Updates from 2023 Anaphylaxis Practice Parameter

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Learning Objective

After participation, the learner will be able to:

- Relate selected recommendations for diagnosis and management of anaphylaxis that will appear in the 2023 Anaphylaxis Practice Parameter.

Anaphylaxis Update 2023

- Diagnosis
- Infants and Toddlers
- Community Settings
- Autoinjectors: How & When To Prescribe
- Beta Blockers & ACE Inhibitors
- Mast Cell Disorders
- Perioperative Anaphylaxis

Anaphylaxis Update 2023

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Summary – Perioperative Anaphylaxis

- May present as cardiovascular collapse, airway obstruction, and/or skin manifestations (less likely).
- During anesthesia and the pre/post anesthesia period, patients receive a variety of drugs, colloids and may also exposed to other anaphylactogenic factors including latex and chlorhexidine.
- Management requires a diligent history and review of anesthetic record, and close collaboration between the surgeon, anesthesiologist, and allergy/immunology consultant.

Classifying Recommendations

- Strong / Weak
- Unconditional / Conditional
- Unqualified / Qualified
- We Recommend / We Suggest
- Clinicians should / Clinicians might

Classifying Recommendations

Strong

- Desirable effects clearly outweigh undesirable effects.
- Low resource allocation
- High quality evidence with large, precise effect
- Low degree of variation in patient values and preferences

Conditional/Weak

- Desirable effects and undesirable effects more closely balanced.
- High resource allocation
- Low quality evidence with imprecise estimate
- Patient values and preferences important

Brozek J et al. Allergy 2011;66:588-95

Two Questions…

①Skin Test To:

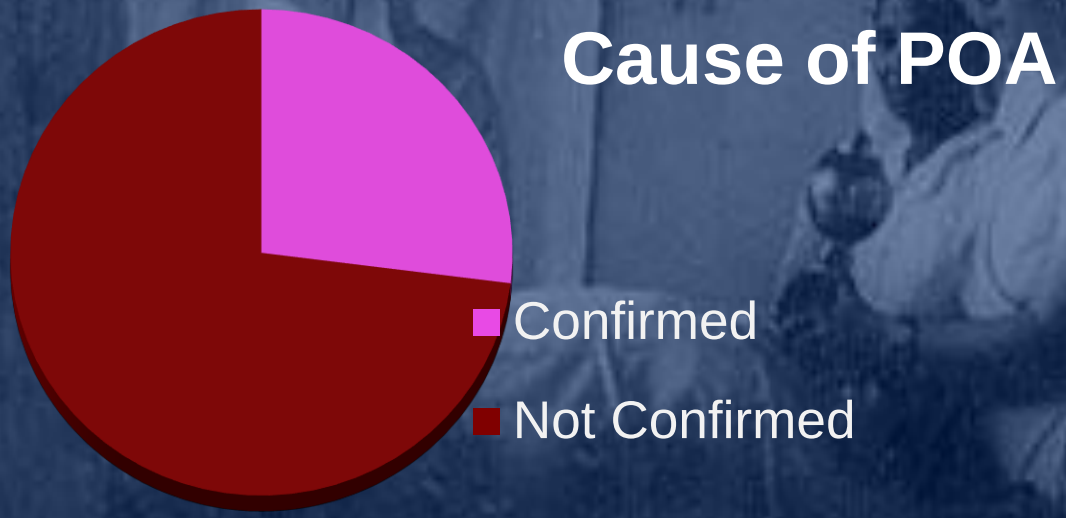
a. Selected drugs?
b. All drugs?

②Timing:

a. Now?
b. Wait 4-6 weeks?

