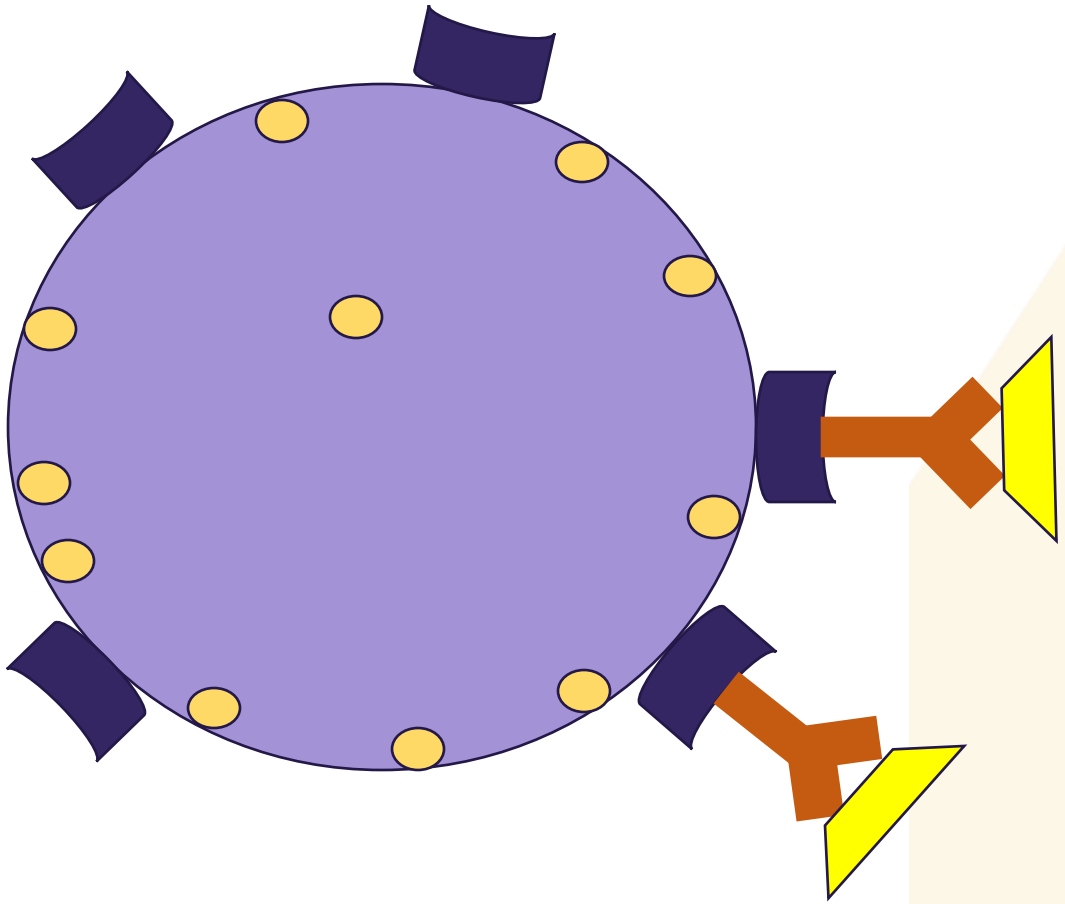


Basic pathophysiology



Degranulation and histamine release

Basic pathophysiology



Degranulation and histamine release

↓

Urticaria
Angioedema
Anaphylaxis

Basic pathophysiology

H1 receptors are located:

- ENT (also H2, H3, H4) and bronchial epithelium
- Smooth muscle and vascular endothelial cells
- Brain and adrenal medulla
- Immune cells (mast, dendritic cells, lymphocytes, neutrophils)

H2 receptors are located:

- Gastric mucosa
- Cardiac muscle and vascular smooth muscle
- Uterus

There are H3 (neuro, respiratory) and H4 (immune) receptors, too!

Basic pathophysiology

- Type I hypersensitivity reactions – Histamine- and IgE-mediated

Basic pathophysiology

- Type I hypersensitivity reactions – Histamine- and IgE-mediated
- Type II – IgG or IgM – transfusion reactions, AIHA, Goodpasture's
- Type III – Ab-Ag complexes – serum sickness, post-Strep GN, SLE
- Type IV – T lymphocytes – poison ivy/oak, PPD reactions, transplant rjx

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- Inflammation and edema
- Superficial – **urticaria/hives**
- Deeper cutaneous/mucosal – **angioedema**
- Skin, facial skin, GI mucosa, airway mucosa
- Vascular and cardiovascular system

Basic pathophysiology

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→ Anaphylaxis

Potential causes of any allergic reaction

- Medication
  - NSAIDs and antibiotics common
- Food
- Hymenoptera and horsefly stings
- Other venoms - sting rays, jelly fish, venomous fish and snakes, fire ants
- IV contrast
- Heat and cold
- Exercise
- Latex

Food intolerance vs food allergy

- Intolerance – gassiness, bloating, abdominal pain, diarrhea
- Hard to tell if there's only GI mucosal angioedema
- Most common allergies:
  - Cow's milk
  - Eggs
  - Soy
  - Wheat
  - Peanuts
  - Tree nuts
  - Sesame seeds
  - Shellfish
  - Other seafood

Source: AMA News Wire. What doctors wish patients knew about food allergies. Feb 20, 2026. Accessed March 3, 2026.

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Source: AMA News Wire. What doctors wish patients knew about food allergies. Feb 20, 2026. Accessed March 3, 2026.

History and Exam

History

- Onset, symptoms, organ systems involved (ROS)
- Prior similar symptoms, diagnosis and any treatment
- Known allergens, recent exposures
- Medications, including beta-blockers, ACE-I's, OTCs
- Comorbidities – RAD, COPD, CHF, CAD
- Recent illness

Exam

- VS, general appearance – general or resp distress, LOC/MS, work of breathing/stridor/ wheezing
- Eyelids/lips/oropharynx
- Lungs
- Skin

Table 2. Red Flags

- Prior severe reaction
- Nut or hymenoptera exposure[1]
- Beta blocker use [2,3]
- Cardiac or pulmonary comorbidities
- Hoarseness
- Swelling of lips, tongue, or uvula
- Respiratory distress
- Hypotension refractory to epinephrine

Sources:

1. Australasian Society of Clinical Immunology and Allergy. ASCIA guidelines for adrenaline autoinjector prescription. Available at: http://www.allergy.org.au/anaphylaxis/epipen_guidelines.htm. Accessed May 17, 2011.
2. Sampson H, Muñoz-Furlong A, Campbell R, et al. 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. *Ann Emerg Med.* 2006;47(4):373-380.
3. Andeae DA, Andreae MH. Should antihistamines be used to treat anaphylaxis? *BMJ.* 2009;339:290-291.

JUCM. June 2011. 9-15

Testing

- **Almost always - none**
- Serum tryptase – recurrent, idiopathic, or severe anaphylaxis, Hymenoptera venom anaphylaxis, or suspected mastocytosis[1]
- Plasma histamine
- Paraprotein
- Complement testing – for angioedema
  - C4
  - C1-q
  - C1-INH antigenic and functional levels

1. Golden DBK, et al *Ann Allergy Asthma Immunol*. 2024 Feb;132(2):124-176.

Clinical presentation - urticaria

Clinical presentation - angioedema

Source: https://dermnetnz.org

Clinical presentation - angioedema

- Stridor
- Difficulty swallowing, drooling
- Wheezing
- Nausea and vomiting
- Abdominal pain
- Diarrhea

Anaphylaxis

WAO 2011 (1)	EAACI 2013 (2)	AAAAI/ACAAI 2010 (11)	ASCIA 2016 (16)	NIAID 2006 (13)	WHO ICD-11 2019 (14)
A serious life-threatening generalized or systemic hypersensitivity reaction.	A severe life-threatening generalized or systemic hypersensitivity reaction.	An acute life-threatening systemic reaction with varied mechanisms, clinical presentations, and severity that results from the sudden release of mediators from mast cells and basophils.	Any acute onset illness with typical skin features (urticarial rash or erythema/flushing, and/or angioedema), PLUS involvement of respiratory and/or cardiovascular and/or persistent severe gastrointestinal symptoms; or Any acute onset of hypotension or bronchospasm or upper airway obstruction where anaphylaxis is considered possible, even if typical skin features are not present.	Anaphylaxis is a serious allergic reaction that involves more than one organ system (for example, skin, respiratory tract, and/or gastrointestinal tract). It can begin very rapidly, and symptoms may be severe or life-threatening.	Anaphylaxis is a severe, life-threatening systemic hypersensitivity reaction characterized by being rapid in onset with potentially life-threatening airway, breathing, or circulatory problems and is usually, although not always, associated with skin and mucosal changes.
A serious allergic reaction that is rapid in onset and might cause death	An acute, potentially fatal, multi-organ system, allergic reaction.				

