

# The Epi-Center: Cracking the code on pediatric food allergies

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CENTER FOR  
IMMUNOLOGY AND  
INFLAMMATORY  
DISEASES



**HARVARD**  
UNIVERSITY



MASSACHUSETTS  
GENERAL HOSPITAL

**RHEUMATOLOGY, ALLERGY  
AND IMMUNOLOGY**

# Disclosures

none

# Cracking the code on pediatric food allergies

## OBJECTIVES:

1. Define the problem: definition and epidemiology
2. Review how we got here...
3. Run the food allergy culprits list
4. Demystify food allergy diagnostics (and how you can help!)
5. Understand eczema and food allergy
6. Explain food allergy treatments
7. Highlight food allergy prevention



# DEFINITIONS

# Adverse Food Reaction versus Food Allergy

## **NIAID Expert Panel Definition of Food Allergy:**

“adverse health effect arising from specific immune response that occurs reproducibly on exposure to a given food”

Boyce et al. JACI 2010

- Adverse food reactions include all reactions to a food
  - Immune reactions = food allergies
  - Non-immune reactions
    - often mislabeled as “food allergies”
- Non-immunologic reactions are highly prevalent.
- Although we focus on food allergy, providers should be familiar with both categories.

Sampson et al, JACI 2014

# Non-Immune Adverse Food Reactions

## Food Intolerances

- Lactose deficiency / malabsorption / sensitivity
- Caffeine
- Alcohol
- Non-celiac gluten sensitivity
- Intolerance of short-chain fermentable carbohydrates (FODMAPs; wheat, certain fruits, vegetables, milk, legumes)
- Naturally occurring components & additives
  - Theobromine (tea, chocolate)
  - Histamine (berries, wine, fish, sauerkraut)
  - Tyramine (cheeses, pickled fish, avocado, orange)
  - Tryptamine (aged cheeses, pickled fish)
  - Serotonin (banana, tomato)
  - Phenylethylamine (chocolate)
  - Glycosidal alkaloid solanine (potatoes)
  - Sodium metabisulfate
  - Monosodium glutamate
  - Salicylates (preservative in canned foods)
  - Capsaicin (chili peppers)

## Gastrointestinal Disorders

- Irritable bowel syndrome
- Gastrointestinal reflux
- Yeast overgrowth syndrome
- Pancreatic exocrine insufficiency
- Peptic ulcer disease
- Gallbladder disease

## Toxic Reactions

- Seafood
  - Scombroid (fresh tuna fish or mackerel)
  - Ciguatera poisoning (grouper, snapper)
  - Saxitoxin (shellfish)
- Other food poisoning
- Fungal toxins

## Other

- Neurologic reactions (auriculotemporal syndrome)
- Psychologic reactions
  - Food phobias
  - Food aversions
- Accidental Contaminations
  - Pesticides
  - Antibiotic (if allergic)

# The Spectrum of Food Allergy: Immune

## IgE Mediated

- Typical IgE Mediated Food Allergy (e.g. urticaria, angioedema, anaphylaxis)
- Oral Allergy Syndrome / Pollen Food Allergy Syndrome
- Food-dependent exercise-induced anaphylaxis

## Mixed IgE & Non-IgE Mediated

- Eosinophilic Gastrointestinal Diseases (EGIDs: esophagitis, gastroenteritis)
- Food-triggered atopic dermatitis

## Non-IgE Mediated

- Celiac disease
- Food Protein Induced Enterocolitis Syndrome (FPIES)
- Food protein induced allergic Proctocolitis (FPIAP)

## Cell Mediated

- Allergic Contact Dermatitis (foods containing balsam of peru, nickel, propylene glycol, chamomile)

EVERYONE HAS FOOD ALLERGIES....

WHY!!!???

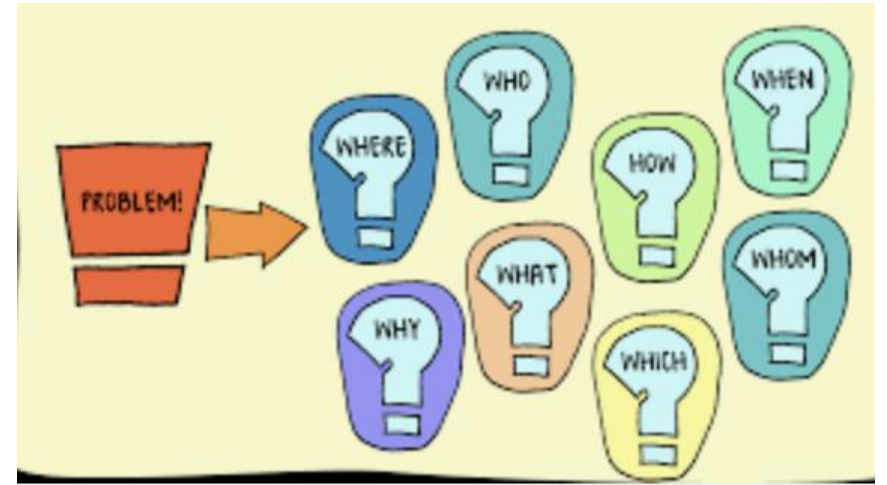


I don't know.....



If I knew....





# DEFINE THE PROBLEM



# THE FOOD ALLERGY EPIDEMIC



**1 in 10**  
adults



**1 in 13**  
children



More than half of adults with food allergies have experienced a severe reaction.



More than 40 percent of children with food allergies have experienced a severe reaction.



Claim lines with diagnoses of anaphylactic food reactions increased 377 percent between 2007 and 2016.

# Cracking the code on pediatric food allergies: Define the problem

- Perception by public: 19-25%<sup>1</sup>
- Estimated convincing food allergy:  
Adults: 10.8%<sup>1</sup> and infants/young children: 7.6%<sup>2</sup>
- Specific allergens: Geographical and cultural variations
- Prevalence increasing – 18% increase between 1997-2007<sup>6</sup>

<sup>1</sup> Gupta et al. JAMA Netw Open 2019, Jan 4;2(1):e185630

<sup>2</sup> Gupta RS et al. Pediatrics. 2018 Dec;142(6):e20181235

<sup>3</sup> Di Palmo, E, et al. Medicina (Kaunas). 2019 Sep;55(9): 509.

<sup>4</sup> Goksor, E, et al. Acta Paediatr. 2016 Dec; 105(12):1472-1479.

<sup>5</sup> Papapostolou, N, et al. J Clin Med. 2022;11(14):4232

<sup>6</sup> Branum AM, Lukacs SL. Pediatrics 2009;124;1549-55.

# Cracking the code on pediatric food allergies: Guidelines disaster...

- **Pre-2010:** ABP/AAAAI- avoidance of peanut until age 2 years
  - ? Avoidance in pregnancy- YES
  - Avoidance during breast feeding- YES
- **2010:** NIAID updated Food allergy guidelines:
  - “... insufficient evidence exists for delaying introduction of... Potentially allergenic foods beyond 4-6 months of age...”
  - But HOW to introduce?
  - Avoidance during pregnancy and BF *not recommended*
- **2014:** NIAID updated food allergy guidelines:
  - No avoidance in maternal diet
  - ? Introduction of highly allergenic foods early
  - NO DELAYED introduction of solid foods beyond 4-6 months

# Cracking the code on pediatric food allergies: Culprit foods



43-86% of food allergic children are allergic to multiple foods

# Cracking the code on pediatric food allergies: Culprit foods

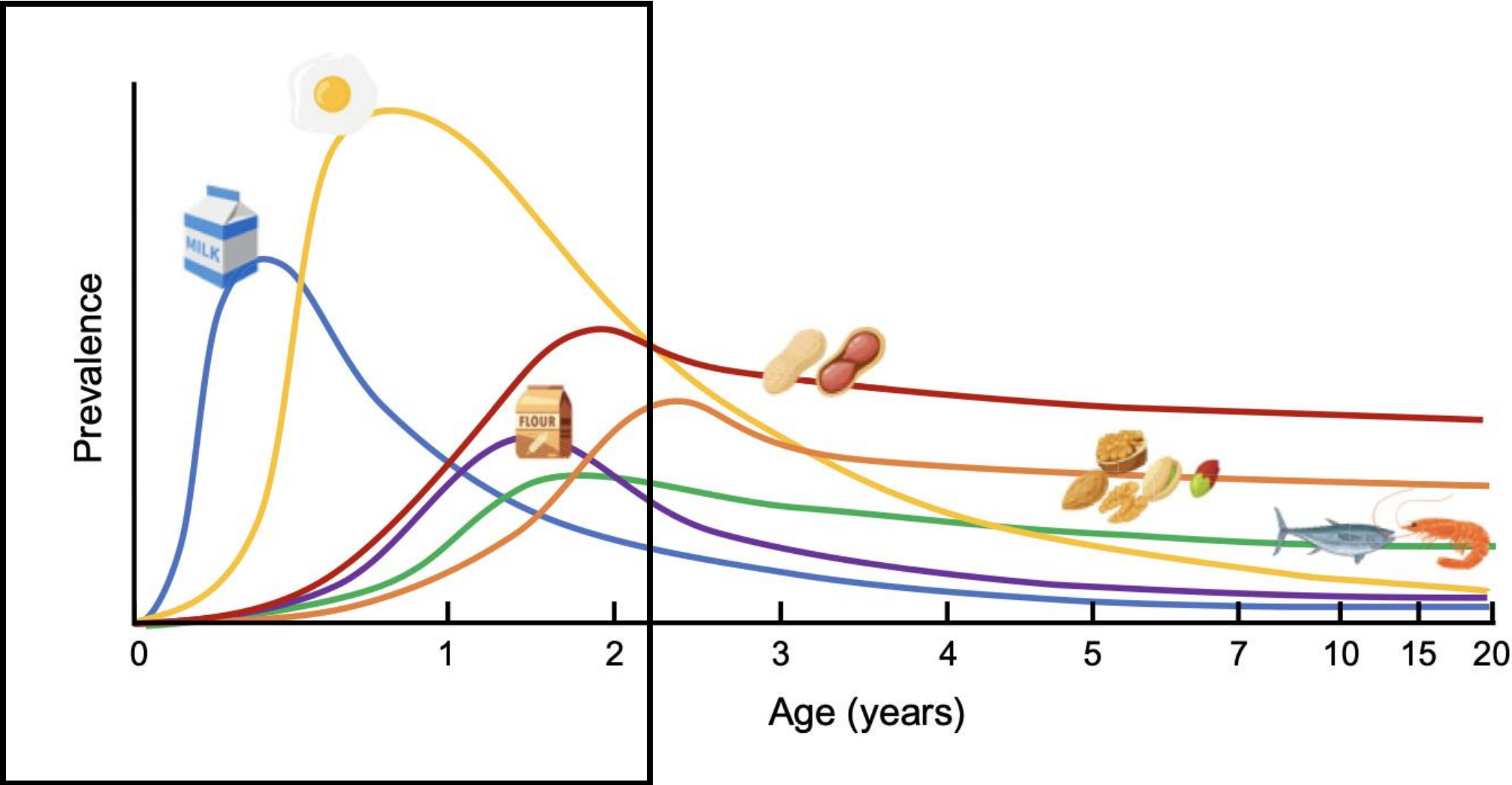
## To Which Foods Are People Allergic?

