

# Risk Factors for Anaphylaxis

Applying the Evidence to OIT Practice

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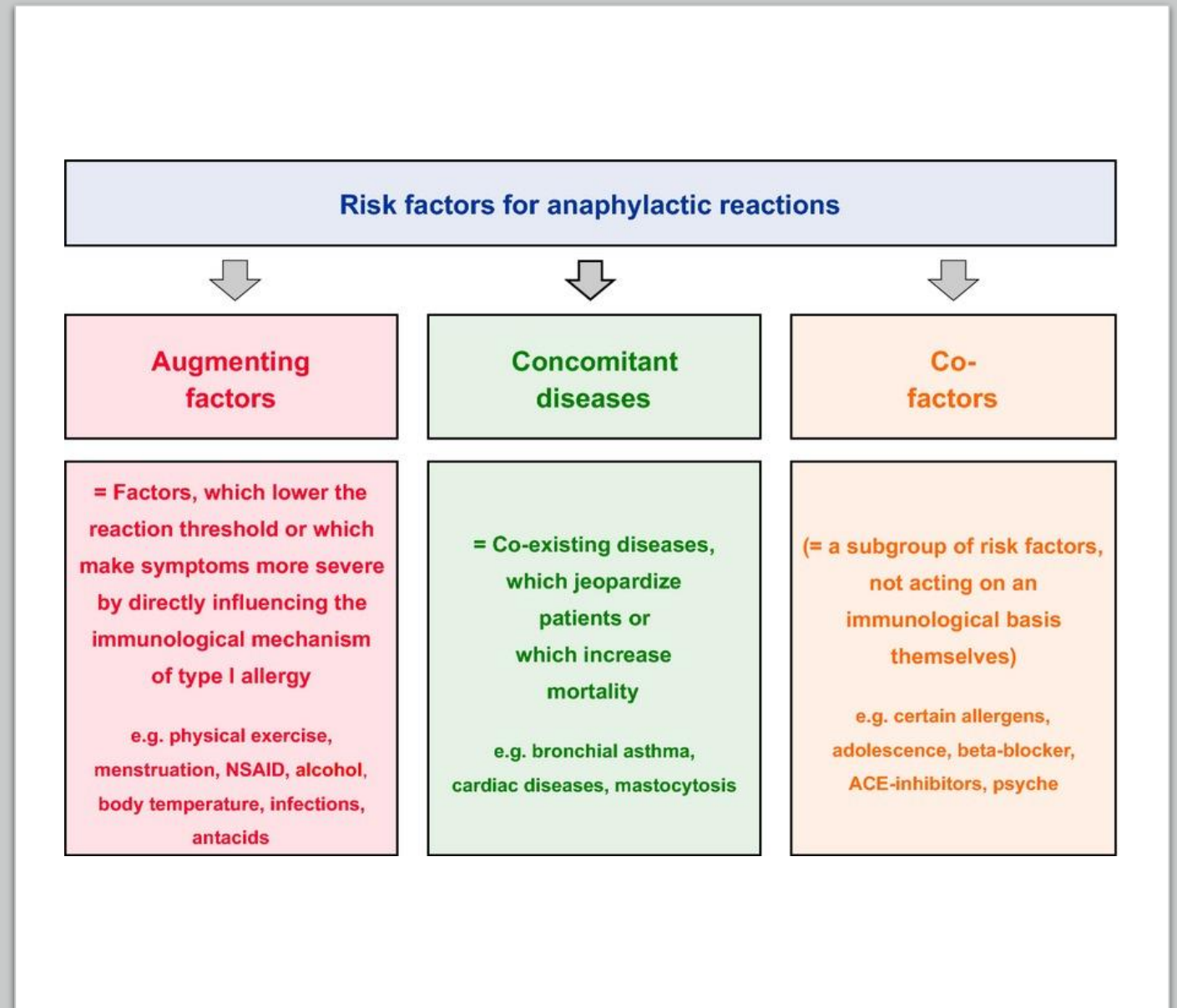
# Pertinent Disclosures

- Owner & Medical Director – Kaneland Allergy & Asthma Center
- Executive Director – Kaneland Food Allergy Foundation
- Owner – Wise Prince Holdings, LLC
  - Developer of Food Allergy Fix Mobile App & Web Portal