Table 1. Current definitions of anaphylaxis in the literature. *AAAAI/ACAAI: American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma, and Immunology; ASCIA: Australasian Society of Clinical Immunology and Allergy; EAACI: European Academy of Allergy Asthma and Clinical Immunology; NIAID: National Institute of Allergy and Infectious Diseases; WAO: World Allergy Organization; WHO ICD-11: World Health Organization International Classification of Diseases 11th Edition*

Cardona et al. World Allergy Organization Journal (2020) 13:100472
http://doi.org/10.1016/j.waojou.2020.100472

Anaphylaxis

Anaphylaxis is highly likely when any 1 of the following 2 criteria is fulfilled:

- Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized hives, pruritus or flushing, swollen lips-tongue-uvula) AND AT LEAST ONE OF THE FOLLOWING:
  - Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced peak expiratory flow, hypoxemia)
  - Reduced blood pressure or associated symptoms of end-organ dysfunction (eg, hypotonia , syncope, incontinence)
  - Severe gastrointestinal symptoms (eg, severe crampy abdominal pain, repetitive vomiting), especially after exposure to non-food allergens
- Acute onset of hypotension or bronchospasm or laryngeal involvement after exposure to a known or highly probable allergen for that patient (minutes to several hours), even in the absence of typical skin involvement.

Anaphylaxis definition, overview, and clinical support tool: 2024 consensus report

Study Summary

- A 46-member expert panel developed a consensus anaphylaxis definition, overview, and clinical support tool based on feedback from medical and patient advocacy organizations.
- The outputs are designed to be generalizable to different medical fields and to help standardize research outcomes.

Consensus anaphylaxis definition

93.5% 43/46 Expert Agreement

Anaphylaxis is a serious allergic (hypersensitivity) reaction that can progress rapidly and may cause death. It may involve the skin/mucosa (includes lip/tongue), respiratory (lungs, breathing), cardiovascular (heart, blood pressure), and/or gastrointestinal (stomach/gut) systems. Life-threatening anaphylaxis is characterized by respiratory and/or cardiovascular involvement and may occur without skin/mucosa involvement.

Consensus anaphylaxis overview

97.8% 45/46 Expert Agreement

The overview conveys important anaphylaxis information, including anaphylaxis presentations, distinct infant findings, common allergens, courses, outcomes, pathogenesis, diagnosis, and management.

Anaphylaxis Clinical Support Tool

For Healthcare Professionals

Anaphylaxis is likely when any one of the following three criteria are fulfilled

1. **No Known† Allergen Exposure**
   Sudden onset of an illness (minutes to several hours) with **Skin / Mucosal** involvement AND **either:**
   - **Respiratory** involvement
   - **Cardiovascular** involvement
2. **Likely or Known† Allergen Exposure**
   Sudden onset of **two** or more of the following:
   - **Skin / Mucosal** involvement
   - **Respiratory** involvement
   - **Cardiovascular** involvement
   - Severe **Gastrointestinal** involvement ‡
3. **Known† Allergen Exposure**
   Sudden onset of **either:**
   - **Respiratory** involvement after exposure to a non-inhaled allergen
   - **Cardiovascular** involvement

Intramuscular Epinephrine / Adrenaline*
- Should be given immediately for suspected anaphylaxis
- Can be given for patients that do not yet fulfill the criteria, based on clinical judgement

Administer in the middle third of the anterolateral thigh; repeat every 5-15 minutes if the patient does not respond

Manual
- 0.01 mg/kg = 0.01 mL/kg of 1 mg/mL (1:1000) solution
- Max single dose 0.5 mg

Auto-injectors
- < 13 kg: 0.1 mg or 0.15 mg
- 13 to < 25 kg: 0.15 mg
- ≥ 25 kg: 0.3 mg (≥ 50 kg: 0.3 mg or 0.5 mg)

Anaphylaxis Organ Systems§

Respiratory
wheezing, increased work of breathing¶, hypoxemia, cough, dyspnea
Laryngeal: stridor, voice change
Infants may also have a hoarse cry

Skin
urticaria, flushing, erythema, facial swelling
Infants may also have mottling

Cardiovascular
hypotension, syncope, dizziness, unexplained change in mental status
Infants may also have persistent unexplained tachycardia

Mucosal
lip, tongue, or oropharyngeal swelling, severe throat tightness, difficulty swallowing
Infants may also have repetitive lip licking

Gastrointestinal
severe crampy abdominal pain, repetitive vomiting, diarrhea

Clinical support tool

Expert Agreement 93.5% 43/46

New clinical criteria to help determine the likelihood that patients are having anaphylaxis.

Intramuscular epinephrine / adrenaline indications and dosing.

Common findings from the anaphylaxis organ systems.

Source: Dribin TE et al. *J Allergy Clin Immunol*. 2025 Aug;156(2):406-417.e6. doi: 10.1016/j.jaci.2025.01.021

Anaphylaxis

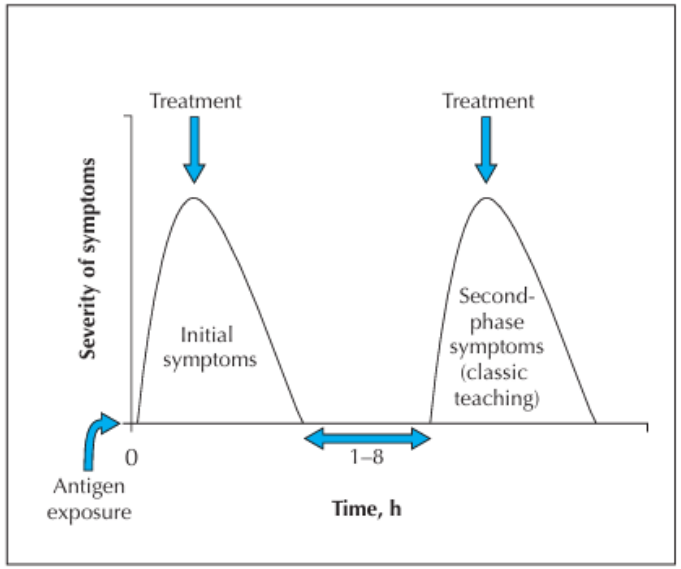
- Potentially life-threatening
  - 1% risk of death
  - ~ 500-1000 deaths in US annually
- Lifetime prevalence of anaphylaxis – 2-5%
- Treatment errors stem from lack of recognition and lack of use of epinephrine
- Think “epi, epi, epi”

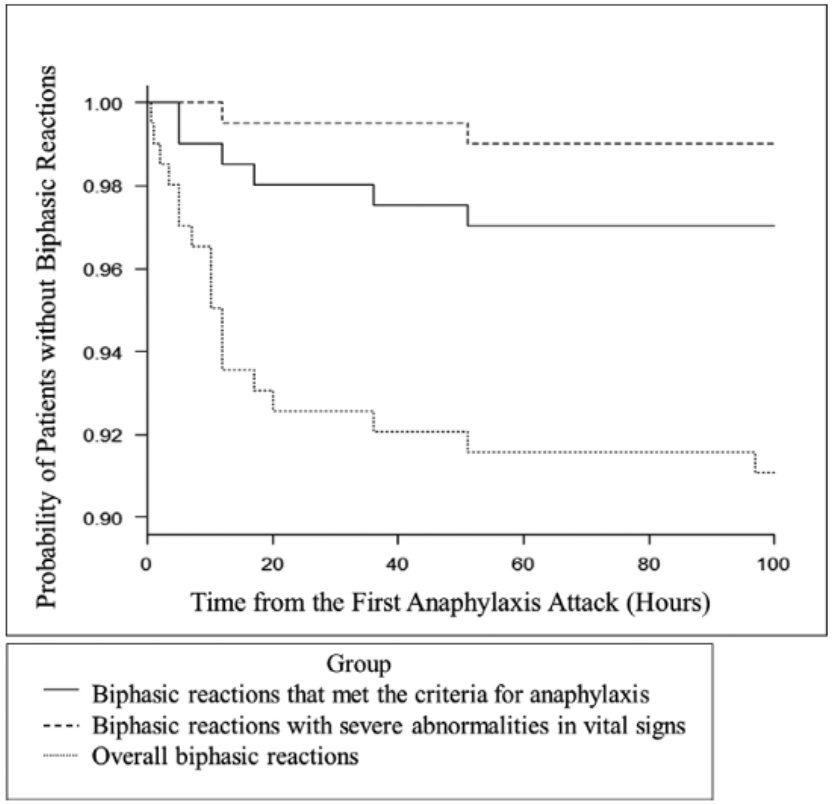
Anaphylactoid reaction?

