

Safety in Food Immunotherapy

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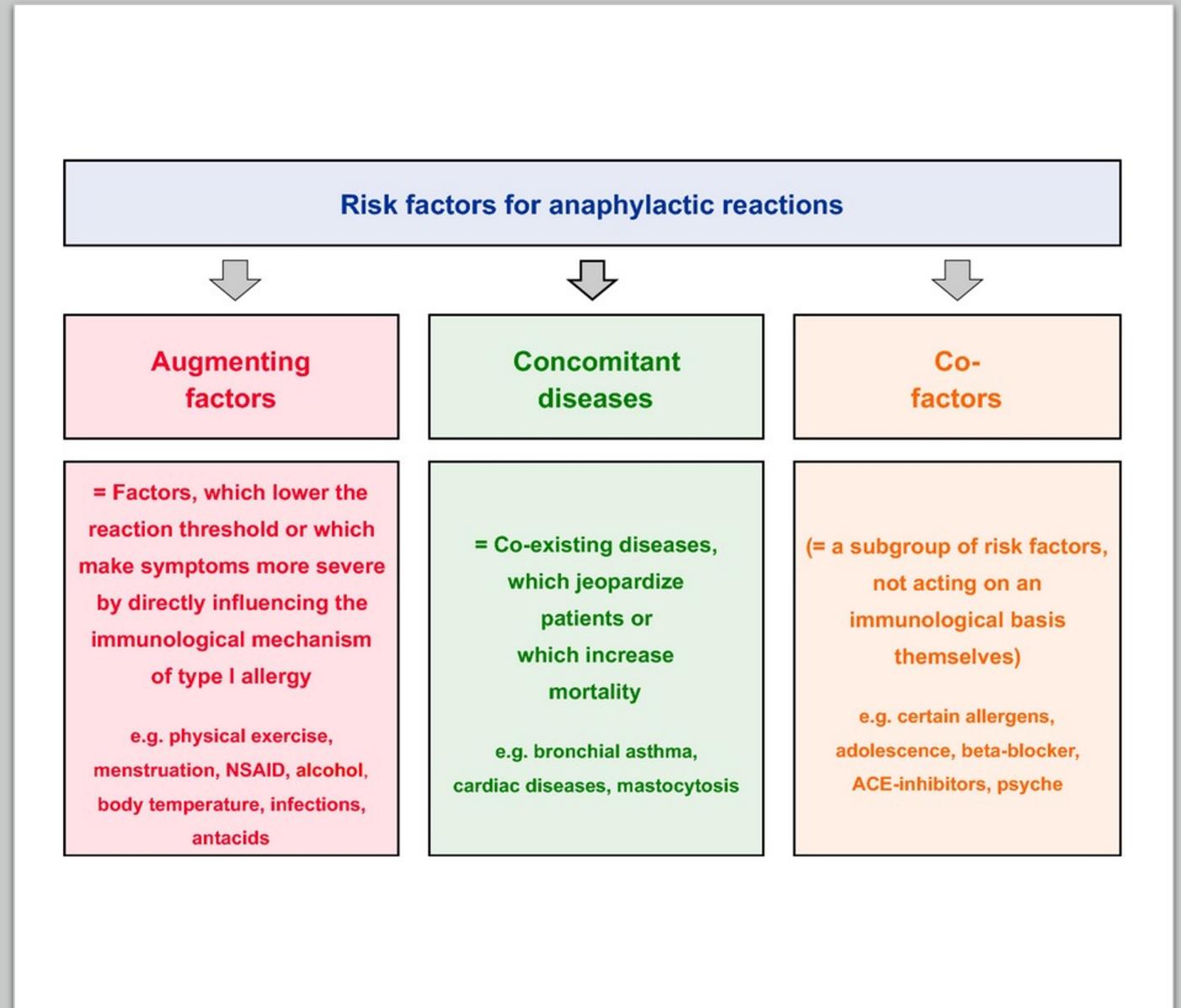
Outline

- Safety: Risk Factors for Anaphylaxis, Applying the Evidence to OIT Practice
(Courtesy of Dr. Sakina Bajowala, Kaneland Allergy)
- Safety Rules Checklist
- Controlling Atopic Disease
 - Maintaining asthma control
- Special Situations
 - Teens dosing alone
- Compliance