# Risk factors for anaphylactic reactions

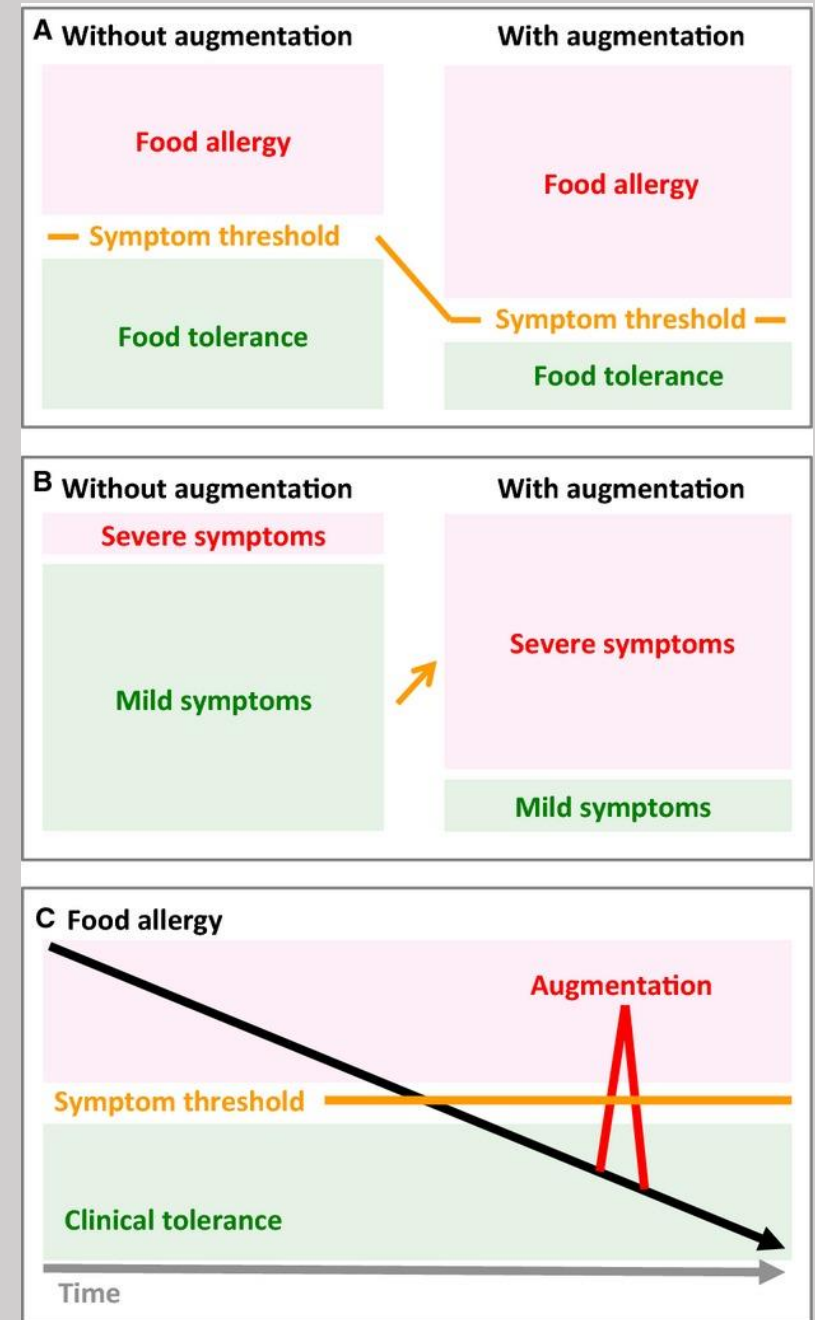
- A. Augmenting factors
- B. Concomitant diseases
- C. Co-factors