- Looks like anaphylaxis; pathophysiology is similar
- Can occur after first exposure to what seems like it could be a potential allergen
- More common with:
  - Radiocontrast dye
  - NSAIDs
  - Opioids
  - Certain antibiotics
  - Dextran
- Risk factors – prior anaphylaxis or anaphylactoid reaction
- World Allergy Organization has recommended not using the term
- Treatment is the same.

Biphasic allergic reaction[1,2]

- Occurs in 1.4% – 20% of cases
- Classically 1-8 hour delay (reports of up to 24-38 hrs)
- Second reaction may be more severe than the first

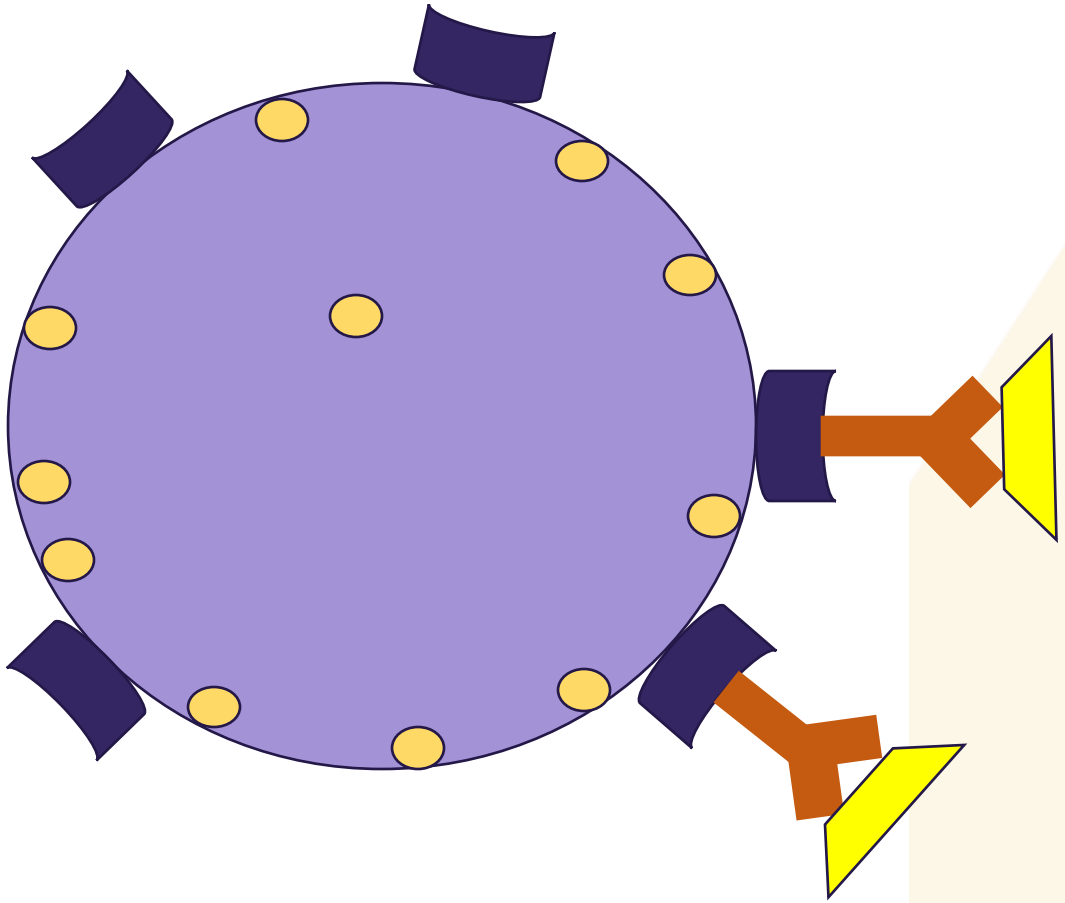




1. CMAJ. Aug 19, 2023. p 308

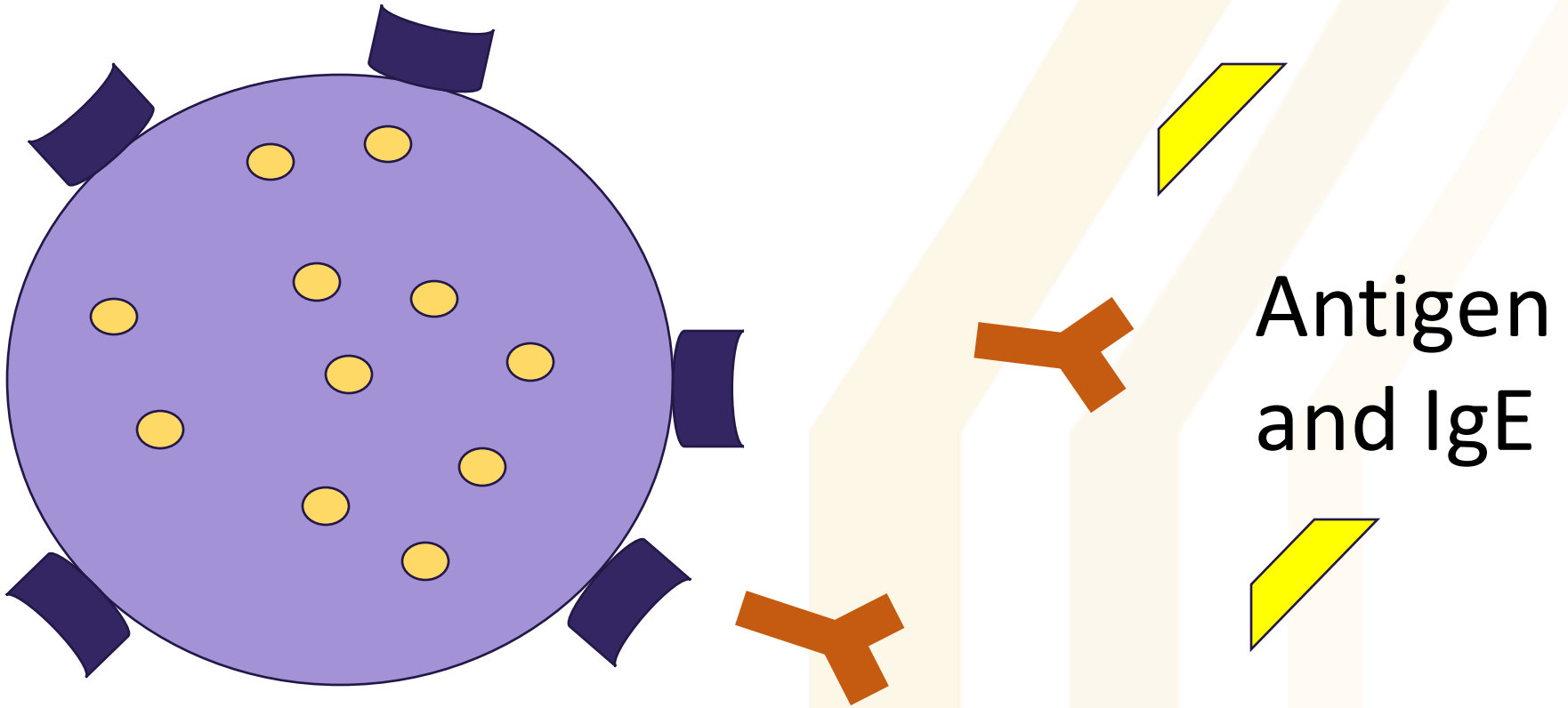
2. *Acute Med Surg*. 2021 Jul 30;8(1):e689. p 6