- More than 170 foods have been reported to cause food allergy reactions in the U.S.<sup>1</sup>
- In 2004, **eight major food allergens**—milk, egg, peanut, tree nuts, wheat, soy, fish and crustacean shellfish—were identified as responsible for at least 90 percent of the serious food allergy reactions in the U.S.<sup>1</sup>
- In 2021, the U.S. added sesame as the **ninth major food allergen**.<sup>70</sup>
- The most common food allergies in children are allergies to peanut, milk, shellfish, and tree nut.<sup>9</sup>
- The most common food allergies in adults are allergies to shellfish, milk, peanut, and tree nut.<sup>7</sup>
- Studies published in 2018 and 2019 can be used to estimate the current number of U.S. children and adults who are allergic to specific foods.<sup>2,7,8,9</sup>
  - shellfish: 8.4 million
  - milk: 6.2 million
  - peanut: 6.2 million
  - tree nuts: 3.9 million
  - egg: 2.7 million
  - fin fish: 2.7 million
  - wheat: 2.4 million
  - soy: 1.9 million
  - sesame: 0.7 million

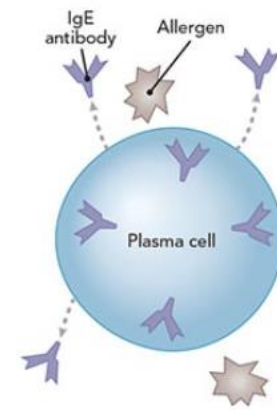


# Cracking the code on pediatric food allergies: Culprit foods, natural history

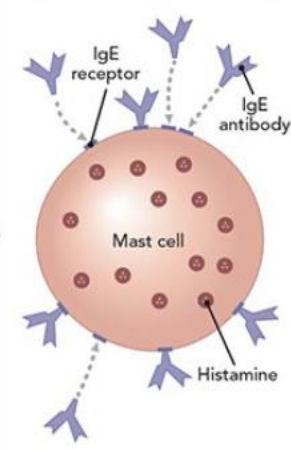
Natural history of food allergy by common food type



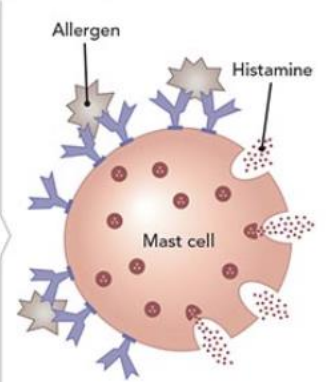
## IMMUNE CELLS ON HIGH ALERT



**1 You're exposed.**  
Immune cells called plasma cells (or B cells) release immunoglobulin E (IgE) antibodies after you eat an allergen.



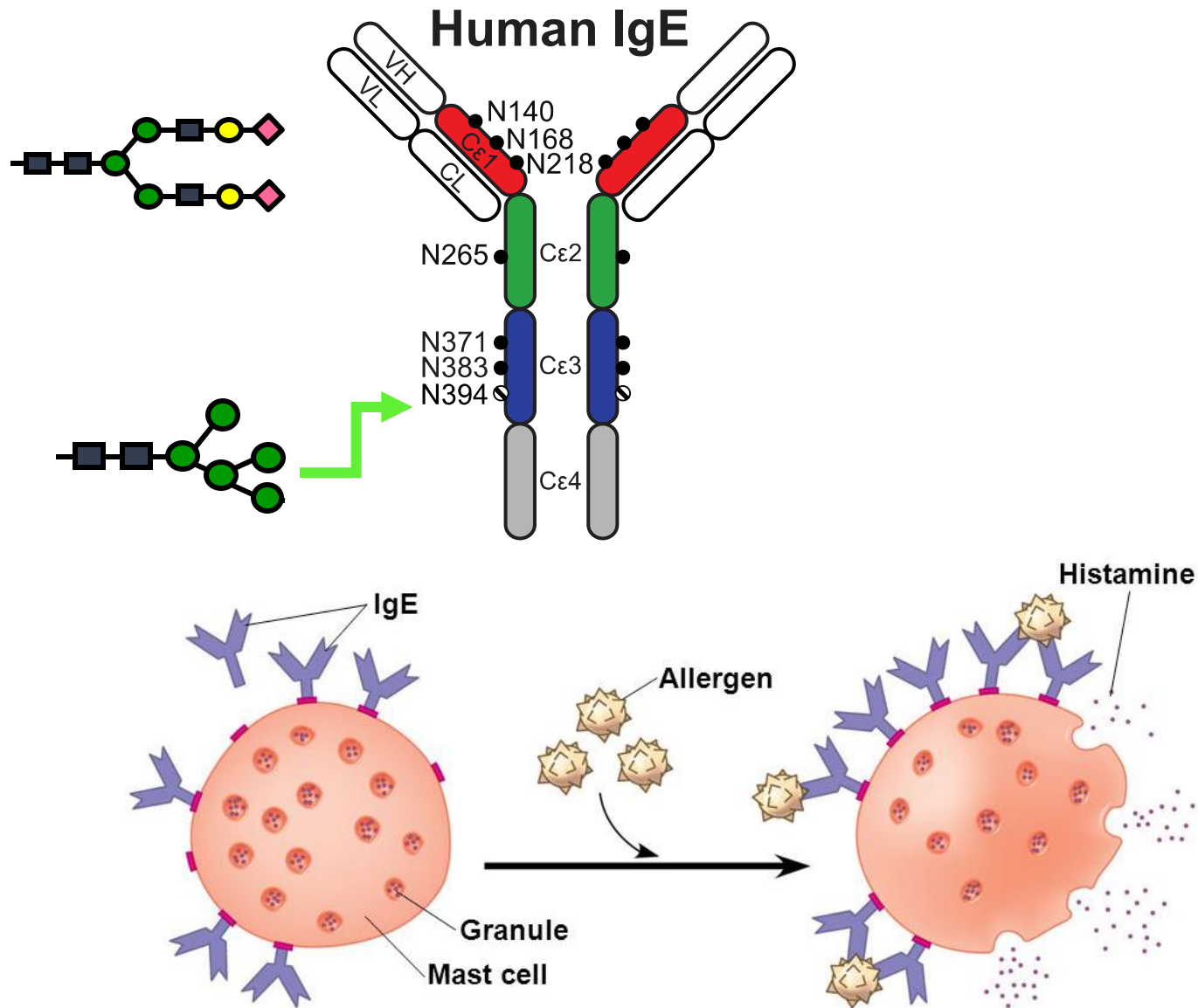
**2 You get sensitized.**  
IgE antibodies bind to the surface of two other types of immune cells: mast cells and basophils.



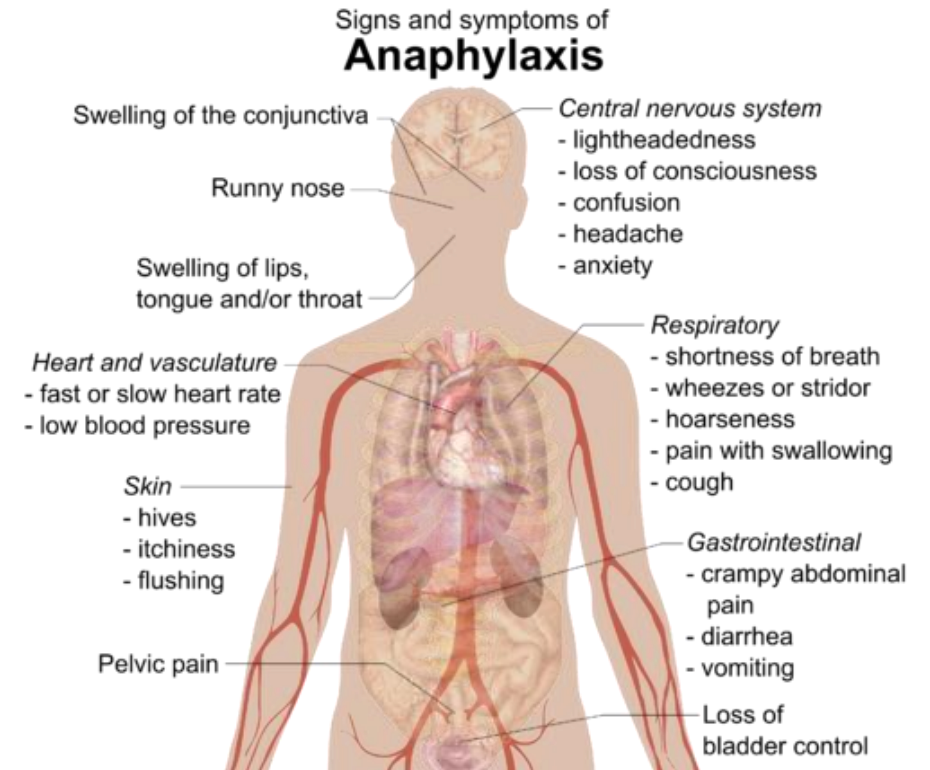
**3 You're exposed again...and react.**  
When an allergen binds to IgE on a mast cell, the cell releases histamine and other chemicals that cause allergy symptoms.

# FOOD ALLERGY BIOLOGY

# IgE antibody biology



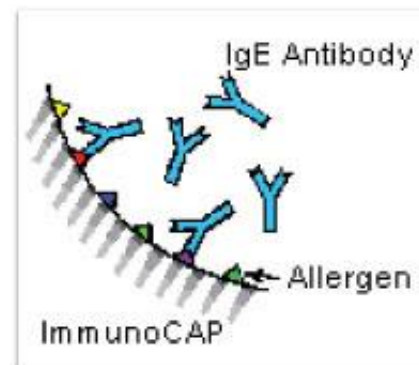
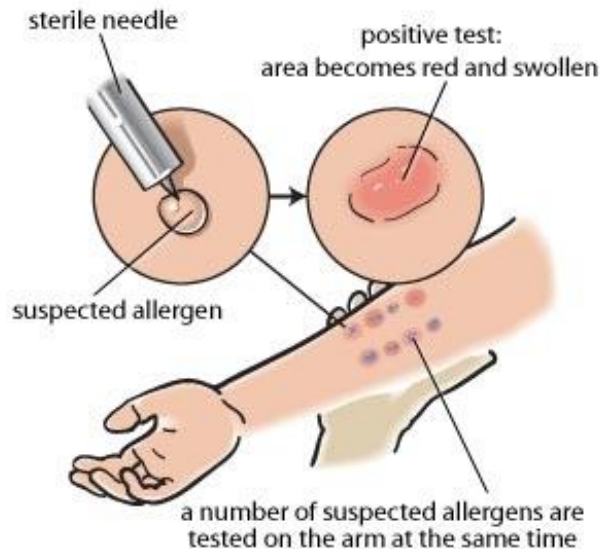
© 2011 Pearson Education, Inc.



# Diagnosis of IgE Mediated Food Allergy: Testing

Positive SPT/sIgE do not correlate well enough with clinical allergy and will over diagnose (~90% sensitivity; ~50% specificity **~50% asymptomatic sensitization**)

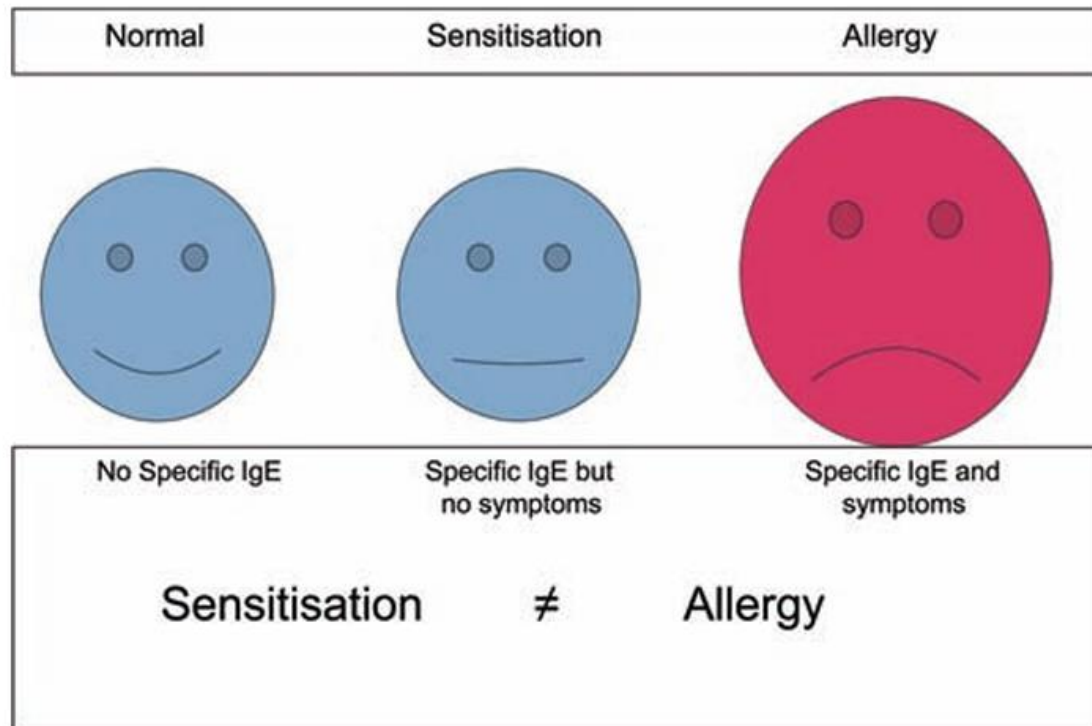
Negative SPT/sIgE essentially exclude IgE antibody (>95% specific)



Boyce J, et al. JACI 2010; 126(6 Suppl):S1-S58;  
Sampson HA, et al. JACI 2014; 134(5):1016-25.e43  
Greenhawt et al. JACI 2020 Dec;146(6):1302-1334.