Risk factors for anaphylactic reactions

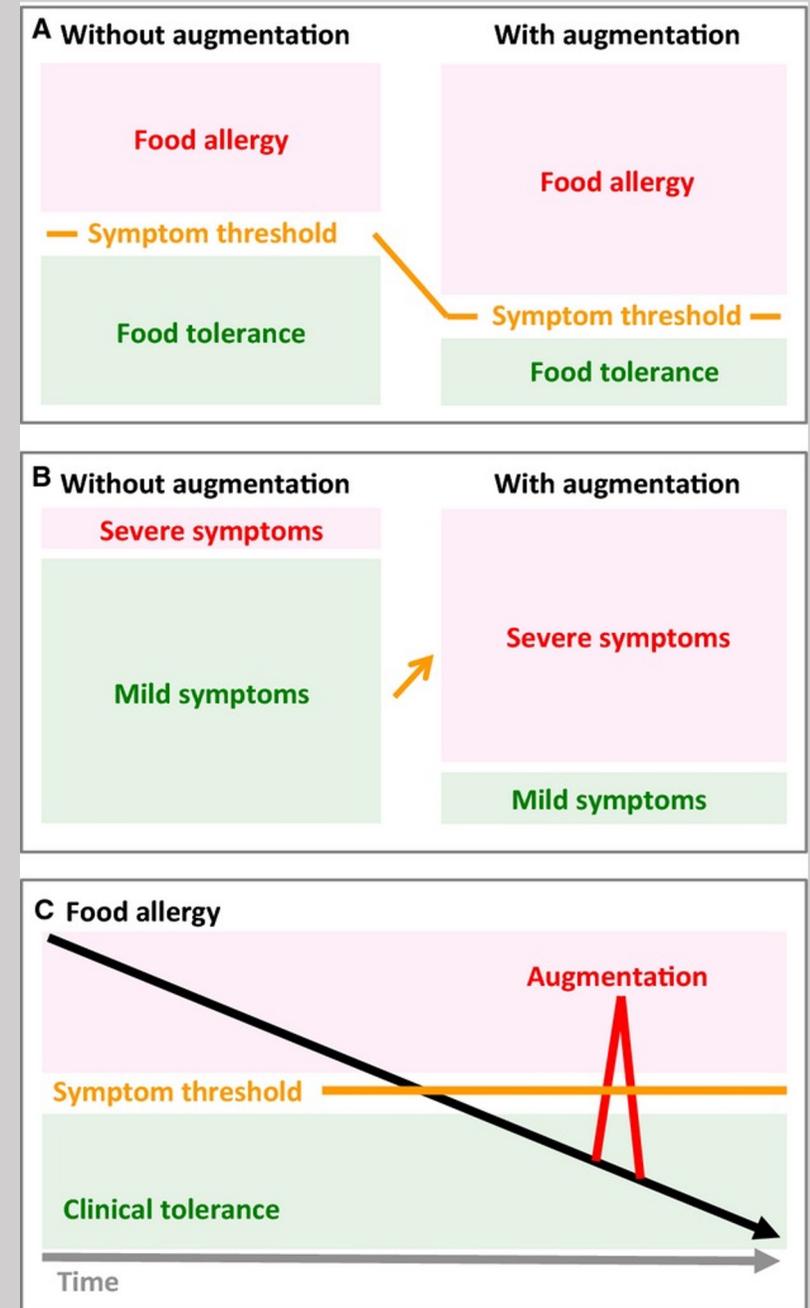
- A. Augmenting factors
- B. Concomitant diseases
- C. Co-factors

Niggemann B, Beyer K. Factors augmenting allergic reactions. Allergy. 2014 Dec;69(12):1582-7. doi: 10.1111/all.12532. PMID: 25306896.