Danish Anesthetists

Clinical Suspicion Not Reliable

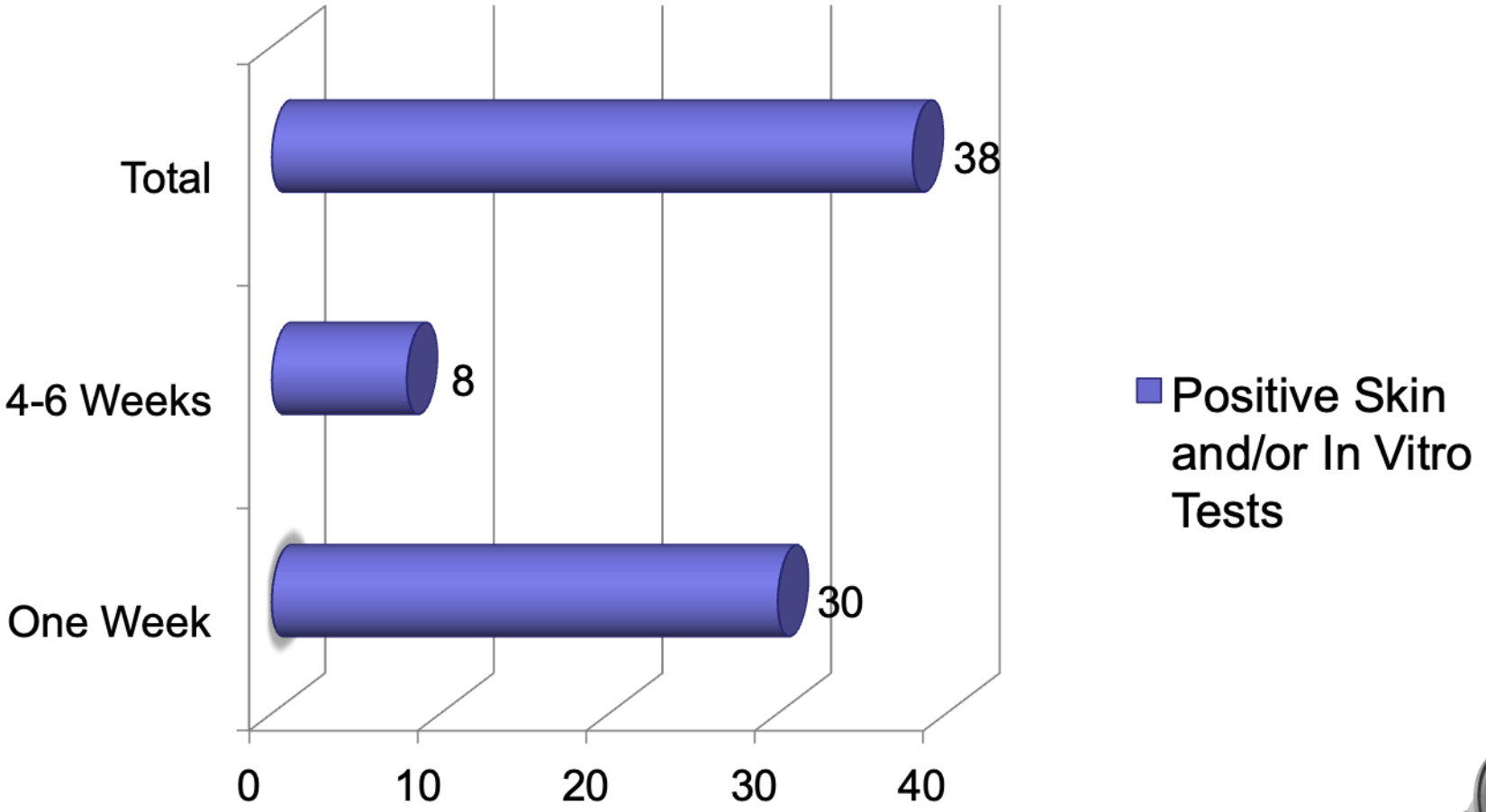


- Referring anesthetists at a Danish Anesthesia Allergy Center were asked to provide their pre-testing causes for POA
- These data provide support for the assertion that testing for *all* potential culprits is required in diagnostic evaluation of patients with perioperative anaphylaxis.

Krøigaard et al. British Journal of Anaesthesia 2005; 95 (4): 468–71.

Skin Testing After Systemic Sting Reaction

N = 41 patients with suspected IgE mediated reactions to hymenoptera venom



Goldberg A, Confino-Cohen R. J Allergy Clin Immunol 1997; 100:183-4.