Initial allergic reaction

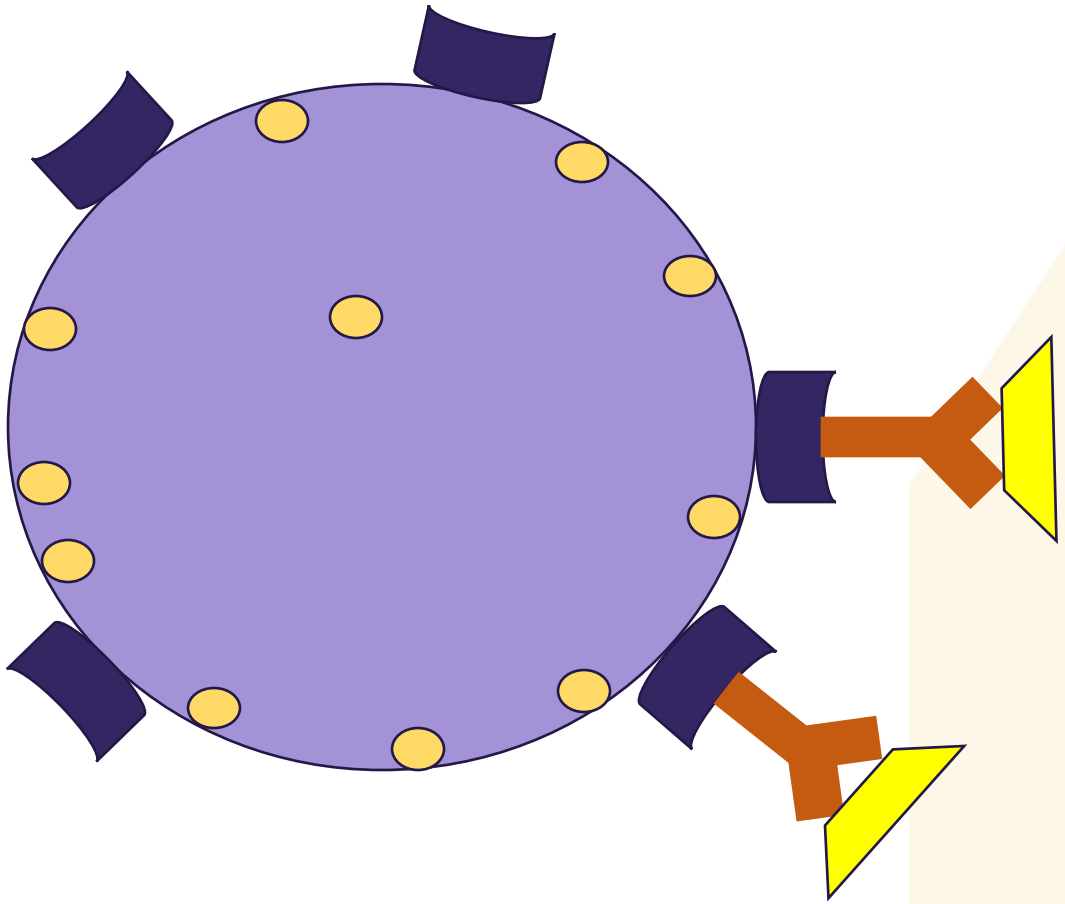


Degranulation and histamine release

Quiescent period



Biphasic allergic reaction



Recurrent degranulation and histamine release

Differential Diagnosis - urticaria/angioedema

- Nonallergic urticaria
  - Viral and other infections
- Nonallergic angioedema
  - Types I, II and III Hereditary Angioedema
  - ACE-inhibitor-mediated angioedema
  - Other medications: gliptins, ARBs, sirolimus and similar meds
- Asthma/COPD exacerbation
- Chronic/“idiopathic” urticaria and angioedema
- Other causes of localized edema – infection, venous obstruction

Differential Diagnosis - dermatologic

Differential Diagnosis - dermatologic

Differential Diagnosis - anaphylaxis

- Other causes of respiratory distress and distributive shock
- Other causes of hypotension/syncope
- Asthma/COPD exacerbation
- Pheochromocytoma
- Carcinoid syndrome
- Mastocytosis
- Scombroidosis, MSG reaction

Treatment - Antihistamines

“H1” antihistamines

- Lots of evidence in urticaria and angioedema, much less in anaphylaxis
- First generation
  - Chlorpheniramine, diphenhydramine (25-50mg q6-8h), hydroxyzine (25-200 mg qHS)
- Second generation
  - Cetirizine (5-10mg qD), fexofenadine (180 mg qD or 60mg BID), loratadine (10mg qD or 5mg BID)
- Third generation
  - Desloratadine (5mg qD), levocetirizine (5mg qD)

H2 antihistamines - little evidence except in urticaria

- Famotidine (20mg BID), cimetidine (200 mg BID), ~~ranitidine~~

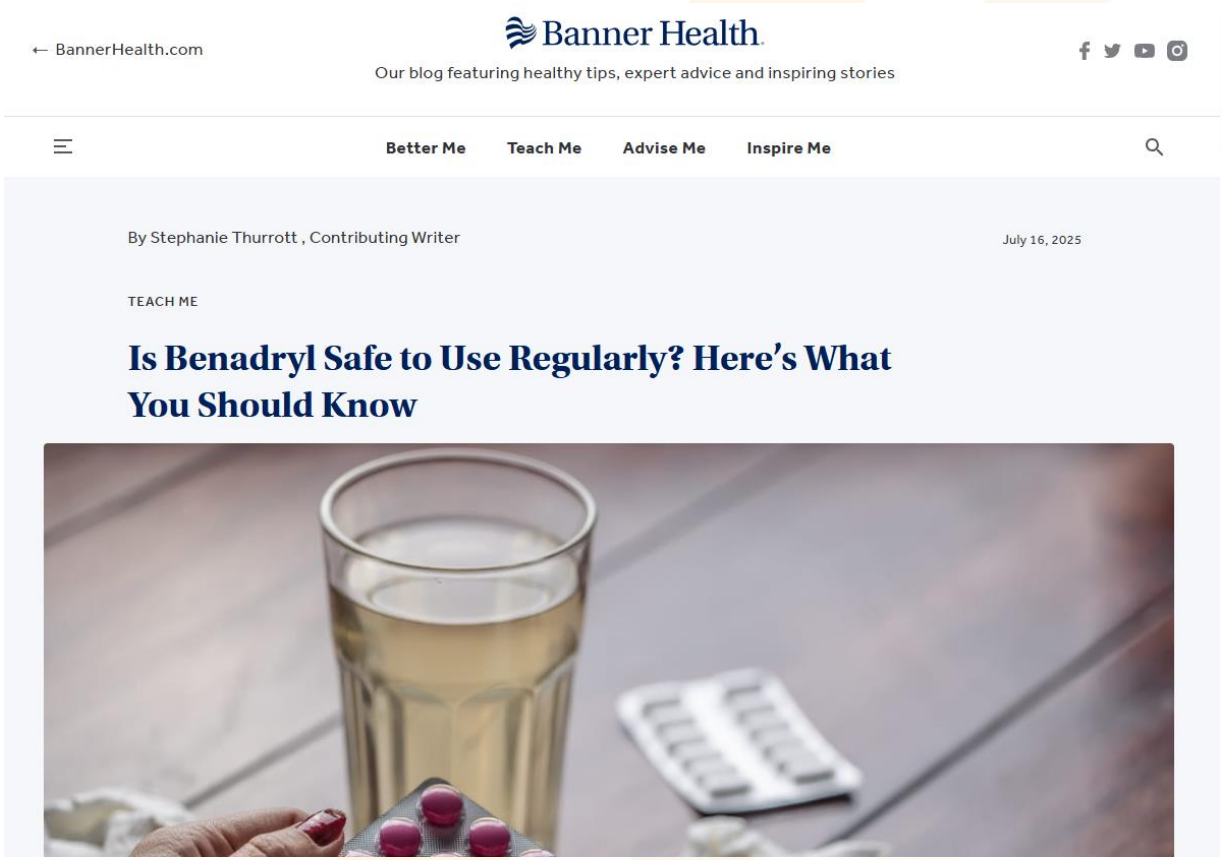
Treatment - Antihistamines

- All are available PO
- Most are available in pediatric formulations – chewable, elixirs, ODTs
- Peds dosing applies – have a reference handy
- Data from treating chronic urticaria indicates higher doses (up to 4x) can be given safely[1]
- Parenteral options in US
  - diphenhydramine - IV or IM
  - hydroxyzine - IM only
  - cetirizine - IV only

1. van den Elzen et al. *Clin Transl Allergy*. 2017 Feb 14:7:4.