# SENSITIZATION DOES NOT ALWAYS MEAN ALLERGY!!!!!!

(and this is why allergists are *obsessed* with food challenges...)



	Specific IgE levels (IU/ml) associated with 95% PPV
Egg	≥7
Egg (infants ≤2 years)	≥2
Milk	≥15
Milk (infants ≤2 years)	≥5
Peanuts	≥15
Peanuts (infants ≤2 years)	–
Tree nuts	≥15
Fish	≥20

PPV, positive predictive value.

# IgE antibody biology- False positives

**Table II.** OFC results on foods avoided due to immunoassay or PST

Food group	Avoiding on admission	OFC positive result	OFC negative result	Avoiding on discharge	% Negative
Egg	10	1	9	1	90%
Fruits	10	2*	8	2	80%
Meats	13	0	13	0	100%
Milk	9	0	9	0	100%
Oats	4	0	4	0	100%
Peanut	7	1	6	1	86%
Shellfish	2	0	2	0	100%
Soy	19	1	18	1	95%
Vegetables	6	0	6	0	100%
Wheat	13	3	10	3	77%
Other	18	0	18	0	100%
Totals	111	8	103	8	93%

\*Two positive tests to banana.



TESTING



# How does an allergist test for food allergies?

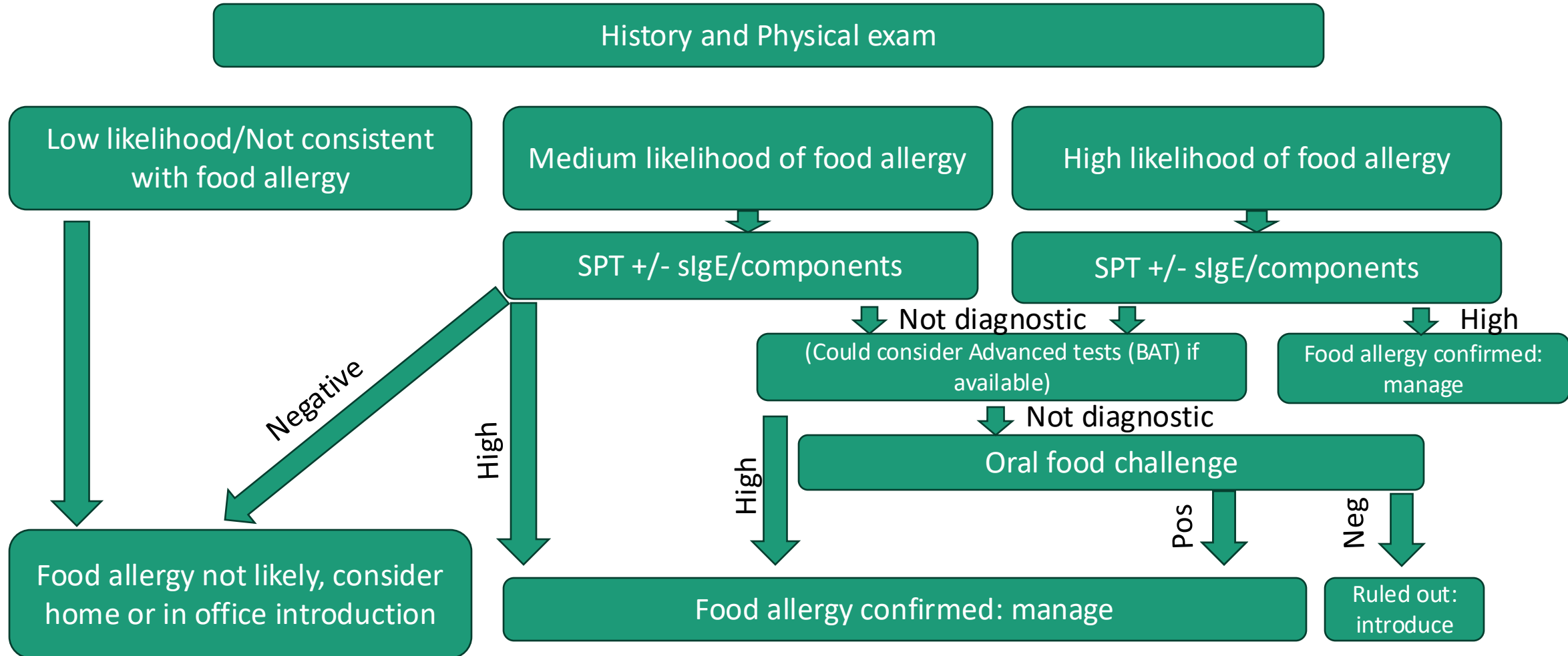
- Differing opinions....
- My approach
  - HISTORY
  - TIMING— symptoms 2+ hours post ingestion very unlikely IgE mediated allergy
  - SKIN TEST
  - SERUM IgE

## 3 possible outcomes

- not allergic, home introduction
- allergic, continued restriction
- unclear → food challenge



# Diagnostic Algorithm for IgE Mediated Food Allergy



# Test before allergist evaluation?

YES! This can help a lot....

BUT ONLY FOR CULPRIT FOOD OR FOODS.



## E 66 Specific Allergens

### Mold /

C. h

A

A

hair

epithelia

mix

Codfish

Salmon

Tuna

### Vegetables

Celery

Broccoli

Bean

Pepper

### Grain

Rice

Wheat

Corn

Soy

Peanut

### Meat

Pork

Beef

Lamb

Chicken

Gelatin

Tomato

Mushroom

Onion

### Mite

D. pterod

D. farinae

B. tropicalis

Cockroach mix

Egg

Shell

Honey

# Cracking the code on pediatric food allergies: Define the problem

- Perception by public: 19-25%<sup>1</sup>
- Estimated convincing food allergy:  
Adults: 10.8%<sup>1</sup> and infants/young children: 7.6%<sup>2</sup>
- Specific allergens: Geographical and cultural variations
- Common comorbidities: asthma (39-48%)<sup>3</sup> **4. atopic dermatitis** (33-80%)<sup>5</sup>, allergic rhinitis (40% in infancy)<sup>4</sup>, latex allergy (28.8%), urticaria (27.8%), and insect sting allergy (22.9%)<sup>1</sup>
- Prevalence increasing – 18% increase between 1997-2007<sup>6</sup>

<sup>1</sup> Gupta et al. JAMA Netw Open 2019, Jan 4;2(1):e185630

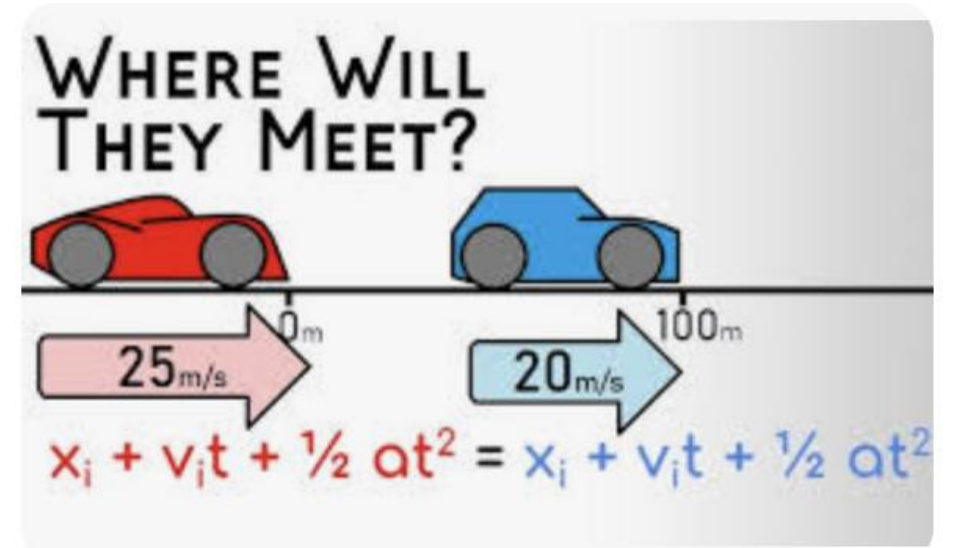
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# FOOD ALLERGIES AND ECZEMA

# Food allergies and eczema



What good data do we have?

HealthNuts study, Australia: 11% kids with FA at age 1, 4% by age 4

- Eval for eczema and oral food challenges (peanut, egg, sesame)

20% of kids with eczema were allergic one of these foods vs. 4% of kids without eczema

1 yo w/eczema has 6X rate of egg allergy, 11X rate of PN allergy compared to those kids without eczema

So... ECZEMA IS A RISK FACTOR FOR FOOD ALLERGY.

# Food allergies and eczema

What good data do we have?



1985 landmark study: 113 kids with severe eczema had 101 positive DBPCFCs:  
84% with skin symptoms

Recent systematic review: 18 studies → food sensitization 6X higher in AD kids  
AD earlier and persistent → higher risk of FA

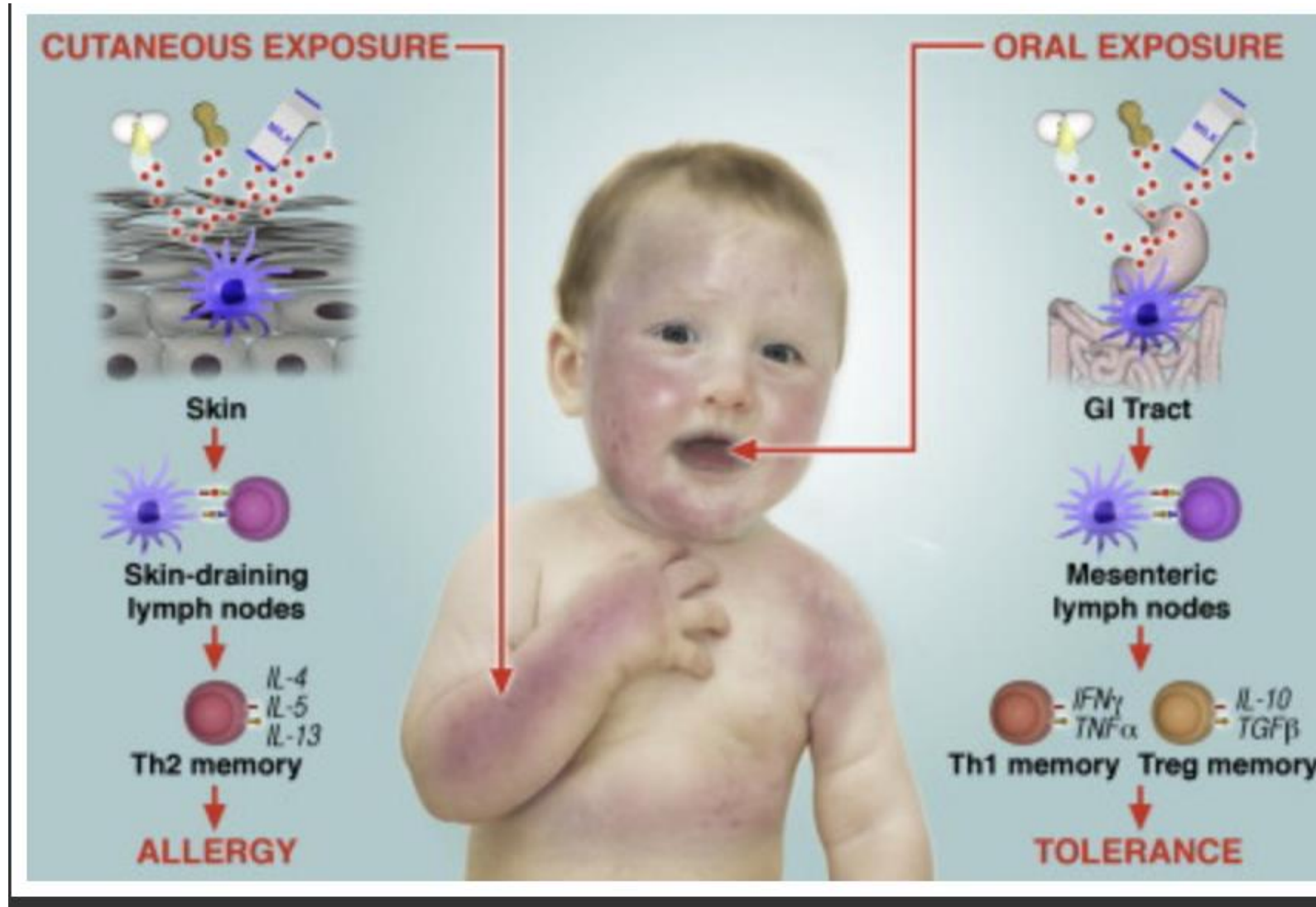
Danish Allergy Research Center: cohort study of 562 babies → AD preceeds FA

J Pediatr 1985;107:669-75.