POA: Diagnostic Evaluation

	Recommendation	Strength of Recommendation	Certainty of Evidence
CBS 45	We suggest that immediate hypersensitivity skin testing (percutaneous and intradermal) and/or in vitro specific-IgE testing should be performed, when available, to all potential pharmacologic and non-pharmacologic culprits used during the perioperative period.	Conditional	Very low
CBS 46	We suggest immediate hypersensitivity testing to suspected culprit (and alternative) agents should be delayed after POA, unless repeat surgery cannot be postponed. If surgery with general anesthesia is needed sooner, then testing should be performed as soon as possible.	Conditional	Moderate
CBS 47	We suggest challenges should be performed to all culprit agents to which skin and/or in vitro testing is negative.	Conditional	Moderate

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Skin Tests - POA

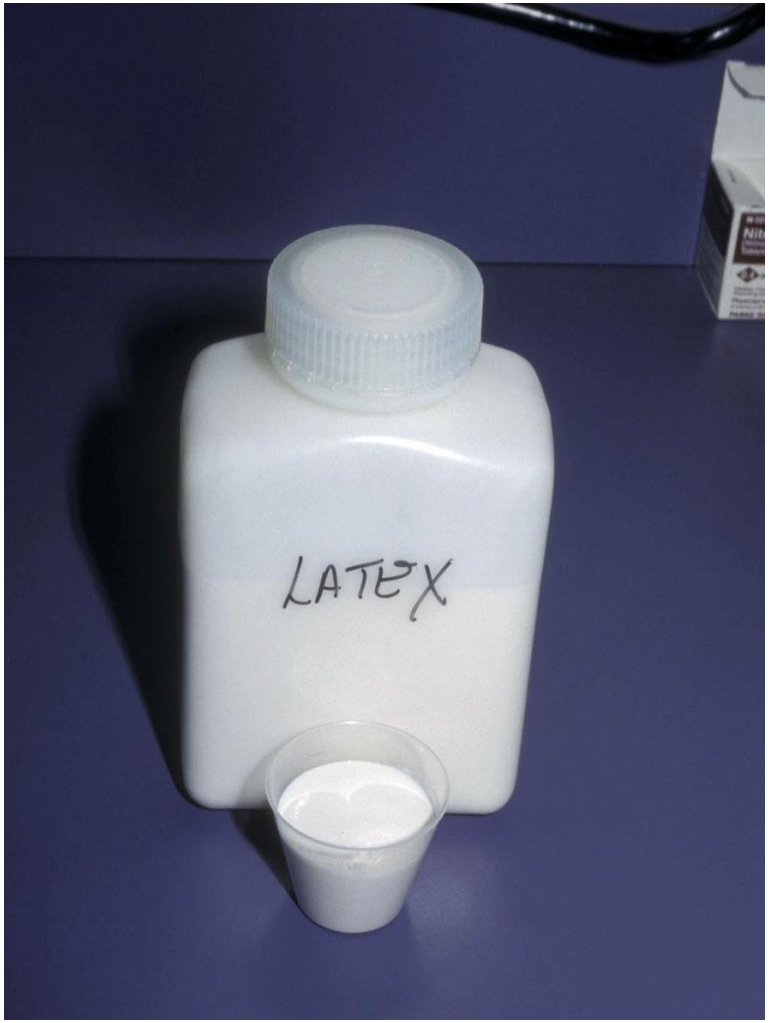
	SPT Concentration	IDT Concentration
NMBAs		
Atracurium	1 mg/mL	0.01 mg/mL
Cisatracurium	2 mg/mL	0.02 mg/mL
Mivacurium	0.2 mg/mL	0.002 mg/mL
Pancuronium	2 mg/mL	0.2 mg/mL
Rocuronium	10 mg/mL	0.05 mg/mL
Vecuronium	4 mg/mL	0.4 mg/mL
Suxamethonium	10 mg/mL	0.1 mg/mL
Hypnotics		
Etomidate	2 mg/mL	0.2 mg/mL
Ketamine	10 mg/mL	1 mg/mL
Propofol	10 mg/mL	1 mg/mL
Thiopental	25 mg/mL	2.5 mg/mL
Midazolam	5 mg/mL	0.5 mg/mL
Opioids*		
Alfentanil	0.5 mg/mL	0.05 mg/mL
Fentanyl	0.05 mg/mL	0.005 mg/mL
Remifentanil	0.05 mg/mL	0.005 mg/mL
Sufentanil	0.05 mg/mL	0.0005 mg/mL
Morphine	1 mg/mL	0.01 mg/mL

	SPT Concentration	IDT Concentration
Sugammadex	Undiluted	1/100
b-lactams		
BPO-OL	0.04	0.04
MD	0.5	0.5
Amoxicillin	20 mg/mL	20 mg/mL
Cephalosporins	20 mg/mL	2 mg/mL
Local anesthetics	Undiluted	1/10
Heparins	Undiluted	1/10
Tranexamic acid	Undiluted	1/10
Protamine	Undiluted	1/1000 – 1/10,000
Aprotinin	1/5	1/500
Hyaluronidase	Undiluted	1/10
Antiseptics		
Chlorhexidine	5 mg/mL	0.002 mg/mL
Dyes		
Patent blue	Undiluted	1/10
Methylene blue	Undiluted	1/10

Laguna et al, J Investig Allergol Clin Immunol 2018; 28:216-32.