The buzz with diphenhydramine

https://www.acepnow.com/article/the-death-of-diphenhydramine/



https://www.bannerhealth.com/healthcareblog/teach-me/is-benadryl-safe-to-use-regularly-here-is-what-you-should-know

The buzz with diphenhydramine

verywell health

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5 Serious Side Effects of Benadryl

By Stephanie Brown | Updated on December 15, 2025

Medically reviewed by Patricia Mikula, PharmD

Key Takeaways

- Benadryl can cause drowsiness and should not be used when driving.
- Taking large doses of Benadryl can lead to serious health issues like cardiac arrest and death.
- People with glaucoma should talk to a doctor before using Benadryl because it can cause vision problems.

Benadryl (diphenhydramine), an antihistamine used to relieve allergy and cold symptoms, can cause some serious side effects, especially when taken incorrectly.

A new review published in the *World Allergy Organization Journal* urges a reevaluation of the drug's safety, arguing its risks now outweigh its benefits. [1]

https://www.verywellhealth.com/benadryl-side-effects-review-11786255

Clark, Meltzer, Naclerio World Allergy Organization Journal (2025) 18:101027
http://doi.org/10.1016/j.waojou.2025.101027

WORLD ALLERGY ORGANIZATION JOURNAL

REVIEW Open Access

Diphenhydramine: It is time to say a final goodbye

James H. Clark,MD[a]*, Eli O. Meltzer,MD[b] and Robert M. Naclerio,MD[a]

ABSTRACT

Diphenhydramine, once a pioneering antihistamine, is now overshadowed by second-generation antihistamines with similar efficacy and fewer adverse effects. Current data suggest that the adverse side-effect profile of diphenhydramine is higher among children and older adults. This has led to countries such as Germany and Sweden restricting access to first-generation antihistamines and societal guidelines advocating for the use of second-generation antihistamines. Despite its well-documented problematic therapeutic ratio, diphenhydramine remains available in over 300 formulations, most of which are over-the-counter.

Based on a comprehensive evaluation of practice patterns and the prevalence and incidence of adverse clinical events, we believe that diphenhydramine has reached the end of its life cycle, and in its class of therapies it is a relatively greater public health hazard. We recommend it should no longer be widely prescribed or continue to be readily available over the counter.

Keywords: Diphenhydramine, Histamine H1 antagonists, Antihistamines, Second-generation

INTRODUCTION

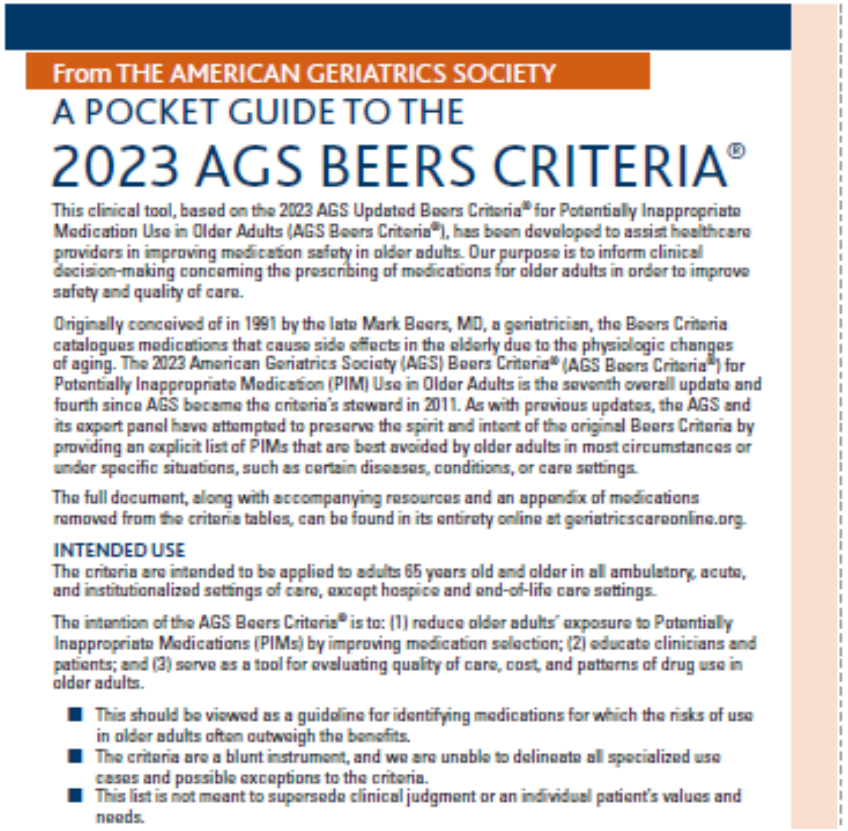
Similar to humans, medications have natural life cycles. They are discovered and researched with the hope of providing effective interventions for the underlying causes and symptoms of specific diseases. Over time, as a medicine's usage grows, its indications may be expanded, and its safety

is a relatively greater public health hazard. We recommend it should no longer be widely prescribed or continue to be readily available over the counter.

PREVALENCE AND USE OF DIPHENHYDRAMINE

https://www.worldallergyorganizationjournal.org/action/showPdf?pii=S1939-4551%2825%2900002-X

Beers' Criteria – Amer Geriatric Society



From THE AMERICAN GERIATRICS SOCIETY

A POCKET GUIDE TO THE

2023 AGS BEERS CRITERIA®

This clinical tool, based on the 2023 AGS Updated Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults (AGS Beers Criteria®), has been developed to assist healthcare providers in improving medication safety in older adults. Our purpose is to inform clinical decision-making concerning the prescribing of medications for older adults in order to improve safety and quality of care.

Originally conceived of in 1991 by the late Mark Beers, MD, a geriatrician, the Beers Criteria catalogues medications that cause side effects in the elderly due to the physiologic changes of aging. The 2023 American Geriatrics Society (AGS) Beers Criteria® (AGS Beers Criteria®) for Potentially Inappropriate Medication (PIM) Use in Older Adults is the seventh overall update and fourth since AGS became the criteria's steward in 2011. As with previous updates, the AGS and its expert panel have attempted to preserve the spirit and intent of the original Beers Criteria by providing an explicit list of PIMs that are best avoided by older adults in most circumstances or under specific situations, such as certain diseases, conditions, or care settings.

The full document, along with accompanying resources and an appendix of medications removed from the criteria tables, can be found in its entirety online at geriatricscareonline.org.

INTENDED USE

The criteria are intended to be applied to adults 65 years old and older in all ambulatory, acute, and institutionalized settings of care, except hospice and end-of-life care settings.

The intention of the AGS Beers Criteria® is to: (1) reduce older adults' exposure to Potentially Inappropriate Medications (PIMs) by improving medication selection; (2) educate clinicians and patients; and (3) serve as a tool for evaluating quality of care, cost, and patterns of drug use in older adults.

- This should be viewed as a guideline for identifying medications for which the risks of use in older adults often outweigh the benefits.
- The criteria are a blunt instrument, and we are unable to delineate all specialized use cases and possible exceptions to the criteria.
- This list is not meant to supersede clinical judgment or an individual patient's values and needs.