J Allergy Clin Immunol 2016;137:1071-8.



# Food allergies and eczema



Clin Exp Allergy 2018;48:586-93.

Nat Genet 2006;38:441-6.

J Allergy Clin Immunol 2013;132:239-42.

J Allergy Clin Immunol 2014;134:867-875.e1.

J Allergy Clin Immunol Pract 2020;8:1721-1724.e6

J Allergy Clin Immunol 2021;147:967-976.e1.



# Food allergies and eczema

It's complicated!!??! Why?

Eczema and food allergy rising in incidence

Diagnosing FA is nuanced and testing quite imperfect

Dry skin isn't eczema

FA introduction recs have changed dramatically....

**SENSITIZATION DOES NOT EQUAL ALLERGY**



# Food allergies and eczema



## Laboratory findings

*n/N (%)*

Elevated total serum IgE	1303/2496 (52.2)
Eosinophilia	740/2327 (31.8)
Positive allergen-specific IgE	355/1153 (30.8)
Elevated total serum IgE and/or eosinophilia and/or positive allergen-specific IgE	1548/2662 (58.2)

# Food allergies and eczema

You have no food allergy but do have food specific IgE...

Take out the food... and you GET ALLERGY

- Food removal in AD may promote immediate FA symptoms, in as many as 13% to 20% of participants with AD



Wheat



Tree Nuts



Peanuts



Eggs



Shellfish



Milk



Fish



Soy



Sesame

# Food allergies and eczema

## Guidelines:

### NIH/NIAID (and others): 2010

“For children less than 5 years of age with moderate-to-severe eczema, the EP recommended that clinicians consider evaluation for milk, egg, peanut, wheat, and soy sensitization, if at least one of the following conditions were present: (1) **the child has persistent AD in spite of optimized management and topical therapy** or (2) the child has a reliable history of an immediate reaction after ingestion of a specific food.”

# Tide turning?

## Primary Prevention of Allergic Disease Through Nutritional Interventions

---

David M. Fleischer, MD<sup>a</sup>, Jonathan M. Spergel, MD, PhD<sup>b</sup>, Amal H. Assa'ad, MD<sup>c</sup>, and Jacqueline A. Pongratic, MD<sup>d</sup>

*Denver, Colo; Philadelphia, Pa; Cincinnati, Ohio; and Chicago, Ill*

- Delayed introduction of solid foods, especially the highly allergenic foods, may increase the risk of food allergy or eczema.<sup>81-87</sup>

- Taken collectively, the above-mentioned studies support the general notion that the highly allergenic foods may be introduced earlier into the diet, that is, as complementary foods. Whether the earlier introduction of these highly allergenic foods proves to truly prevent the individual food allergies remains to be seen, because interventional studies need to be performed to support the limited data reported here from these observational studies.

# Guidelines disaster...

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  - ? Avoidance in pregnancy- YES
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Taking the LEAP

# Big breakthrough.... January 2015



*The NEW ENGLAND JOURNAL of MEDICINE*

## ORIGINAL ARTICLE

### Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy

George Du Toit, M.B., B.Ch., Graham Roberts, D.M., Peter H. Sayre, M.D., Ph.D.,  
Henry T. Bahnson, M.P.H., Suzana Radulovic, M.D., Alexandra F. Santos, M.D.,  
Helen A. Brough, M.B., B.S., Deborah Phippard, Ph.D., Monica Basting, M.A.,  
Mary Feeney, M.Sc., R.D., Victor Turcanu, M.D., Ph.D.,  
Michelle L. Sever, M.S.P.H., Ph.D., Margarita Gomez Lorenzo, M.D.,  
Marshall Plaut, M.D., and Gideon Lack, M.B., B.Ch., for the LEAP Study Team\*





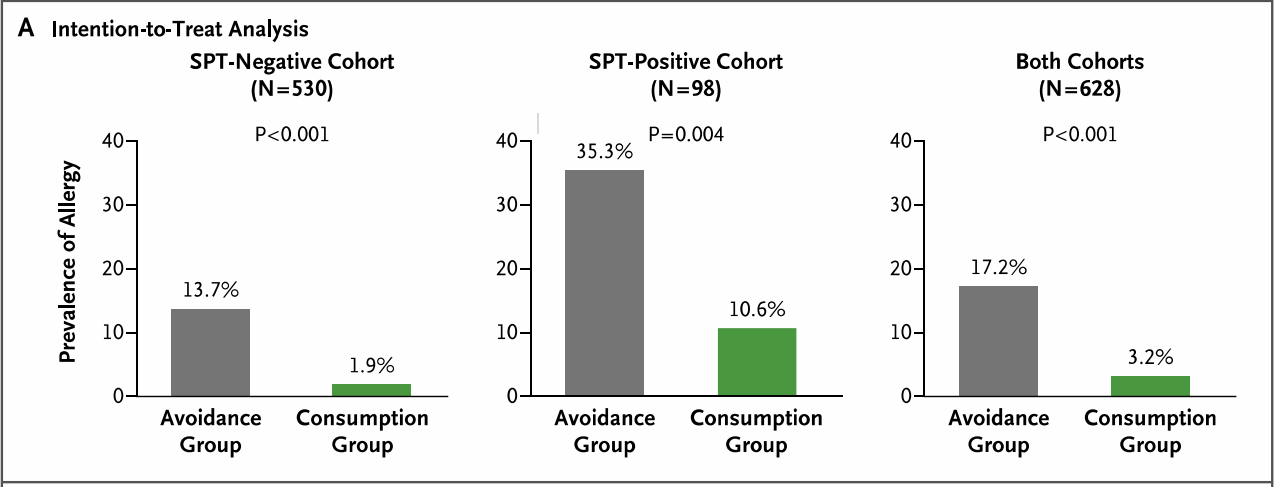
# LEAP (Learning early about peanut allergy)



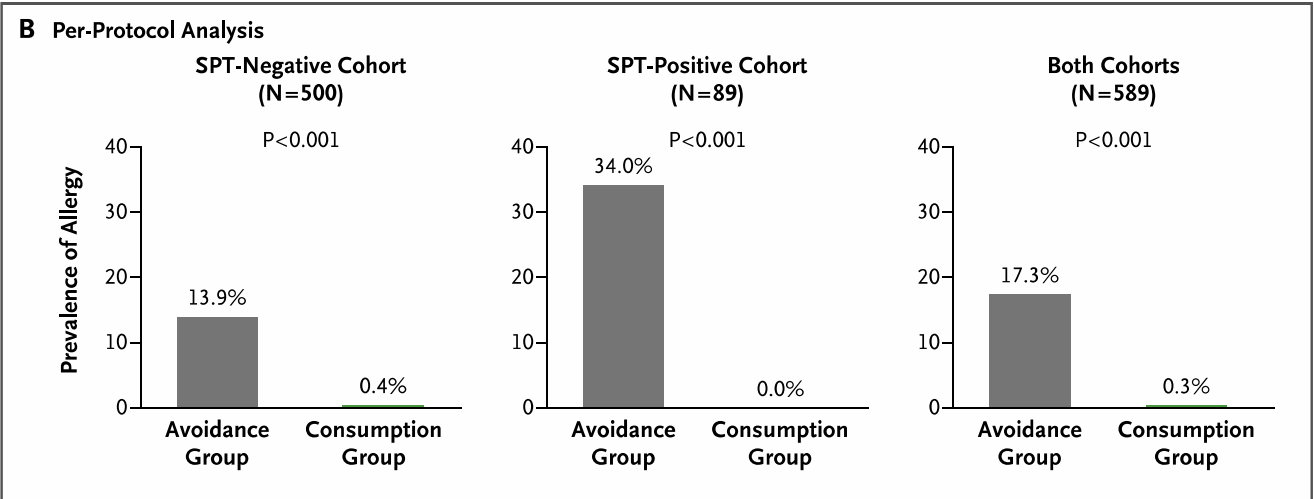
**Idea**: determine whether early introduction of dietary PN → primary and secondary prevention of PN allergy

- Randomized, open label controlled trial
- Enrollment 12/06-5/09: infants >4 months, < 11 months
- Infants *with severe eczema, egg allergy or both*
- Divided into 2 cohorts...

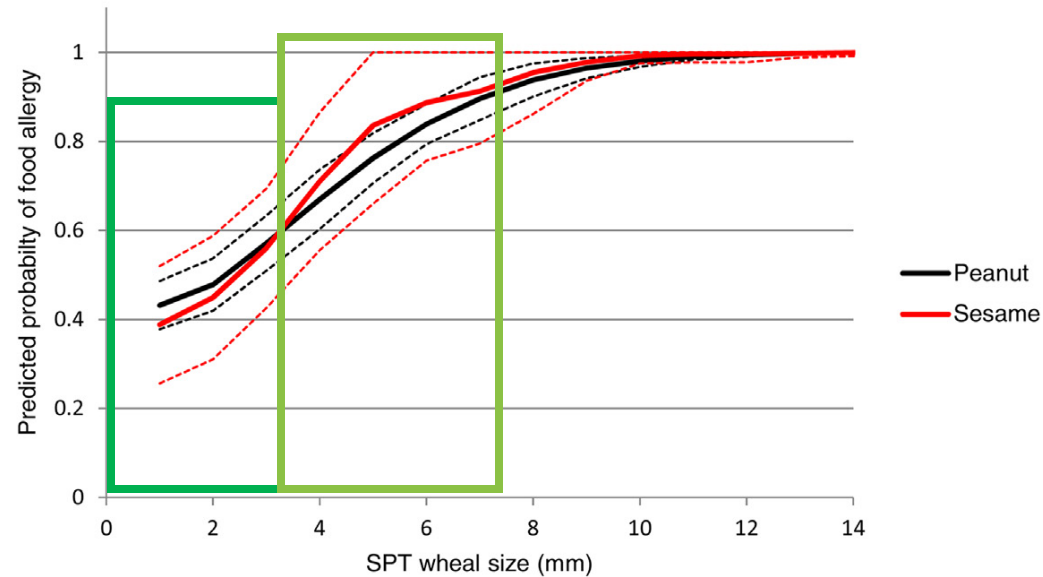
# LEAP (Learning early about peanut allergy)



**86% reduction in PN allergy w/ NEG SPT**  
**70% reduction in PN allergy w/POS SPT**



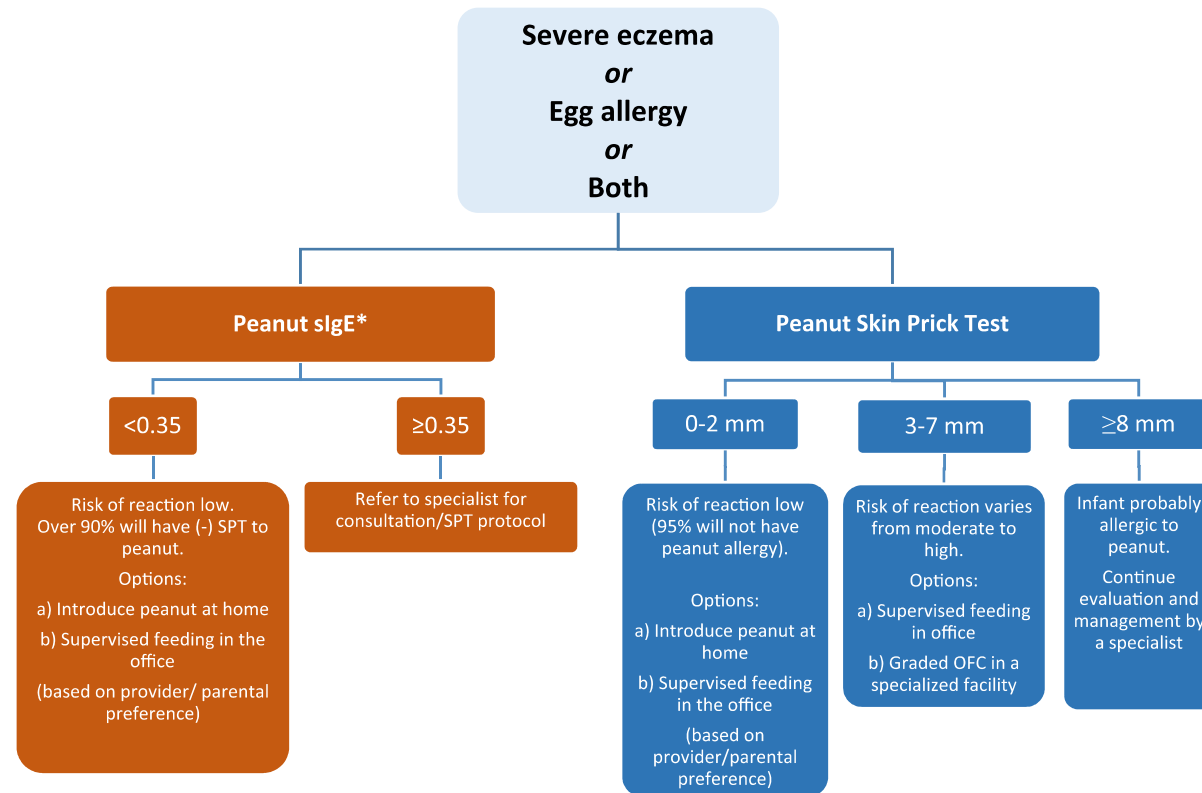
# HealthNuts Study



**FIG 2.** The probability of food allergy for infants with SPT responses and sIgE levels equal to or greater than the stated threshold.