Different Effects of Augmenting Factors

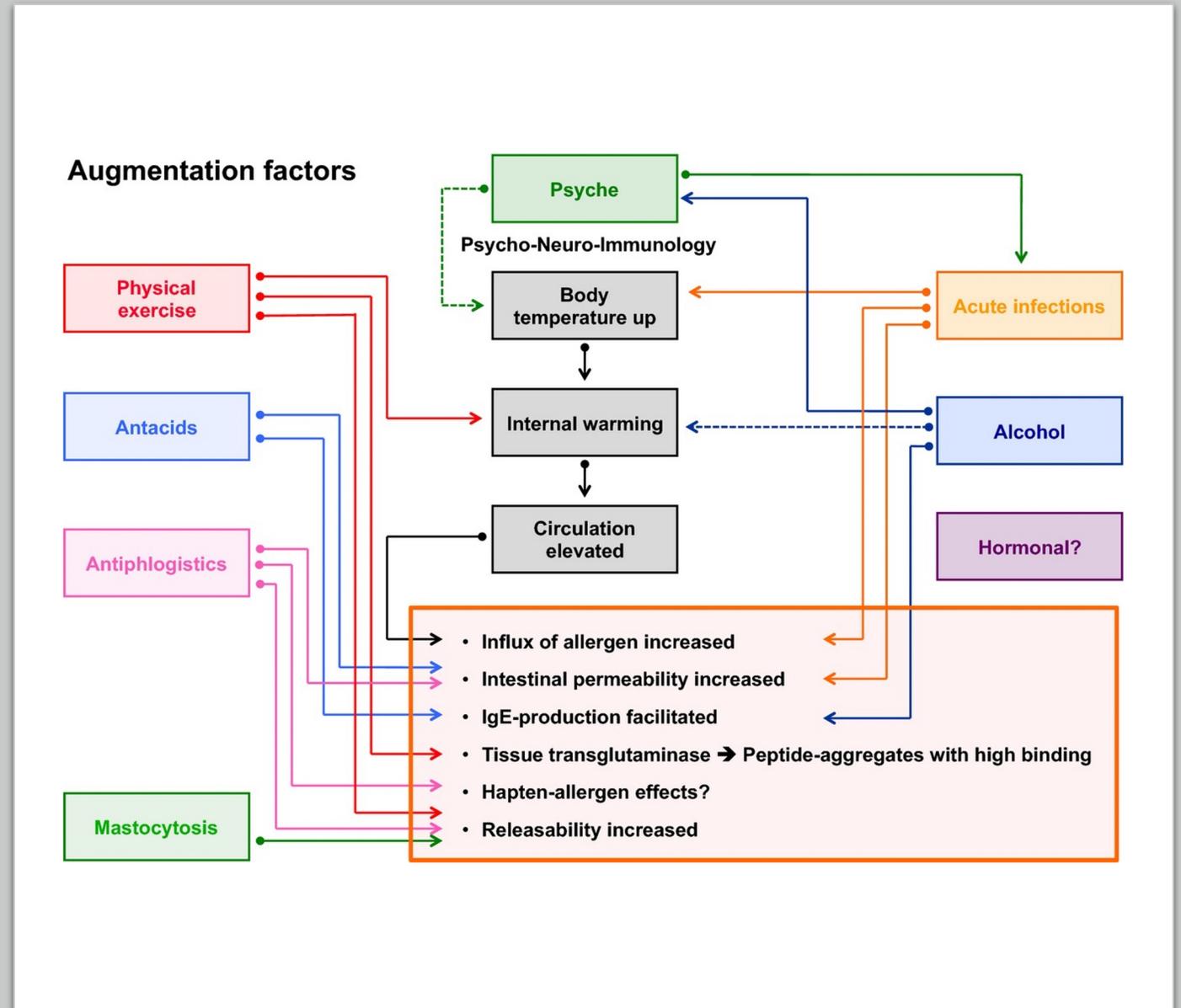
- A. Lowers threshold for reactivity
 - A. Takes less allergen to elicit reaction
- B. Increases severity of reaction
 - A. Same dose elicits more severe symptoms over time
- C. Reverses acquired clinical tolerance
 - A. Allergic reactions suddenly re-occur due to acute influence of augmenting factors



Possible Interacting Mechanisms of Augmentation

- Increased allergen influx
- Increased intestinal permeability
- IgE production
- Allergen binding
- Hapten effects
- Mast cell mediator release

Niggemann B, Beyer K. Factors augmenting allergic reactions. *Allergy*. 2014 Dec;69(12):1582-7. doi: 10.1111/all.12532. PMID: 25306896.