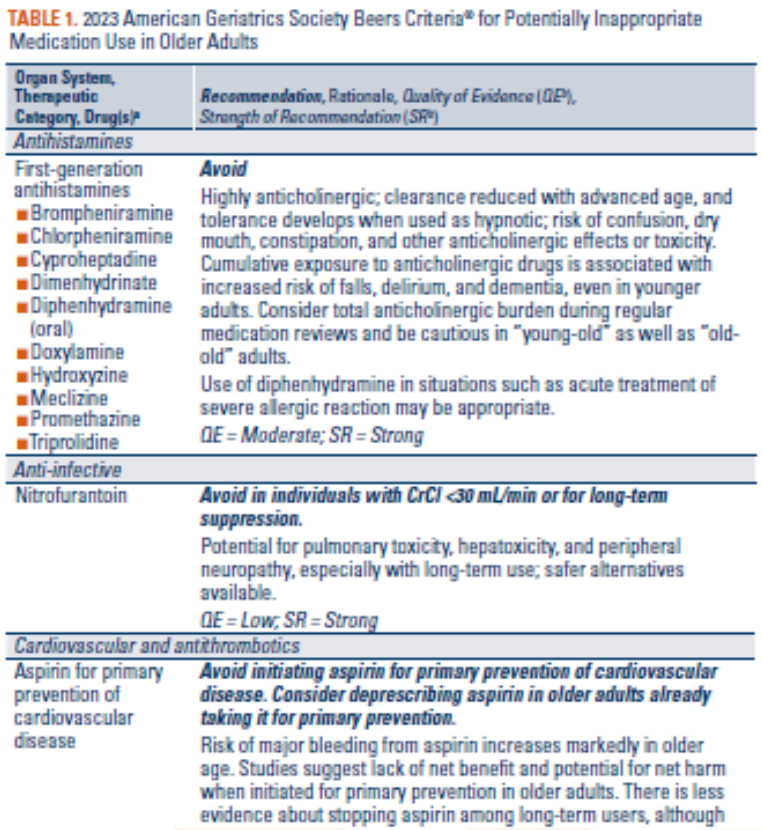
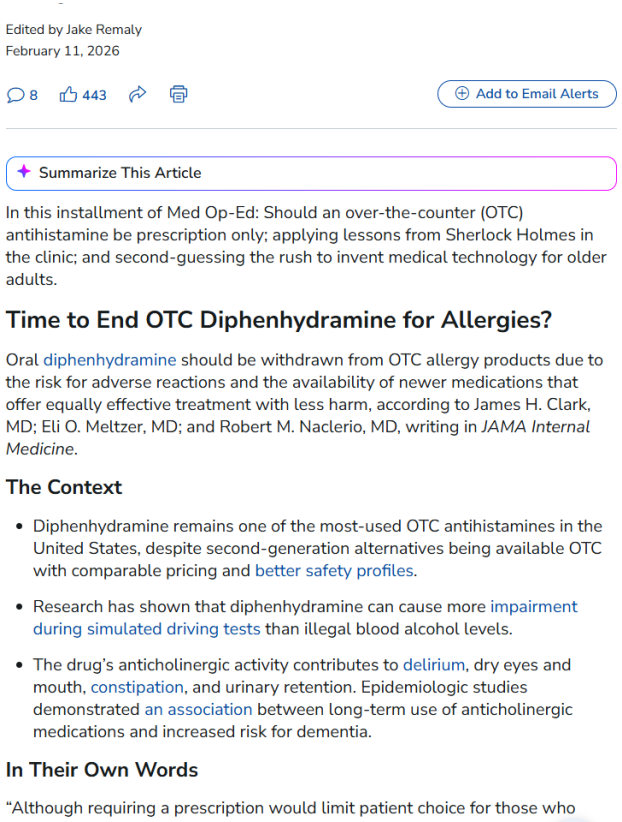


TABLE 1. 2023 American Geriatrics Society Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults

Organ System, Therapeutic Category, Drug(s)[a]	*Recommendation*, Rationale, *Quality of Evidence (QE)*, *Strength of Recommendation (SR)*
Antihistamines	
First-generation antihistamines ■ Brompheniramine ■ Chlorpheniramine ■ Cyproheptadine ■ Dimenhydrinate ■ Diphenhydramine (oral) ■ Doxylamine ■ Hydroxyzine ■ Meclizine ■ Promethazine ■ Triprolidine	***Avoid*** Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; risk of confusion, dry mouth, constipation, and other anticholinergic effects or toxicity. Cumulative exposure to anticholinergic drugs is associated with increased risk of falls, delirium, and dementia, even in younger adults. Consider total anticholinergic burden during regular medication reviews and be cautious in "young-old" as well as "old-old" adults. Use of diphenhydramine in situations such as acute treatment of severe allergic reaction may be appropriate. *QE = Moderate; SR = Strong*
Anti-infective	
Nitrofurantoin	***Avoid in individuals with CrCl <30 mL/min or for long-term suppression.*** Potential for pulmonary toxicity, hepatoxicity, and peripheral neuropathy, especially with long-term use; safer alternatives available. *QE = Low; SR = Strong*
Cardiovascular and antithrombotics	
Aspirin for primary prevention of cardiovascular disease	***Avoid initiating aspirin for primary prevention of cardiovascular disease. Consider deprescribing aspirin in older adults already taking it for primary prevention.*** Risk of major bleeding from aspirin increases markedly in older age. Studies suggest lack of net benefit and potential for net harm when initiated for primary prevention in older adults. There is less evidence about stopping aspirin among long-term users, although

https://thecarepartnerproject.org/wp-content/uploads/The-Beers-List.pdf

The buzz with diphenhydramine



Edited by Jake Remaly
February 11, 2026

8 443 Add to Email Alerts

Summarize This Article

In this installment of Med Op-Ed: Should an over-the-counter (OTC) antihistamine be prescription only; applying lessons from Sherlock Holmes in the clinic; and second-guessing the rush to invent medical technology for older adults.

Time to End OTC Diphenhydramine for Allergies?

Oral diphenhydramine should be withdrawn from OTC allergy products due to the risk for adverse reactions and the availability of newer medications that offer equally effective treatment with less harm, according to James H. Clark, MD; Eli O. Meltzer, MD; and Robert M. Naclerio, MD, writing in *JAMA Internal Medicine*.

The Context

- Diphenhydramine remains one of the most-used OTC antihistamines in the United States, despite second-generation alternatives being available OTC with comparable pricing and better safety profiles.
- Research has shown that diphenhydramine can cause more impairment during simulated driving tests than illegal blood alcohol levels.
- The drug's anticholinergic activity contributes to delirium, dry eyes and mouth, constipation, and urinary retention. Epidemiologic studies demonstrated an association between long-term use of anticholinergic medications and increased risk for dementia.

In Their Own Words

"Although requiring a prescription would limit patient choice for those who

https://www.medscape.com/viewarticle/med-op-ed-otc-drug-flagged-sherlockian-diagnosis-and-more-2026a10004cn

Slashing the Use of Harmful Antihistamines in Pediatric Patients

Brittany Vargas
February 13, 2026

9 520 Add to Email Alerts

Summarize This Article

First-generation oral antihistamines long entrenched in pediatric care can be displaced with the safer alternative cetirizine through relatively simple system changes, according to new research published in *Pediatrics*.

Despite long-standing safety concerns, first-generation antihistamines such as diphenhydramine remain common in pediatric settings, even though second-generation agents are recommended as first-line therapy. The findings suggest that overuse of older, more sedating antihistamines may be less a matter of clinical necessity than of habit and system design.

"Health systems should strongly consider the use of quality improvement methodology to reduce the use of first-generation antihistamines in favor of second-generation antihistamines [SGAs]," said Katelyn Wong, MD, assistant professor in the Department of Pediatric Pulmonology, Allergy, Immunology and Sleep Medicine at the Yale School of Medicine in New Haven, Connecticut, who led the study. "These interventions are applicable to various clinical settings as they are not overly time- or resource-intensive."