- 0-2 mm low risk (LEAP too)
- 3-7 mm moderate to high risk of reactions

# New NIAID EP guidelines... 2017



\* To minimize a delay in peanut introduction for children who may test negative, testing for peanut-specific IgE may be the preferred initial approach in certain health care settings. Food allergen panel testing or the addition of sIgE testing for foods other than peanut is not recommended due to poor positive predictive value.

**FIG 1.** Recommended approaches for evaluation of children with severe eczema and/or egg allergy before peanut introduction.

# Food allergies and eczema

Guidelines:

NIH/NIAID (and others): updated 2017

“For infants with severe eczema, egg allergy, or both, exposure to age-appropriate peanut-containing foods was recommended as early as 4 to 6 months of age (after appropriate evaluation).”

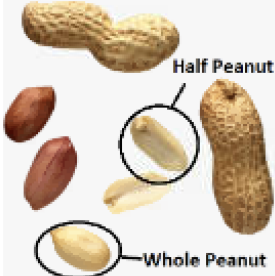



But... only test for relevant foods bc of POTENTIAL FOR IATROGENIC HARM...





Do not recommend elimination based solely on positive blood and skin tests



TREATMENT

# Treatments: “Bite safety” goal

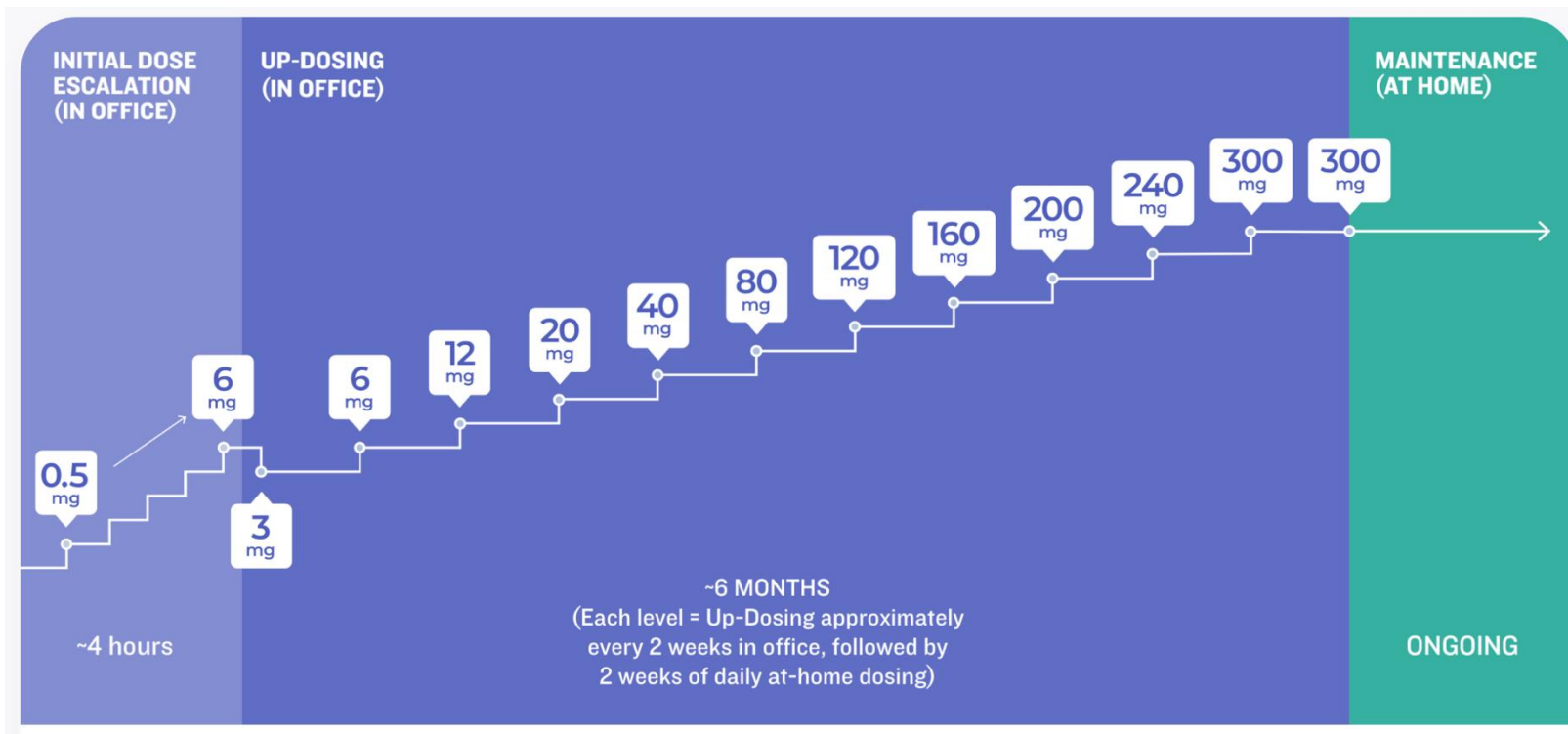
Food	Picture	Amount to Eat
<b>Peanuts</b> shelled peanut kernel, dry roasted Please choose regular size (not jumbo sized) peanuts  Label states: 1 oz = 7 g Protein  Not recommended for children under 5 due to choking risk.		1 and ½ peanuts (or 3 peanut halves)  Peanuts can be eaten with or without the skin on.  Equals approximately ~330 - 360 mg of peanut protein
<b>Peanut Butter</b> Any brand with equivalent protein content (7-8 g protein per 2 tbsp serving)  Label states: 2 Tbsp = 7g – 8g Protein		¼ teaspoon (level)  May be thinned with water or other food (e.g. applesauce)  Equals approximately 290 - 330 mg of peanut protein
<b>PB2 (powdered peanut butter)</b> PB2 Original, PB2 Organic, or PB2 Pure (Do not use PB2 Performance or flavored varieties)  Label states: 2 Tbsp = 6 g Protein		⅓ teaspoon (level) Or ⅝ teaspoon (level)  Link for measuring spoon: <a href="#">Beryler 1/3 Teaspoon Single Measuring Spoon</a>  Equals approximately 333 mg of peanut protein (375 mg for ⅝ tsp)
<b>Bamba</b> <i>*Must use Osem Brand Bamba*</i> Other brands may contain more or less peanut protein.  Label states: 1 oz = 5 g Protein		3 puffs  Note: Some brands of Bamba contain gluten  Equals approximately 285 mg of peanut protein

<b>Reese's Pieces</b> <i>*Must use Reese's Brand*</i> Other brands may contain more or less peanut protein.  Label states: 51 pieces (40 g) = 4 g protein  Not recommended for children under 5 due to choking risk.		4 Reese's Pieces  Equals approximately 340 mg of peanut protein
<b>Reese's Peanut Butter Cups Unwrapped Minis</b> <i>*Must use Reese's Brand*</i> Other brands may contain more or less peanut protein.  Label States: 9 Pieces = 3 g protein		2 mini cups  Note: Contains milk  Equals approximately 365 mg of peanut protein
<b>Reese's Peanut Butter Cups Miniatures (wrapped)</b> <i>*Must use Reese's Brand*</i> Other brands may contain more or less peanut protein.  Label States: 5 Pieces = 4 g protein		½ miniature cup  Note: Contains milk  Equals approximately 300 mg of peanut protein
<b>Peanut M&amp;Ms</b> <i>*Must use M&amp;M's Brand*</i> Other brands may contain more or less peanut protein.  Label states: 1.5 ounce (¼ cup) = 4 g protein  Not recommended for children under 5 due to choking risk.		2 peanut M&Ms  Note: Contains milk  Equals approximately 295 mg of peanut protein



# Treatments: Oral immunotherapy

- Daily ingestion of food allergen with incremental up dosing under allergist supervision until goal maintenance dose is reached.
- Clinical trial meta-analyses suggest OIT successful desensitization rates range up to 84%.
- Palforzia FDA approved in 2020: **ages 4-17yo**



# Treatments: Oral immunotherapy

## ***DON'Ts***



Do not have the child eat peanuts or peanut products as part of their diet.



Do not give the child their daily dose of PALFORZIA on the day of an appointment, since they will be receiving some from their allergist.



Do not take more than one dose of PALFORZIA in a single day.



Do not give any more doses if the child has missed a dose of PALFORZIA. Instead, contact their allergist for next steps in continuing treatment.



Do not let the child swallow the capsule or inhale the powder.



Do not give the child PALFORZIA if they are very hot or have just participated in any strenuous physical activity, like a game or sport, and still have a high heart rate.



Do not let the child participate in sports or other strenuous physical activity or take a hot bath or shower within three hours after taking PALFORZIA.