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

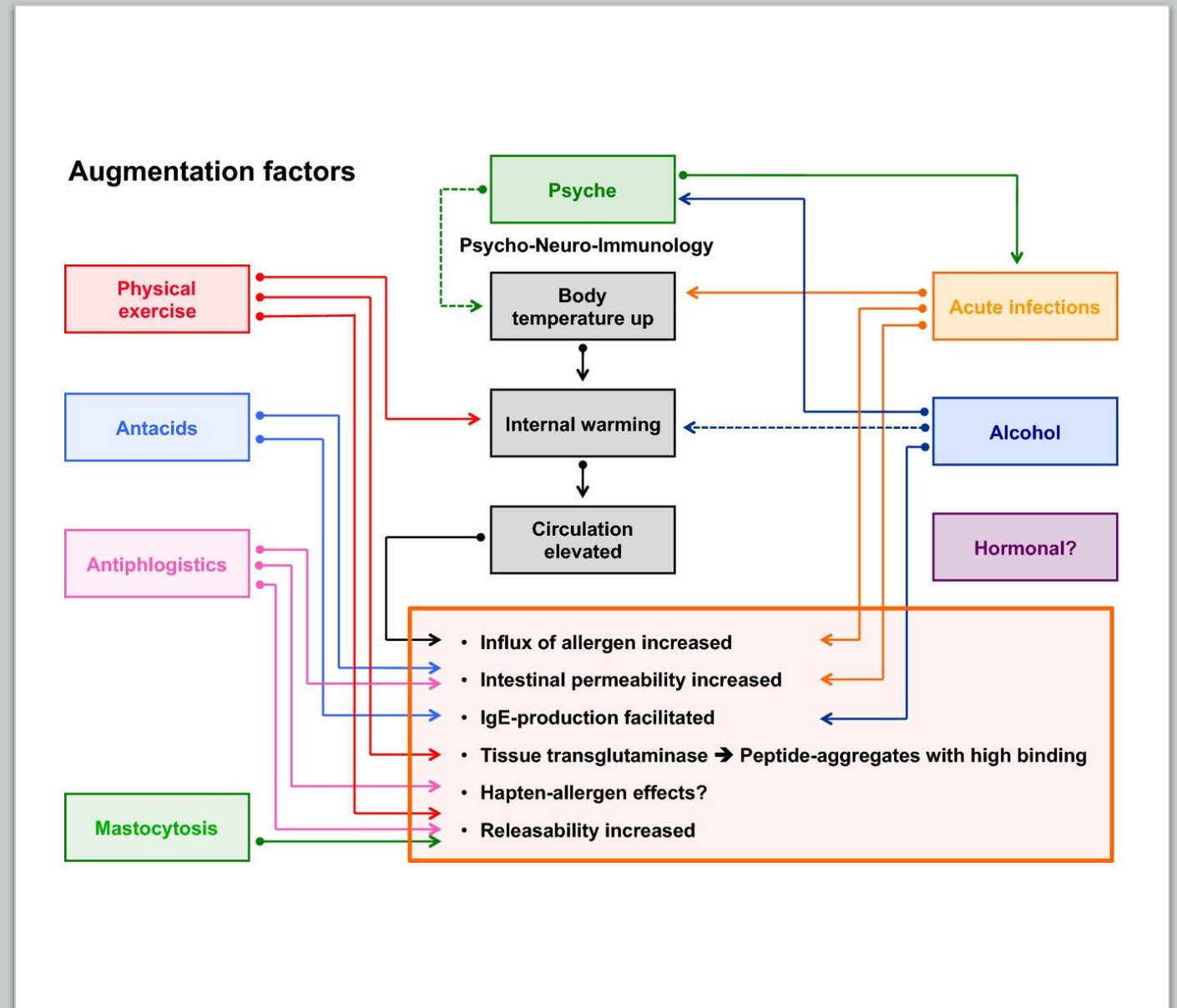
- A. Lowers threshold for reactivity
  - A. Takes less allergen to elicit reaction
- B. Increases severity of reaction
  - A. Same dose elicits more severe symptoms over time
- C. Reverses acquired clinical tolerance
  - A. Allergic reactions suddenly re-occur due to acute influence of augmenting factors



# 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-Gęszicka 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.

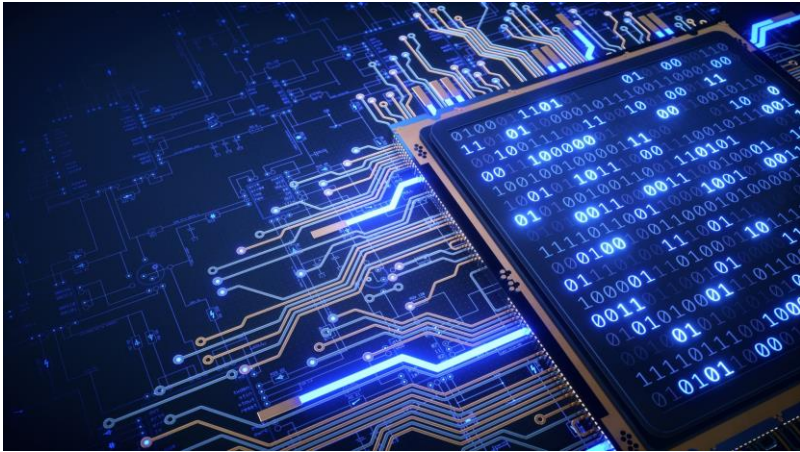
Lam HCY, Turner PJ, Hemming D, Jarvis DL.  
Seasonality of food-related anaphylaxis admissions and associations with temperature and pollen levels. *J Allergy Clin Immunol Pract*. 2021 Jan;9(1):518-520.e2. doi: 10.1016/j.jaip.2020.07.032. Epub 2020 Jul 31. PMID: 32745700; PMCID: PMC7794659.

- 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 <sup>st</sup> 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!