Fast Five Quiz: Secondary Stroke Prevention What do you know about antithrombotic therapy & risk factor modification? *Test Your Knowledge*

https://www.medscape.com/viewarticle/slashing-use-harmful-antihistamines-pediatric-patients-2026a10004lj

Antihistamines – what to do……

- Pharmacokinetics – shorter acting, but faster onset of first (30-60 m) vs later generation (1-3 h)
- Begin to get experience using the second- and third-gen medications
- Talk to patients about it
- *Slater et al. 1999* – "For urticaria, cetirizine and mizolastine demonstrate superior suppression of wheal and flare at the dosages recommended by the manufacturer."
- Devillier et al. 2008 – "Based on these pharmacological characteristics, as well as clinical endpoints such as symptom scores, quality-of-life surveys, inflammatory cell counts and investigators' global evaluations, we conclude that desloratadine, fexofenadine and levocetirizine are all efficacious treatments for AR and CIU. However, differences among the antihistamines in relation to a lack of significant interaction with drug transporter molecules and somnolence in excess of placebo may provide some advantages for the overall profile of desloratadine compared with fexofenadine and levocetirizine."
- Watch for more developments and recommendations

Antihistamines – other nuances

- Lowest approved age differs between meds and, sometimes, indications
  - 6 mos and older: cetirizine, desloratadine, levocetirizine
  - 2 years and older: loratadine, fexofenadine (6 mos for CIU), diphenhydramine
- Package dosing for many tablet forms: “Consult a physician” for ≤ 6yo
- Have a ready pediatric medication reference
- Pregnancy “category” - allergies occur in 20-30% of women during pregnancy[1]
  - B = diphenhydramine, cetirizine, loratadine, levocetirizine[1]
  - C = hydroxyzine, desloratadine, fexofenadine[1]
  - **Always weigh risk and benefit**
- Lactation – cetirizine and loratadine preferred (www.sps.nhs.uk and www.breastfeedingnetwork.org.uk)

1. Kar S, et al. J Pharmacol Pharmacother. 2012 Apr-Jun;3(2):105–108

Treatment - epinephrine

- IM and consider inhaled (racemic)
- Alpha and Beta-adrenergic receptor agonist – heart, airway, blood vessels, other tissues
- Consider glucagon if no effect and patient takes beta-blocker
- Stabilizes mast cells
- Dose: 0.01 mg/kg, max dose 0.5 mg for adult; **repeat q 5-10 mins, if/as needed**
  - 0.1 mg (or 0.15mg autoinjector) for those < 15kg[1]
  - 1-5 years old - fixed/max dose 0.15 mg
  - 6-12 years old – fixed/max dose 0.3 mg
- Doses of 0.5 mg less likely to lead to escalation of care than 0.3 mg (*Jackson, et al, 2025*)
- Have a plan for quick administration in the UC

1. Golden DBK, et al *Ann Allergy Asthma Immunol*. 2024 Feb;132(2):124-176.

Treatment - epinephrine

- Many identified patient and clinician barriers → delay, underuse, nonuse
  - Fear, lack of experience, lack of recognition of anaphylaxis
  - Not having the medication available, needing someone's help
  - Stigma, cost/insurance, expiration
- Alternative to IM – intranasal
  - Approved summer 2024
  - 2 mg/0.1 ml spray into one nostril; one spray per device
  - May repeat in 5 minutes in same nostril
  - OK in children down to 30 kg bodyweight
- Sublingual epi is in Phase 3 trials

What's the scoop with corticosteroids?

- Waljee, et al. *BMJ* 2017;357:j1415. http://dx.doi.org/10.1136/bmj.j1415
- 2022: https://urgentcareassociation.org/uca-cucm-position-on-corticosteroid-stewardship/
- Alqurashi and Ellis, 2017 – review of 31 studies – "Because of the potential detrimental adverse effects of corticosteroids and lack of compelling evidence demonstrating an effective role in reducing anaphylaxis severity or preventing biphasic anaphylaxis, we do not advocate for their routine use in anaphylaxis."
- GA^{2}LEN 2024 – list corticosteroids as adjunct – comment period "…the role of and evidence for use of corticosteroids is anaphylaxis is very limited. I would be in favor of caveating the corticosteroid mention - perhaps - limited evidence for the effectiveness of corticosteroids in the management of anaphylaxis outside biphasic and refractory anaphylaxis."

What's the scoop with corticosteroids?

Glucocorticosteroids are commonly used in anaphylaxis, with the objective of preventing protracted symptoms, in particular in patients with asthmatic symptoms, and also to prevent biphasic reactions (eg, intravenous hydrocortisone, or methylprednisolone). However, there is increasing evidence that glucocorticosteroids may be of no benefit in the acute management of anaphylaxis, and may even be harmful; their routine use is becoming controversial.[86,96-100]

Cardona et al. World Allergy Organization Journal (2020) 13:100472
http://doi.org/10.1016/j.waojou.2020.100472

Putting it all together……

Treatment – urticaria

- ABCs, remove allergen if still present
- Observe for worsening/anaphylaxis
- Antihistamines – H1 and H2
- Corticosteroids?

Treatment – urticaria

- ABCs, remove allergen if still present
- Observe for worsening/anaphylaxis
- Antihistamines – H1 and H2
- Corticosteroids – only for truly refractory cases

Treatment – angioedema

- ABCs, remove allergen if still present
- Observe for worsening/anaphylaxis
- Epinephrine IM if airway in jeopardy, stridor, wheezing
- Consider inhaled racemic epi, as well, for visible or symptomatic airway edema (*Stone et al, 2018*)
- Bronchodilators for wheezing
- Antihistamines – H1 and H2
- Corticosteroids – for RAD/wheezing or truly refractory or severe cases
- Keep head elevated
- Observation period?

Treatment – anaphylaxis

- ABCs, remove allergen if still present
- Observe for worsening/anaphylaxis
- Epinephrine IM if airway in jeopardy, stridor, wheezing
- Consider inhaled racemic epi, as well, for visible or symptomatic airway edema (*Stone et al, 2018*)
- Bronchodilators for wheezing
- If possible, IV crystalloid for hypotension, poor perfusion
- Antihistamines – H1 and H2
- Corticosteroids – for RAD/wheezing or truly refractory or severe cases

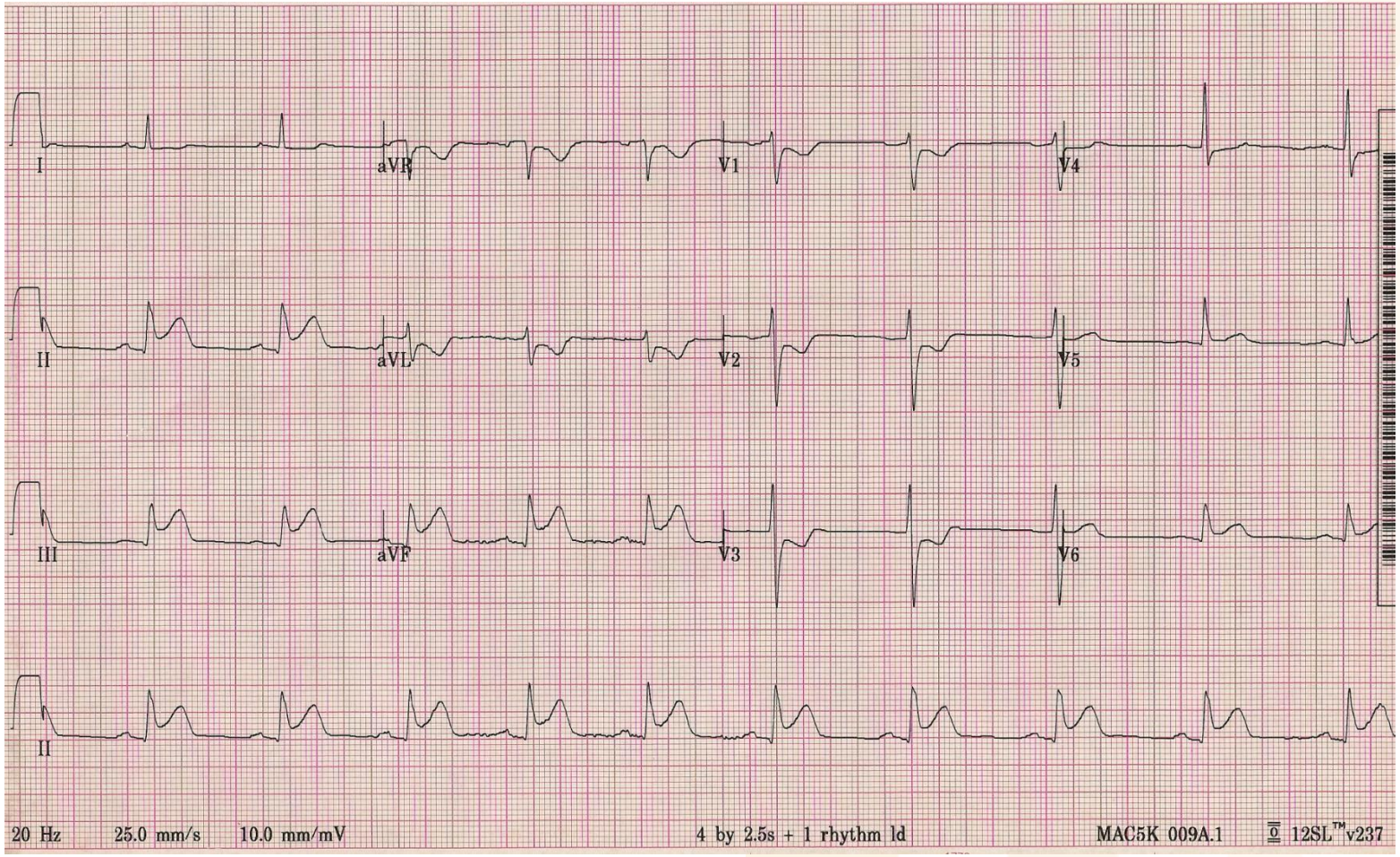
Treatment – Activate EMS?