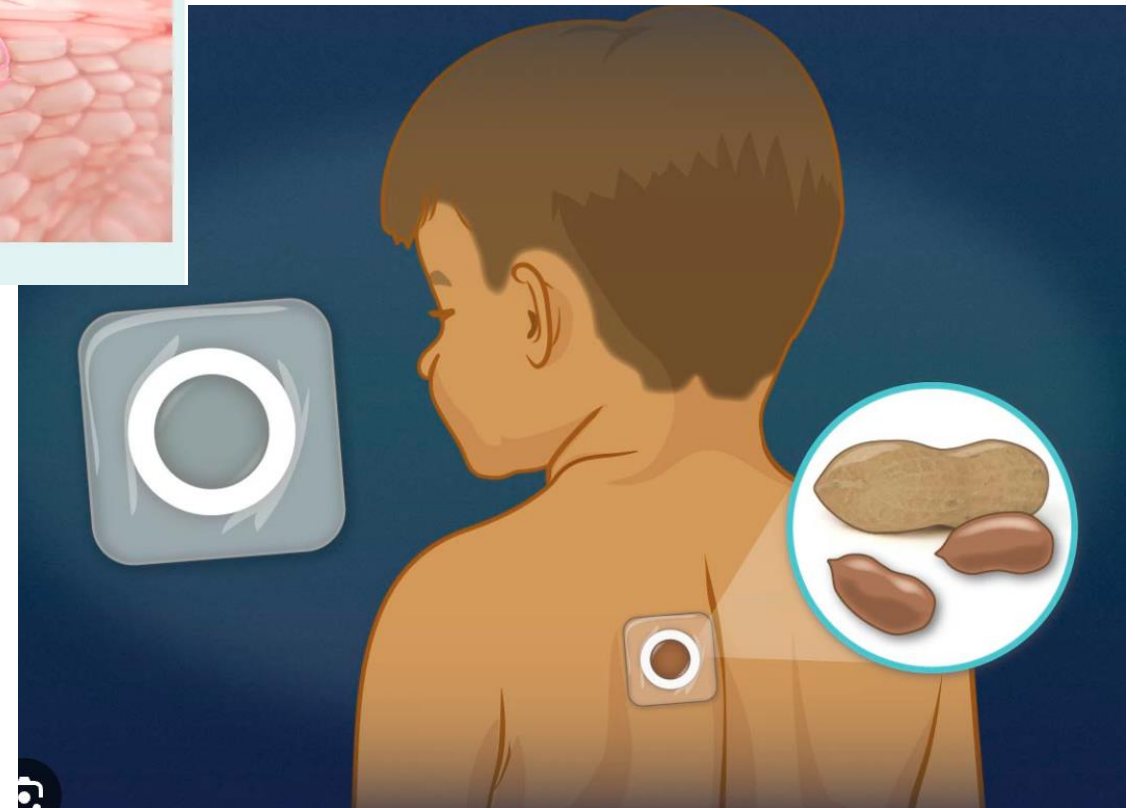
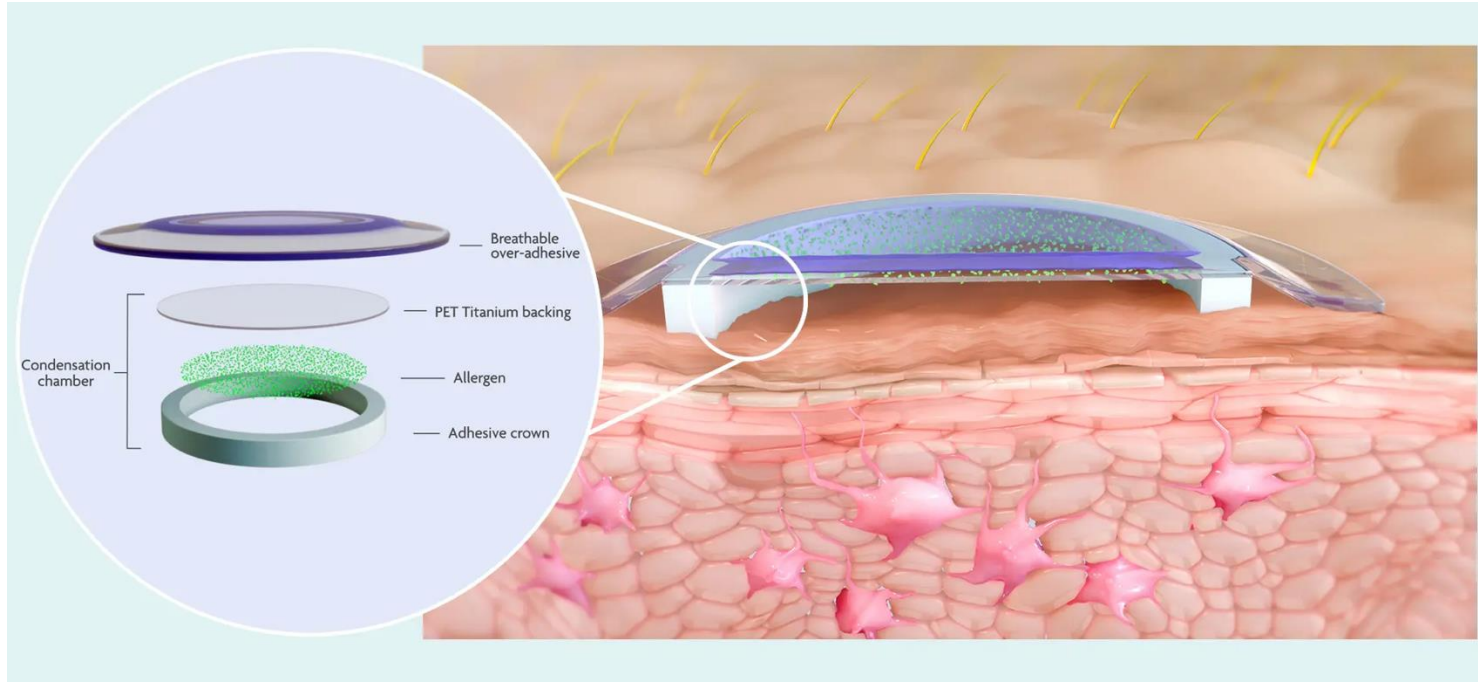
# Treatments: Epicutaneous immunotherapy (patch)

- Epicutaneous immunotherapy (EPIT) uses daily administrations of a proprietary patch containing allergen
- Best studied in peanut in multiple phase 2 and phase 3 studies<sup>1</sup>
- In the most recent phase 3 trial involving peanut allergic **1–3 year-olds**: 67% of tolerated either 300 or 1000 mg peanut depending on baseline reactivity<sup>2</sup>
- All patients had adverse events during EPIT with 99.2% of patients having mild reactions, 92.2% having moderate reactions, 25.8% having severe reactions, and 8.6% having serious reactions according to the Common Terminology Criteria for Adverse Events, version 4.03
- 7.8% of EPIT patients reported anaphylaxis

<sup>1</sup>Kim and Burks. Allergy. 2020 Jun;75(6):1337-1346.

<sup>2</sup>Greenhawt et al. N Engl J Med. 2023; 388(19):1755-1766.

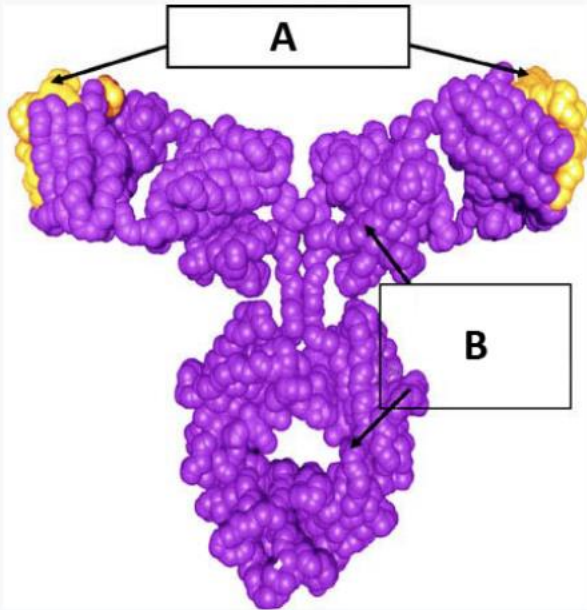
# Treatments: Epicutaneous immunotherapy (patch)



# Treatments: Omalizumab/anti-IgE

Anti-IgE: Omalizumab is the best studied biologic in the setting of food allergy

Shown in Phase 2 studies to improve the speed and efficacy of single or multiple foods when used as an adjuvant



Omalizumab structure: (A) murine complementarity-determining region and (B) IgG1k human framework

Approach is to use a modified asthma-based protocol<sup>4</sup>

Highly dosing has been studied and shown to facilitate sensitization to multiple foods<sup>5</sup>

<sup>1</sup>Andorf S et al. Lancet Gastroenterol Hepatol. 2018;3(2):85-94.

<sup>2</sup>Andorf S et al. EClinicalMedicine. 2019;7:27-38.

<sup>3</sup>MacGinnitie AJ et al. J Allergy Clin Immunol. 2017;139(3):873-881.e8.

<sup>4</sup>Sindher SB et al. Ann Allergy Asthma Immunol. 2023;131(1):29-36.

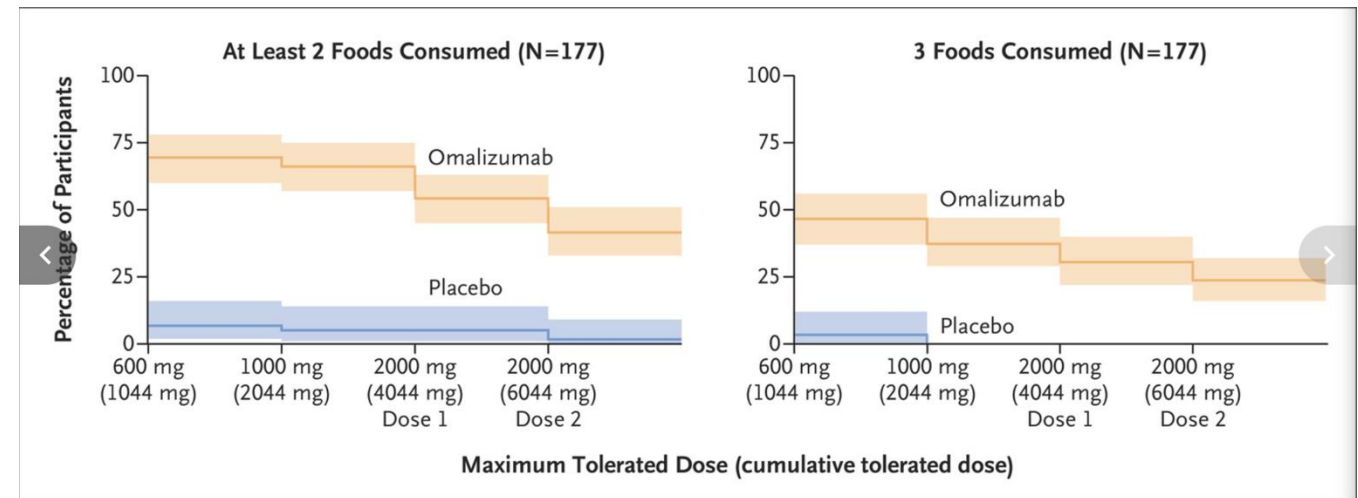
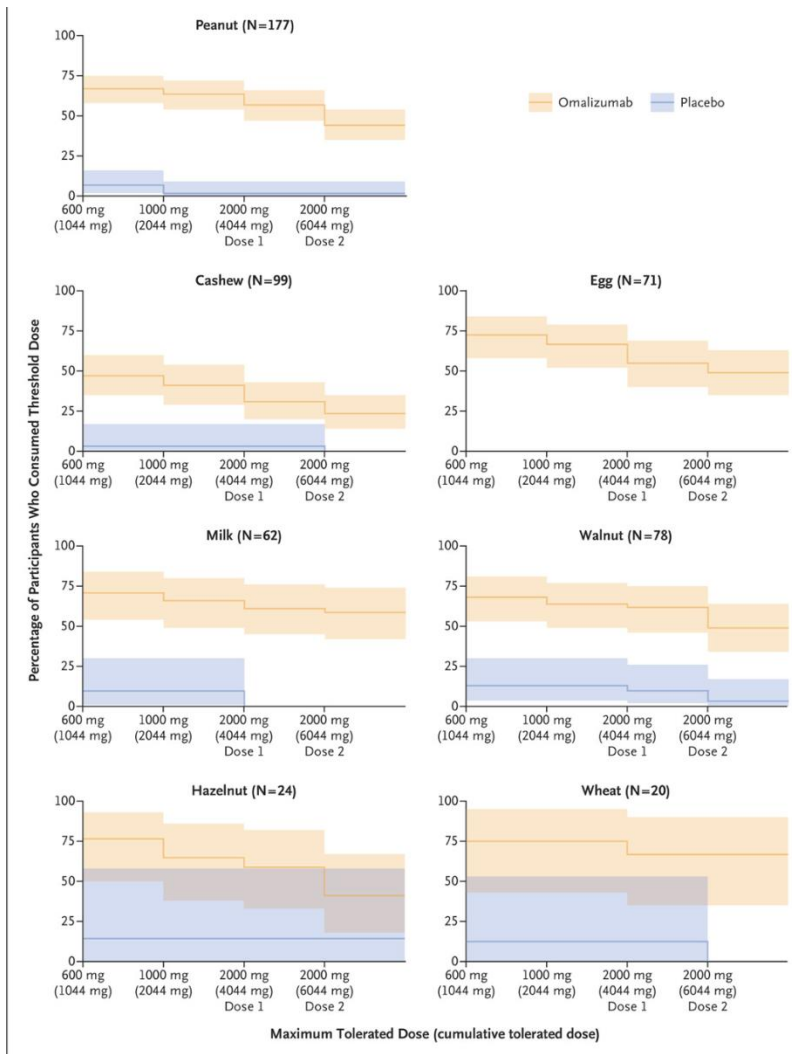
<sup>5</sup>Sindher SB et al. 2022;77(6):1873-1884.



# Treatments: Omalizumab/anti-IgE

## Stage 1 results of the Phase 3 OUtMATCH trial (NCT03881696):

Omalizumab allowed ~2/3 of participants to consume 1000 mg of peanut, egg, milk, walnut, hazelnut, or wheat  
Lower protection observed for consuming cashew (41% could consume 1000 mg)



# Treatments: Omalizumab/anti-IgE

Omalizumab approved by the FDA for immunoglobulin E-mediated food allergy in individuals 1 year or older with allergies to one or more foods

To be used in conjunction with food allergen avoidance

Not approved as an emergency treatment and does not replace epinephrine

Should not be used by individuals who have a history of hypersensitivity reactions to omalizumab or its components







TOWARD **PREVENTION**



**5.6 million children** have food allergies in the US. That's roughly two children in every classroom.

Gupta RS, Warren CM, Smith BM, et al. The public health impact of parent-reported childhood food allergies in the United States. *Pediatrics*. 2018;142(6):e20181235. doi:10.1542/peds.2018-1235



**377% increase** in medical procedures to treat severe food allergy reactions between 2007 and 2016. Two-thirds of these reactions were in children.