An update on epidemiology of anaphylaxis in children and adults.

Koplin JJ, Martin PE, Allen KJ. An update on epidemiology of anaphylaxis in children and adults. *Curr Opin Allergy Clin Immunol*. 2011 Oct;11(5):492-6. doi: 10.1097/ACI.0b013e32834a41a1. PMID: 21760501.

- Children under 5 years at highest risk for hospitalization from food-induced anaphylaxis
- History of asthma (especially severe asthma) raises risk of anaphylaxis
- Relationship between latitude (less sunlight) and prevalence of anaphylaxis
 - Role for Vitamin D?

Factors increasing the risk for a severe reaction in anaphylaxis: An analysis of data from The European Anaphylaxis Registry

Worm M, Francuzik W, Renaudin JM, Bilo MB, Cardona V, Scherer Hofmeier K, Köhli A, Bauer A, Christoff G, Cichocka-Jarosz E, Hawranek T, Hourihane JO', Lange L, Mahler V, Muraro A, Papadopoulos NG, Pföhler C, Poziomkowska-Gęsicka I, Ruëff F, Spindler T, Treudler R, Fernandez-Rivas M, Dölle S. Factors increasing the risk for a severe reaction in anaphylaxis: An analysis of data from The European Anaphylaxis Registry. *Allergy*. 2018 Jun;73(6):1322-1330. doi: 10.1111/all.13380. Epub 2018 Mar 8. PMID: 29318637.

- Higher age & concomitant mastocytosis (OR: 3.1, CI: 2.6-3.7)
- Vigorous physical exercise (OR: 1.5, CI: 1.3-1.7)
- Male sex (OR: 1.2, CI: 1.1-1.3)
- Psychological burden (OR: 1.4, CI: 1.2-1.6)
- Beta-blockers (OR: 1.9, CI: 1.5-2.2)
- ACE-I (OR: 1.28, CI: 1.05-1.51)

Effect of sleep deprivation and exercise on reaction threshold in adults with peanut allergy: A randomized controlled study.

Dua S, Ruiz-Garcia M, Bond S, Durham SR, Kimber I, Mills C, Roberts G, Skypala I, Wason J, Ewan P, Boyle R, Clark A. Effect of sleep deprivation and exercise on reaction threshold in adults with peanut allergy: A randomized controlled study. *J Allergy Clin Immunol*. 2019 Dec;144(6):1584-1594.e2. doi: 10.1016/j.jaci.2019.06.038. Epub 2019 Jul 15. PMID: 31319102; PMCID: PMC6904229.

- Cross-over study
 - Blinded challenge to establish baseline eliciting dose
 - 3 open challenges (in random order)
 - Exercise after each dose
 - Sleep deprivation preceding challenge
 - No intervention
- Exercise and sleep deprivation each significantly reduce the threshold of reactivity in patients with peanut allergy, putting them at greater risk of a reaction.

Seasonality of food-related anaphylaxis admissions and associations with temperature and pollen levels.

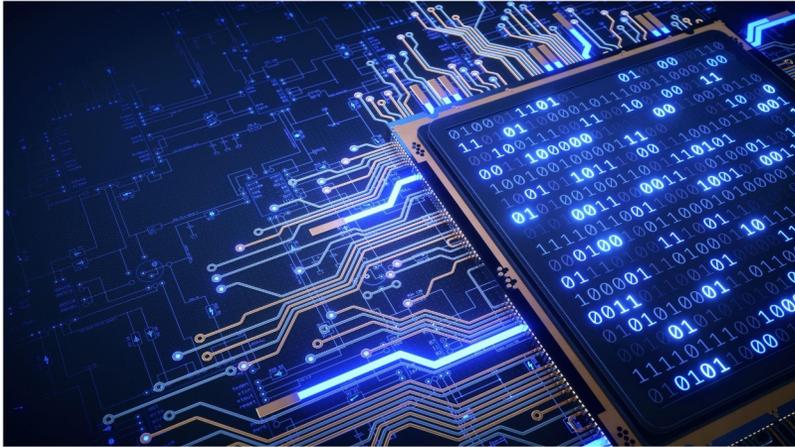
Lam HCY, Turner PJ, Hemming D, Jarvis DL.
Seasonality of food-related anaphylaxis admissions and associations with temperature and pollen levels. *J Allergy Clin Immunol Pract*. 2021 Jan;9(1):518-520.e2. doi: 10.1016/j.jaip.2020.07.032. Epub 2020 Jul 31. PMID: 32745700; PMCID: PMC7794659.