Perioperative Anaphylaxis

Non-Pharmacologic Agents



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Citation	Cases of (Suspected) POA	Contactable and Confirmed POA Cases	Cases of Subsequent Anesthesia	Procedures Performed without POA	Recurrent POA
Fisher	606	246	183	183	0
Guyer	73	73	47	45	2
Miller	174	70	70	67	3
		Total No of Cases	300	Number with POA	5
				Percent	1.7%

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POA: Repeat Anesthesia

	Recommendation	Strength of Recommendation	Certainty of Evidence
CBS 48	We suggest repeat anesthesia may proceed in the context of shared decision making and as directed by history and results of diagnostic evaluation.	Conditional	Low
CBS 49	We suggest avoidance of culprit pharmacologic and non-pharmacologic agents associated with POA may be considered, regardless of test results; if challenge is not feasible and equally efficacious, structurally-unrelated alternatives are available.	Conditional	Low

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Anaphylaxis Parameter 2023
CBS 50

- **We offer no recommendation for or against the use of pretreatment prior to return to the operating room in patients with negative cutaneous (percutaneous and intradermal) and/or in vitro specific-IgE testing (and challenge when possible)**
- **Strength of Recommendation: None**
- **Certainty of Evidence:** Very Low

Beta Blockers & ACE Inhibitors

Increased Risk for More Serious Anaphylaxis

- Practice Parameter recommendations refer to beta blockers and ACE inhibitors together, although mechanism for more severe anaphylaxis differs.
- Confounders
  - Cardiovascular disease
  - Older age
- Contradictory findings

Beta Blockers & ACE Inhibitors

Increased Risk for More Serious Anaphylaxis

- Widely used for management of patients with ischemic heart disease, hypertension, and cardioprotection.
- ACE Inhibitors have similar indications as beta blockers, especially in diabetic patients.
- ACE Inhibitors may have an additive effect on this risk when used in combination with beta blockers – this approach has become common in patients with more severe cardiovascular disease.

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Editorial

Risk of anaphylaxis in patients receiving beta-blocker drugs

A growing number of case reports describe the occurrence of exceptionally severe anaphylaxis in patients receiving β-blocker therapy.[1-13] Clinical allergists should be aware of this risk because it may complicate allergy testing or treatment. The attacks have been characterized by profound hypotension, bradycardia with or without atrioventricular nodal block, severe sustained bronchospasm, urticaria, or angioedema, and typically, they are very refractory to treatment.

PATHOGENESIS

Normally, the production of anaphylactic mediators is modulated by neurohumoral mechanisms acting via cyclic nucleotides.[23-25] Beta-blockade interferes with these systems so as to amplify both the signal and the response. This is evidenced by increases in mediator synthesis and mediator release,[24, 26-28] end organ responsiveness,[29-32] and anaphylactic mortality induced experimentally by immunologic[32] or non-immunologic[31] mechanisms of mediator release.

Toogood JH. J Allergy Clin Immunol 1988; 81: 1-5.

Systematic Review and Meta-Analysis

- 15 studies: 22,313 severe anaphylaxis episodes.
- Increased severity
  - Beta blockers: OR = 2.19 (1.25-3.84)
  - ACE Inhibitors: OR = 1.56 (1.12-2.16)
- “It was not possible to perform an analysis adjusted for cardiovascular diseases … “
- Quality of evidence low, owing to differences in the control of confounders arising from concomitant presence of cardiovascular diseases.

Tehedor-Alonso et al. J Allergy Clin Immunol Pract 2019; 7: 879-97.