FAIR Health. Food allergies: a growing health concern. 2017. Accessed May 8, 2023.



**Up to 80%** of peanut allergies are preventable with early allergen introduction.

Du Toit G, Roberts G, Sayre PH, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med*. 2015;372(9):803-813. doi:10.1056/NEJMoa1414850

# Moving toward food allergy PREVENTION...

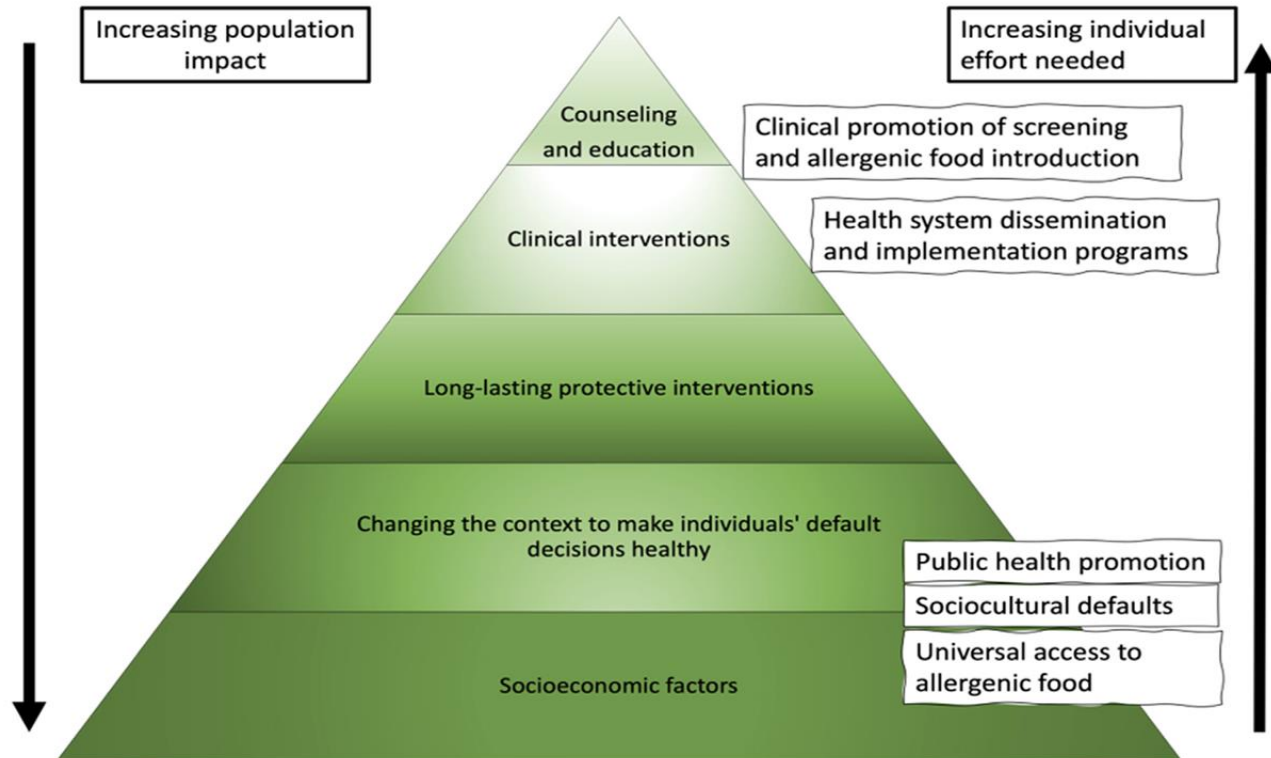
- Where pediatricians are heroes....



# Moving toward food allergy PREVENTION...



FIGURE 1. Conceptual model of latent periods from exposure to sensitization and sensitization to clinical allergy.



# Moving toward food allergy PREVENTION...

<b>TABLE 2</b> Examples to Overcome Barriers to Implementation of Food Allergy Prevention Discussions in the Primary Care Office		
<b>Time in the Office</b>	<b>Discussion Points</b>	<b>Parental Concerns</b>
Incorporate into well-child visits at every age.	Proactively address in a positive manner; don't wait for families to ask.	Do not rub the food on your child's skin before <del>letting them eat it</del>
Use preformed smartphrases in the electronic medical record.	Introducing peanut and other allergenic foods in age-appropriate forms is safe for infants.	Food allergy reactions occur within 1–2 h of ingestion and typically cause hives, swelling, or vomiting. If this does not occur, that is reassuring and can keep in their diet.
Have ancillary staff provide written handouts.	The benefit of preventing food allergy outweighs the risk for severe allergic reaction.	Address common childhood conditions unrelated to food allergy that may wax and wane as new foods are introduced (ie, gastroesophageal reflux, constipation or loose stools, and eczema).
	Testing before introduction can cause a delay in ingestion and false-positive results.	Offer to be available for follow-up questions or concerns.
		You do not need to have epinephrine prescribed or available before introducing foods to infants (unless they have existing food allergy).

Where did the 3 day rule of food introduction come from--- does anyone know????  
Can we move past it????

# Moving toward food allergy PREVENTION...

**TABLE I.** Including potential food allergens for allergy prevention and/or healthy infant feeding during the first year of life

Food allergen	Choose healthy infant foods	How much/how often as part of the infant's complementary diet
Foods known to have prevention benefits of early and sustained introduction (start peanut, egg, and milk when developmentally ready at the beginning of complementary feeding, around 4-6 months of age)		
Peanut	Thinned peanut butter or peanut powder: Peanut butter should be thinned with breast milk, water, or formula or mixed into a pureed food (eg, 2 teaspoons of peanut butter mixed with 2-3 teaspoons of liquid)	Approximately 1-2 teaspoons of peanut butter/powder per serving, served 2-3 times per week as tolerated
Egg	Serve well-cooked egg mashed with pureed foods or chopped and served as finger food	Approximately 1/3 of a well-cooked egg, 2-3 times per week
Cow's milk	Plain, full fat yogurt can be mixed into pureed fruit or vegetable; cow's milk should not substitute for breast milk or infant formula (Note: for infants who were introduced formula in the first few days of life but have fully transitioned to breast milk, continuing regular formula exposure may reduce the risk of cow's milk allergy)	2-4 fluid ounces of yogurt per day (Note: 2-3 fluid ounces of formula per week)
Foods with not known preventions benefits of delay, balanced by not known health harms of introduction with infant-safe forms of food		
Tree nuts	Smooth, thinned nut butters (eg, almond, cashew, hazelnut, pistachio, walnut, and pecan)	≥1/2 ounce of nuts per week (approximately 3 teaspoons of nut butter)
Wheat	Infant wheat cereals (iron-fortified for the breastfed infant); whole-wheat toast, pasta, or crackers for older infants	1/2 to 1 ounce total grains per day; 1/2 ounce wheat serving is equal to 1/4 cup fortified infant wheat cereal, 1/4 cup pasta, or 1/2 slice of bread
Soy	Soft tofu	2 tablespoons per serving
Sesame	Tahini is sesame paste typically served as an ingredient in hummus or as tahini dipping sauce for finger foods like vegetables (blended with water, lemon juice, olive oil, and herbs for flavoring)	≥1/2 ounce seeds per week (approximately 3 teaspoons)
Seafood	Low mercury finfish	1 ounce per serving, 3 times per week



# Moving toward food allergy PREVENTION... Peanut

## Peanut

Thinned peanut butter or peanut powder: Peanut butter should be thinned with breast milk, water, or formula or mixed into a pureed food (eg, 2 teaspoons of peanut butter mixed with 2-3 teaspoons of liquid)

Approximately 1-2 teaspoons of peanut butter/ powder per serving, served 2-3 times per week as tolerated

### Four Recipe Options, Each Containing Approximately 2g of Peanut Protein

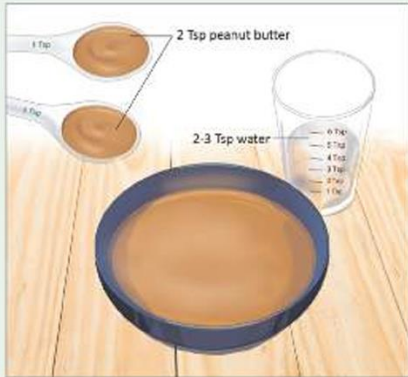
Note: Teaspoons and tablespoons are US measures (5 and 15 mL for a level teaspoon or tablespoon, respectively).



Option 1: Bamba (Osem, Israel), 21 pieces (approximately 2 g of peanut protein)

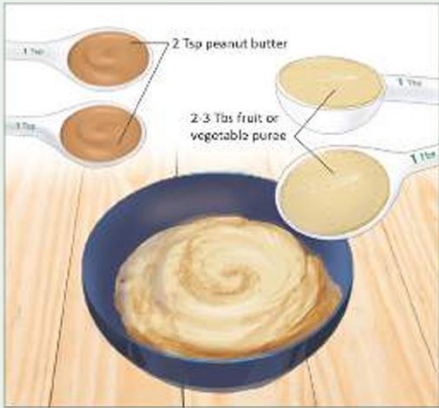
Note: Bamba is named because it was the product used in the LEAP trial and therefore has proven efficacy and safety. Other peanut puff products with similar peanut protein content can be substituted.

- a. For infants less than 7 months of age, soften the Bamba with 4 to 6 teaspoons of water.
- b. For older infants who can manage dissolvable textures, unmodified Bamba can be fed. If dissolvable textures are not yet part of the infant's diet, softened Bamba should be provided.



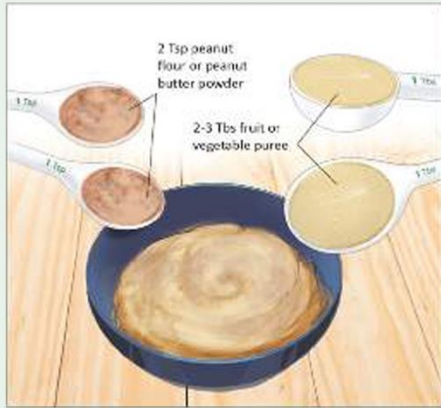
Option 2: Thinned smooth peanut butter, 2 teaspoons (9-10 g of peanut butter; approximately 2 g of peanut protein)

- a. Measure 2 teaspoons of peanut butter and slowly add 2 to 3 teaspoons of hot water.
- b. Stir until peanut butter is dissolved, thinned, and well blended.
- c. Let cool.
- d. Increase water amount if necessary (or add previously tolerated infant cereal) to achieve consistency comfortable for the infant.



Option 3: Smooth peanut butter puree, 2 teaspoons (9-10 g of peanut butter; approximately 2 g of peanut protein)

- a. Measure 2 teaspoons of peanut butter.
- b. Add 2 to 3 tablespoons of pureed tolerated fruit or vegetables to peanut butter. You can increase or reduce volume of puree to achieve desired consistency.



Option 4: Peanut flour and peanut butter powder, 2 teaspoons (4 g of peanut flour or 4 g of peanut butter powder; approximately 2 g of peanut protein)

- Note: Peanut flour and peanut butter powder are 2 distinct products that can be interchanged because they have a very similar peanut protein content.
- a. Measure 2 teaspoons of peanut flour or peanut butter powder.
  - b. Add approximately 2 tablespoons (6-7 teaspoons) of pureed tolerated fruit or vegetables to flour or powder. You can increase or reduce volume of puree to achieve desired consistency.