- This is the first quantification of seasonality of food-related anaphylaxis admissions.
- Risk of food-related anaphylaxis admissions was higher around June in England (22% higher vs January), especially among children younger than 15 years.
- Oak and Ragweed pollen levels associated with increased risk of hospital admission
- Positive association between increased temperature and risk of admission

Creating OIT Dosing Rules to Correct for Augmenting Factors, Concomitant Disease, and Co-Factors

Risk Factor	Dosing Rule
Physical Exercise	Rest period pre- (~20-30 min) and post- (~2 hrs) dose
Acute infection / fever	Dose reduction or deferral during acute illness
Stress / Anxiety	Must be calm during dosing – meditation / breathing
Hormonal factors (menses, etc)	Dose reduction or prophylactic Rx during ovulation/1 st few days of menses
Asthma	No dose during asthma exacerbation
Medications (NSAIDs, PPI)	Avoid NSAIDs 4 hrs before or after dose; Avoid long-term PPI during OIT
Alcohol	“Don’t drink and dose”
Mastocytosis	Antihistamine treatment
Seasonal allergen exposure	Prophylactic antihistamine for active symptoms
Vaccination	Dose reduction or deferral
Dental Work / Mucosal injury	Dose deferral until healed
Sleep deprivation	No dose late at night
Empty stomach	Always dose with healthy food (complex carbs, antioxidants)

Safety Optimization for OIT Home Dosing: Put the Data to Work



- DATA is KING
- Keep meticulous reaction records – preferably digitized
 - Protocol, dose, season, time, augmenting/co-factors
- Don't keep your data in a silo
 - OIT registry
 - Publications
 - Presentations
 - Collaboration
- Crowd-sourcing, Big data, Machine-learning & Artificial Intelligence are the Future
 - The pace of safety optimization will quicken!

Safety Rules Checklist

Temperature / Circulation

Internal

- Fever
- Exercise
- Hormones
- Infections

External

- Hot Baths/Showers
- Hot Tubs
- Weather

Age

Hormonal

- Adolescence, Menstruation, Menarche, Menopause
- Exogenous (Medications)

Medications

- Maintaining Allergy/Asthma Regimen
- Prophylactic Medications
- Other Medications of Special Interest
 - NSAIDS
 - ACE-I
 - Beta Blockers
 - Antacids
 - Immunosuppressants / Biologics

Co-morbidities

Non-Atopic Disease

- Cardiovascular
- Immune / Autoimmune
- Pulmonary
- Gastrointestinal / Oral

Atopic Disease

- Asthma Control
- Dermatitis Control
- Seasonal Variation
- Allergy Shots and Other Immunotherapy

Concomitant Ingestions

- Alcohol
- Tolerated Allergic Foods
- New Foods
- Fasting

Mucosal Integrity

- Dental Work
- Oral Herpes

Infections

- Type
 - Viral vs Bacterial
- Location
 - Pharyngeal, Respiratory
 - Gastrointestinal

Sleep and Scheduling Issues

Controlling Allergy Asthma

- Pre-IT FENO / Spirometry
- Pre-IT Peak Flow
- Recheck with seasonal variation
- ACT and Peak Flows at each up-dosing
- Aggressive Infection and Exacerbation Management
- Advising Against Therapy Change
- Biologics

Special Situations

- Teens
 - Updosing Alone (No)
 - Dosing at Home Alone (No)
- Non-parental Adult At Visit
 - Consent Needed
 - Consent for Treatment Needed
- Divorced / Separated Parents
 - Pre-Visit Touchpoint with Both Parents
 - Consent for Treatment and Release of Information
 - Guardrails for Who and Who Cannot Accompany
- Extremely Anxious Parent / Child

Compliance

The Non-Adherent Patient

The Self-Managing Patient

The Angry/ Overly Anxious Parent or Patient

The Un-Vaccinated or Resistant to Standard Medical Treatment