Framework for Risk Evaluation

Clinical Question	Potential Benefits of Treatment	Potential Risks of Treatment
Indication for Medication? • Post-MI • CHF • Migraine • Glaucoma • Diabetes • Other		
Indication for Intervention? • Skin Test • Inhalant Allergen Immunotherapy • Venom Immunotherapy • EAI Prescription • Other		

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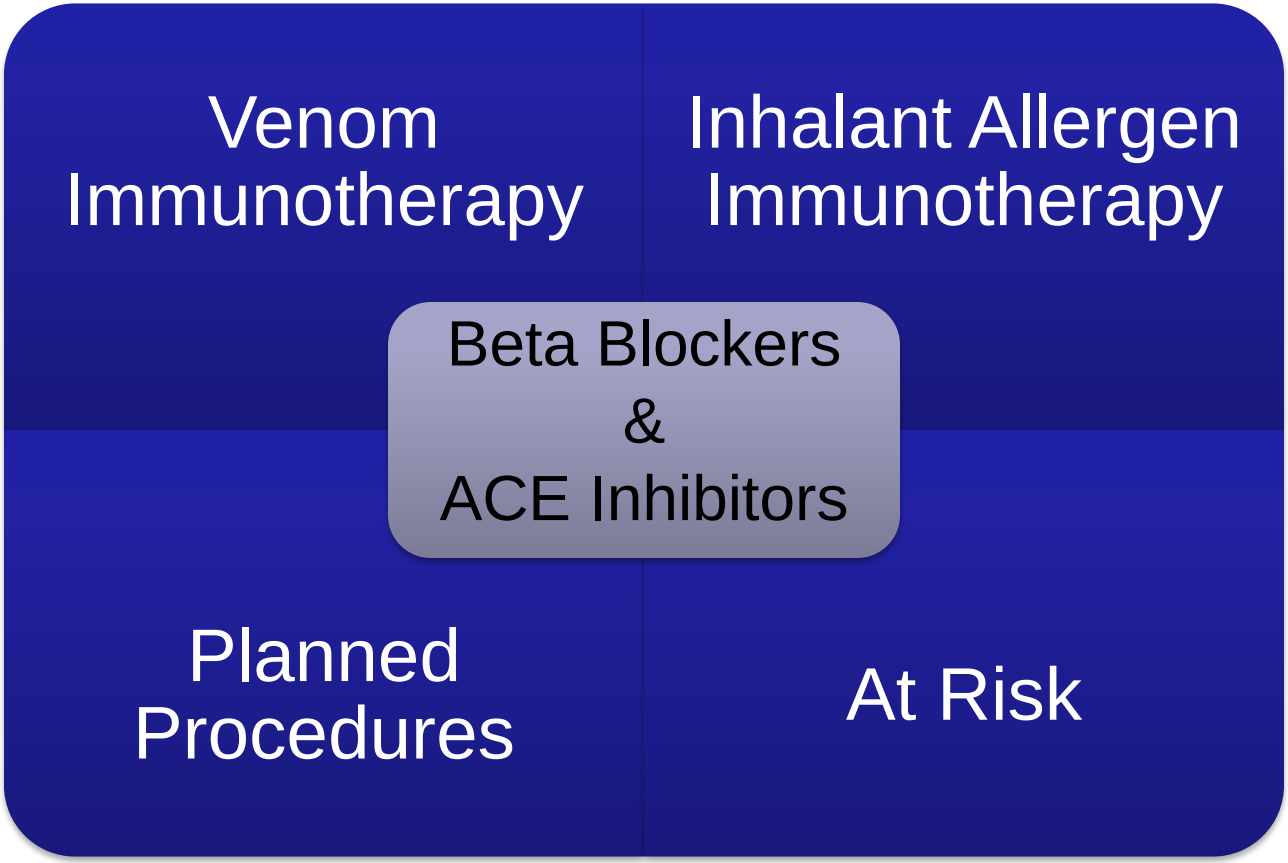

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Management of BB or ACEI in Patients with Anaphylactic Potential to Hymenoptera Venom

Question	Consensus Statement	Strength	Certainty
Discontinue BB or ACEI?	Continue Rx when benefit exceeds risk for more severe anaphylaxis	Conditional	Low
VIT recommended with BB or ACEI?	Yes, via shared decision making, or withholding either Rx or VIT	Conditional	Low
Maintenance VIT with BB or ACEI?	For most medical indications, Rx should not be changed	Conditional	Low