- Activate EMS for abnormal or unstable VS, critical airway or respiratory issues, worsening course, LOC, syncope, cyanosis, true voice change, other severe reaction, if second dose of epi needed
- *Golden DBK, et al, 2023* – no need for patients to activate EMS or go to the hospital if there is a "prompt, complete, and durable response" to the first dose….biphasic anaphylaxis is unlikely if anaphylaxis is not severe and the patient remains symptom-free for one hour of observation following resolution."
- *Dribin, et al 2025 (7717 pts, 30 EDs, retrospective, 6 mos to 17yo)* – 2 hour obs is "probably safe" after epi; 4 hours in those with CV involvement who appear well (time = time from first/only epi dose)
- *Dribin et al 2026 (expert consensus/Delphi method*) – affirmed *Golden DBK, et al, 2023* stay home (*if caregiver and second epi dose available, < 30 mins to nearest hospital*) and *Dribin et al 2025* ≤ 2 hour obs if in medical setting

Disposition/Discharge plan

- Observe for improvement/lack of worsening
- Home - urticaria, angioedema without life-threat, anaphylaxis (1-2 hr)?
- Avoid known/suspected allergens
- Continue H1 and H2 blockers for several days
- Rx: 2 or more epi autoinjectors (0.1 mg, 0.15 mg or 0.3 mg) vs. nasal
- Discuss return precautions – call 911
- Recommend allergist referral for idiopathic, severe, recurrent, refractory cases
- +/- Corticosteroids – not never, <u>but NOT routinely</u>

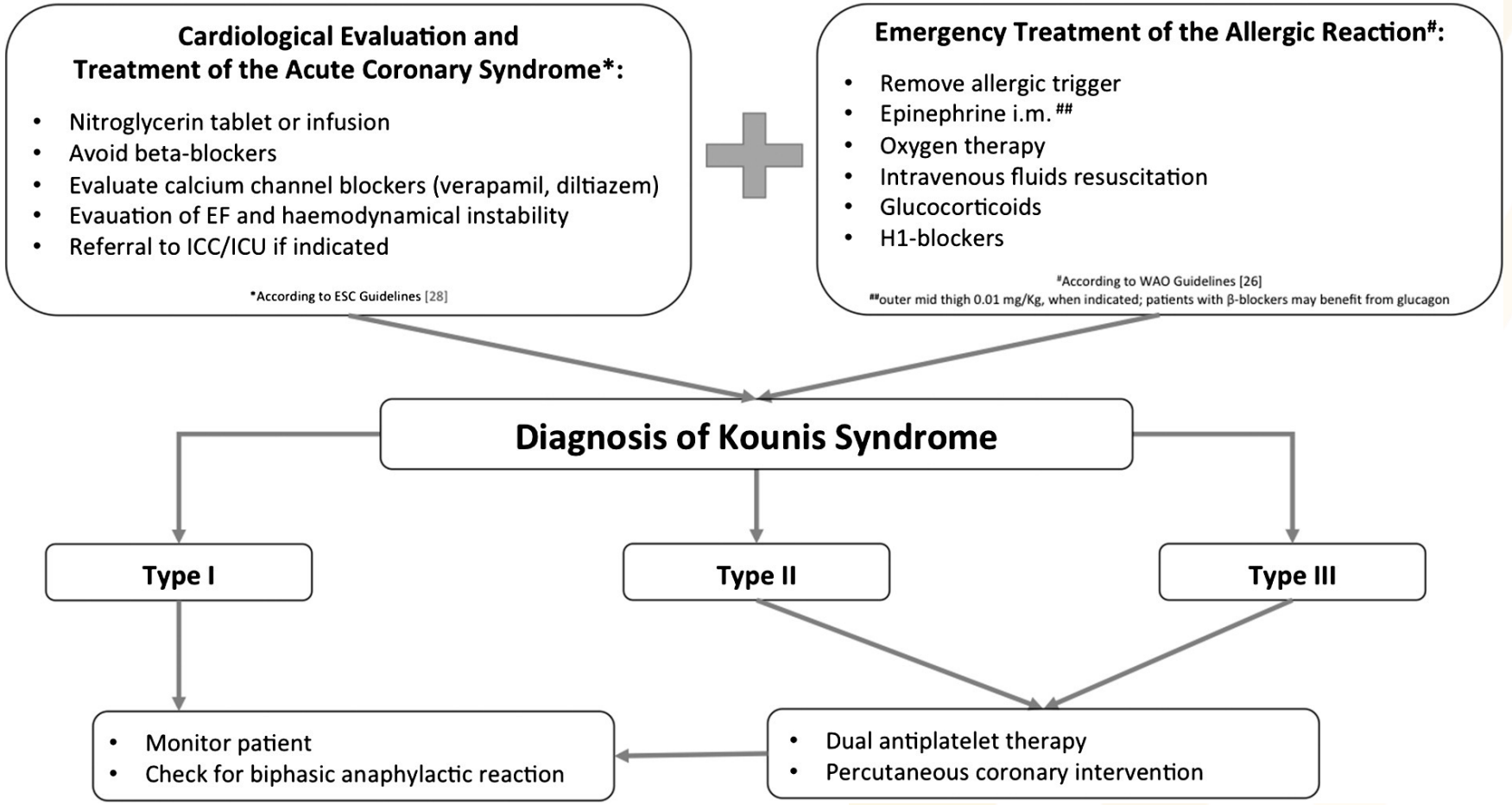
Allergic reaction and MI?



Kounis' syndrome

- Anaphylaxis can include distributive shock, ? cardiogenic
- Inflammation affecting coronary arteries, hypotension
- CP, SOB, syncope, hypotension → 12-lead EKG
- Concurrent time-sensitive emergencies - treat both issues - ASA, 911…
- Maybe 0.3 vs 0.5 mg epi IM?
- Cardiac issues and EKG changes often resolve with treating anaphylaxis
- Three "Types" described
  - Adverse cardiovascular effects of anaphylaxis can affect anyone - Type I
  - Someone with known CAD could have an allergic reaction - Types II and III

Kounis' syndrome



From: Fassio F et al. *Eur J Intern Med*. 2016 May:30:7-10

Take Away Points

- Anaphylaxis → Epi (in the UC and for home) – IM, nasal
- Consider observing nonsevere, resolved, stable patients after single-dose epi
- 911, stabilize, and treat the severe, unstable, or worsening patient
- Don’t forget bronchodilators for wheezing
- Consider inhaled racemic epi for symptomatic airway mucosal edema
- Become more familiar with the more selective antihistamines
- Continue antihistamines for several days
- If you’re prescribing steroids for all of these patients – **STOP**
- Use steroids for associated RAD/COPD or severe or refractory cases only

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