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Management of BB or ACEI in Patients Receiving Allergen Immunotherapy

- Consensus Statement:
  - If AIT initiated or continued via shared decision making, important to document.
  - Preferable to replace BB or ACEI; if not, important to ensure patient understands risk for more severe reaction should anaphylaxis occur.
- Strength: Conditional
- Certainty: Low

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Immunotherapy Practice Parameter

Summary Statement 37: Exposure to beta-adrenergic blocking agents is a risk factor for more serious and treatment-resistant anaphylaxis. Concomitant use of beta-blockers and allergen immunotherapy should be carefully considered from an individualized risk/benefit standpoint and incorporate the patient's preferences in the medical decision- making process.

Cox L, et al. J Allergy Clin Immunol 2011; 127: S1-55

Immunotherapy Practice Parameter

Summary Statement 37: Exposure to beta-adrenergic blocking agents is a risk factor for more serious and treatment-resistant anaphylaxis. Concomitant use of beta-blockers and allergen immunotherapy should be carefully considered from an individualized risk/benefit standpoint and incorporate the patient's preferences in the medical decision- making process.

Cox L, et al. J Allergy Clin Immunol 2011; 127: S1-55

Management of BB or ACEI in Patients Undergoing a Procedure

- Consensus Statement:
  - For planned procedures: contrast infusion, challenge/desensitization, etc.
  - If BB or ACEI cannot safely be interrupted, recommend discussion of medical necessity of procedure, relative risk of anaphylaxis, and possibility of more severe reaction.
- Strength: Conditional
- Certainty: Low

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Management of BB or ACEI in Patients At Risk For Anaphylaxis

- Consensus Statement:
  - For patients with anaphylactic potential to food or venom, idiopathic anaphylaxis, mast cell disorder, etc., at risk for sudden or unexpected anaphylaxis.
  - These patients should be counseled about risk for more severe anaphylaxis, and should avoid, where possible, use of non-selective BB or ACEI
- Strength: Conditional
- Certainty: Low

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Anaphylaxis in Restaurants

- The Food Allergen Labeling and Consumer Protection Act of 2004
  - Requires disclosure of major allergens on packaged food items
  - Does not require restaurants to provide ingredient lists or allergy warnings
  - Some restaurants list allergens on menus.
- Most common locations: cafes, fast food and Asian restaurants.
- Most common allergens: peanut, tree nuts, milk
- Effectiveness of staff training in anaphylaxis mitigation strategies needs to be studied.

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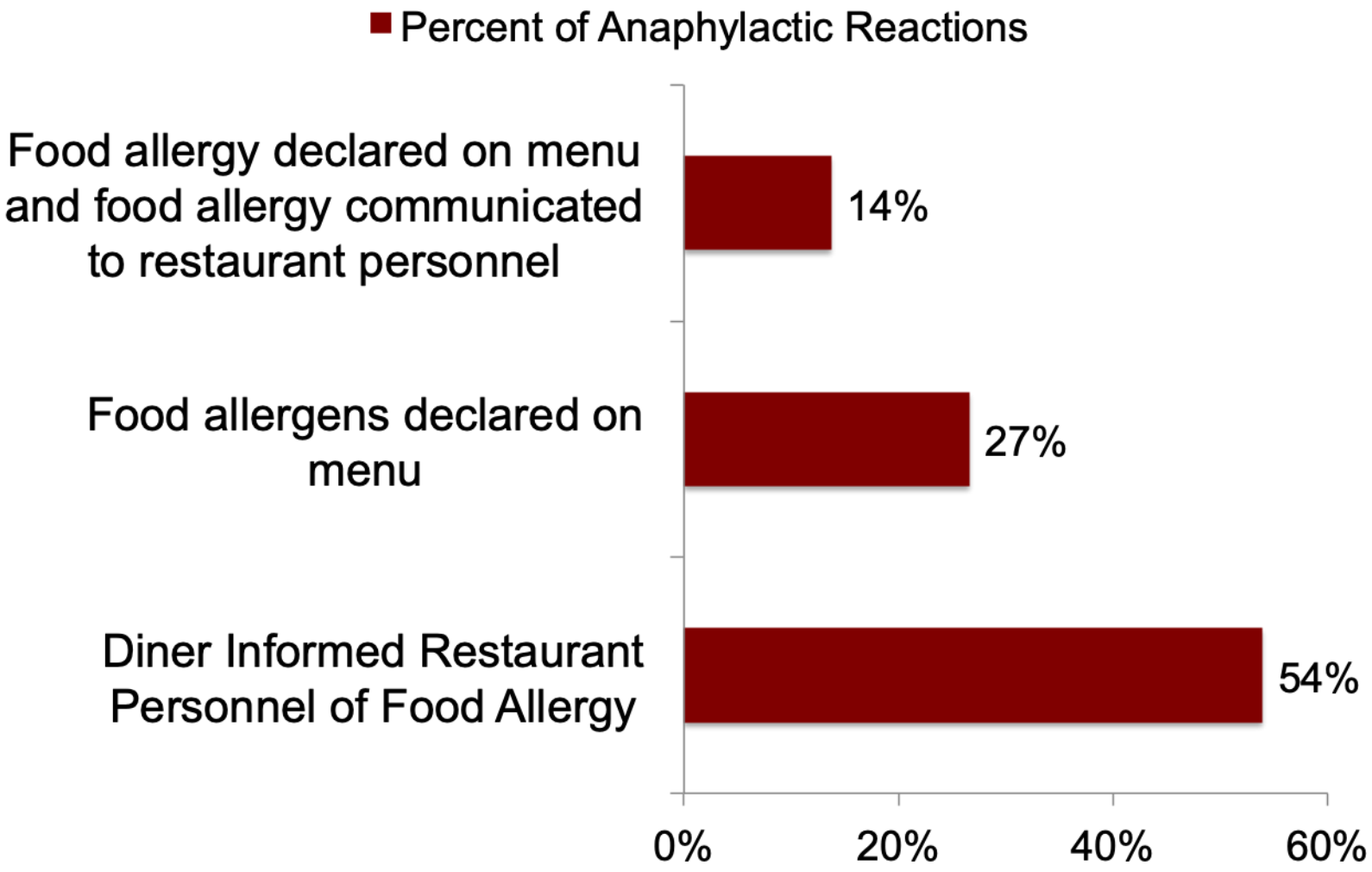
Anaphylaxis in Restaurants



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Recommended Strategies for Safe Dining

- Disclose allergy to knowledgeable and responsible food service staff.
- Be aware there is a higher risk of peanut, tree nut, and/or milk exposure in Asian restaurants, bakeries, and ice cream shops.
- Avoid buffets.
- Consider dining in off peak hours.
- Inform companions of food allergy and steps to take for reaction.

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Anaphylaxis Inflight

- Allergic emergencies reported:
  - 1 out of 37,750 flights
  - for ≤ 1 out of 2 million passengers
- Emergency landings reported for < 5% of episodes of anaphylaxis.
- Most common food allergen

10-15% of infight allergic reactions

- Epinephrine vial 1:1000 w/v & syringe is available on US airlines but not in airports or during transit

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Anaphylaxis in the Community

	Recommendation	Strength of Recommendation	Certainty of Evidence
CBS 13	We recommend clinicians counsel patients at high risk of anaphylaxis to always carry self-injectable epinephrine and teach patients proper indications and use.	Strong	Very low
CBS 14	We recommend clinicians educate patients on avoidance of potential exposure to their allergen(s).	Strong	Very low
CBS 15	We recommend clinicians educate patients that the main route of food induced anaphylaxis is by ingestion and not contact or inhalation.	Strong	Moderate

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Anaphylaxis in the Community

	Recommendation	Strength of Recommendation	Certainty of Evidence
CBS 21	We suggest that advising individuals at risk of anaphylaxis to wear or carry medical identification (eg, jewelry or wallet card) be considered optional. If worn or carried, the wording on medical alert jewelry or wallet cards should be verified for accuracy by a healthcare professional.	Conditional	Very low

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	Implications		
Grade	Patients	Clinicians	Policy
1—strong 'We recommend'	Most people in your situation would want the recommended course of action, only a small proportion would not	Most patients should receive the recommended course of action	The recommendation can be adopted a as policy in most situations
2—weak 'We suggest'	Most people in your situation would want the recommended course of action, but many would not	You should recognize that different choices will be appropriate for different patients [illegible] arrive at a management decision consistent with her or his values and preferences	Policy making will require substantial debate and involvement of many stakeholders

*Adapted from [7].


ONE SIZE
FITS ALL