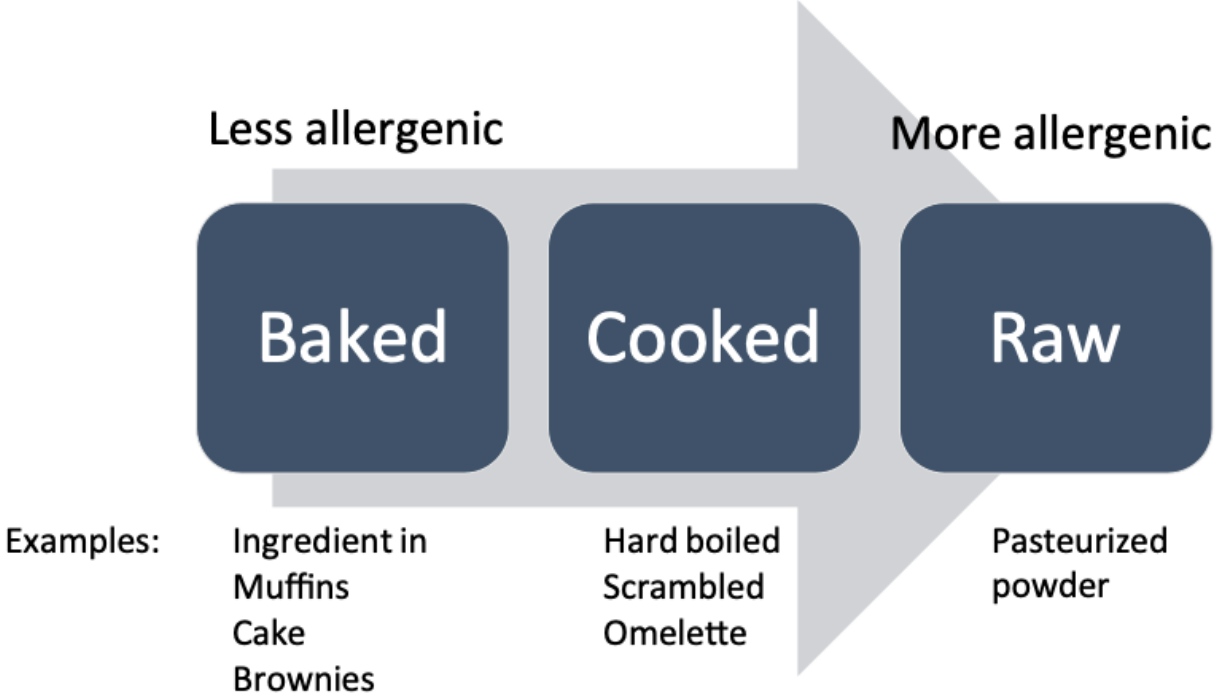
Brands: Skippy/Teddie PBs, PB2 powder

Addendum Guidelines for the  
Prevention of Peanut Allergy  
in the United States

Report of the NIAID-Sponsored Expert Panel



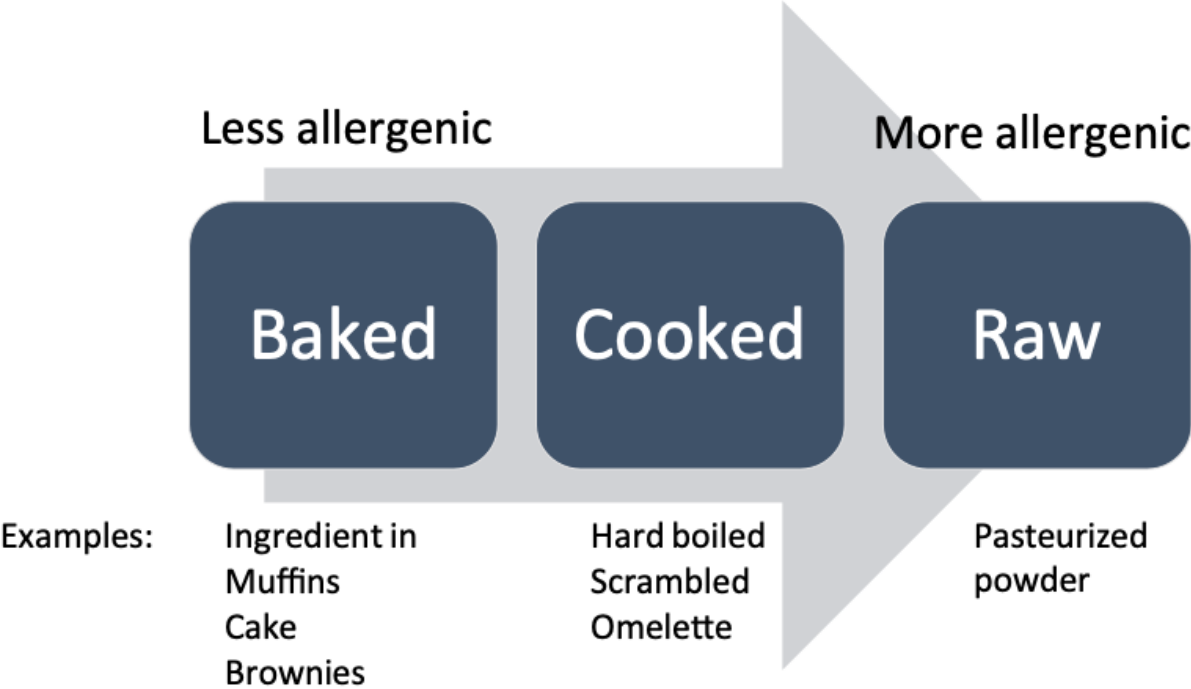
Egg	Serve well-cooked egg mashed with pureed foods or chopped and served as finger food	Approximately 1/3 of a well-cooked egg, 2-3 times per week
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# Moving toward food allergy PREVENTION... Cow's milk

Cow's milk	Plain, full fat yogurt can be mixed into pureed fruit or vegetable; cow's milk should not substitute for breast milk or infant formula (Note: for infants who were introduced formula in the first few days of life but have fully transitioned to breast milk, continuing regular formula exposure may reduce the risk of cow's milk allergy)	2-4 fluid ounces of yogurt per day (Note: 2-3 fluid ounces of formula per week)
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# Moving toward food allergy PREVENTION... Tree nuts, wheat, soy, sesame, seafood

Foods with not known preventions benefits of delay, balanced by not known health harms of introduction with infant-safe forms of food		
Tree nuts	Smooth, thinned nut butters (eg, almond, cashew, hazelnut, pistachio, walnut, and pecan)	≥1/2 ounce of nuts per week (approximately 3 teaspoons of nut butter)
Wheat	Infant wheat cereals (iron-fortified for the breastfed infant); whole-wheat toast, pasta, or crackers for older infants	1/2 to 1 ounce total grains per day; 1/2 ounce wheat serving is equal to 1/4 cup fortified infant wheat cereal, 1/4 cup pasta, or 1/2 slice of bread
Soy	Soft tofu	2 tablespoons per serving
Sesame	Tahini is sesame paste typically served as an ingredient in hummus or as tahini dipping sauce for finger foods like vegetables (blended with water, lemon juice, olive oil, and herbs for flavoring)	≥1/2 ounce seeds per week (approximately 3 teaspoons)
Seafood	Low mercury finfish	1 ounce per serving, 3 times per week

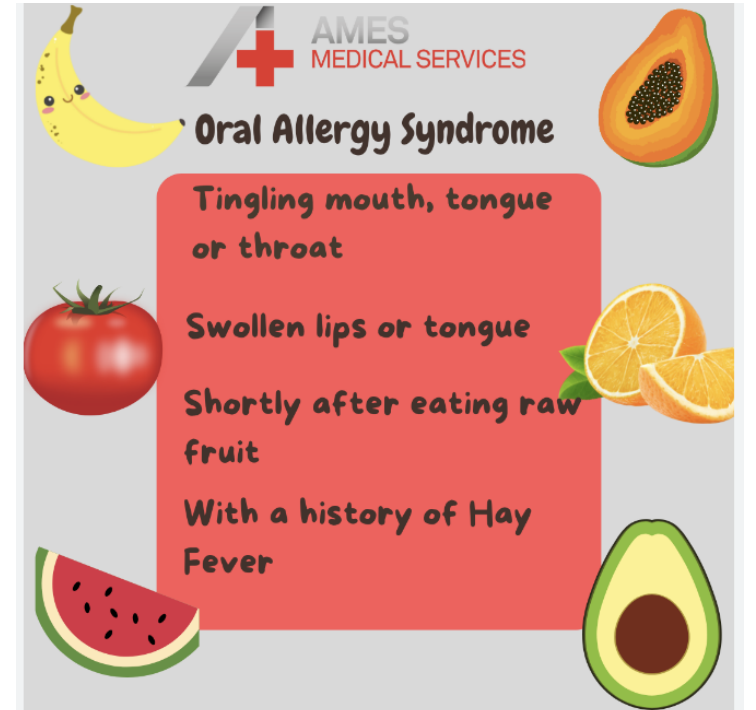
## Brands:

## Tree nuts:

- Walnut**-Crazy Go Nuts walnut butter or shelled diamond walnuts
- Pecan**-Green Valley pecans or Purely Pecans pecan butter
- Brazil nut**- Food to live
- Cashew**- Artisana raw organic cashew butter, Mara Natha cashew butter, or Sunshine nut company cashews
- Pistachio**- Wonderful pistachios
- Almond**- Barney butter, Madi K's whole almonds
- Hazelnut**- Artisana Hazelnut Cacao spread, Trader Joe's hazelnuts
- Macadamia nuts**- Hamakua brand
- Pine nuts**- any brand

# OAS

A rapid fire primer....



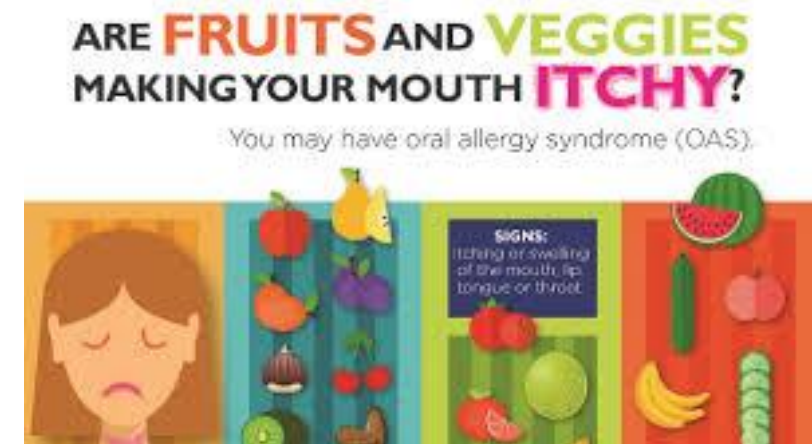
# Oral allergy syndrome (pollen-food syndrome)

- Occurs when pollen antibodies recognise and react to similar proteins in plant foods
- Affects 5-48% of school age children and 20-70% of adults sensitized to pollen<sup>1,2</sup>
- Characterized by the onset of mild oro-pharyngeal symptoms within minutes of eating trigger foods
- $\leq 8\%$  of people with systemic symptoms, typically mild
- Oropharyngeal swelling can sometimes be significant
- Management is avoidance of raw forms of the food trigger, but consumption of the cooked form is usually well-tolerated

Prescribe epi?

Usually not.... Except....

Systemic symptoms, severe OP swelling, multiple nut trigger



<sup>1</sup>Skypala I.J. et al. . Clin Exp Allergy. 2022 Sep;52(9):1018-1034.

<sup>2</sup>Mastrorilli C. et al. Medicina (Kaunas). 2019 Sep 26;55(10):641

# Oral allergy syndrome: triggers



**Birch**



Apple Peach Plum Pear Cherry Apricot Almond

**Rosaceae**



Carrot Celery Parsley Caraway Fennel Coriander Aniseed

**Apiaceae**



Soybean Peanut

**Fabaceae**  
(old Leguminosae)



Hazelnut

**Betulaceae**



**Ragweed**



Cantaloupe Honeydew Watermelon Zucchini Cucumber

**Cucurbitaceae**



Banana

**Musaceae**



**Mugwort**



Celery Carrot Parsley Caraway Fennel Coriander Aniseed

**Apiaceae**



Bell pepper

**Solanaceae**



Black pepper

**Piperaceae**



Mustard

**Brassicaceae**



Cauliflower



Cabbage



Broccoli



Garlic

**Liliaceae**



Onion



Peach

**Rosaceae**



Cantaloupe Honeydew Watermelon

**Cucurbitaceae**



Peanut

**Fabaceae**



White potato Tomato

**Solanaceae**

Cross-reactivity patterns in oral allergy syndrome (pollen-food allergy syndrome) Adapted and extended from: Sicherer SH. Clinical implications of cross-reactive food allergens. *J Allergy Clin Immunol* 2001; 108:881.



# Oral allergy syndrome: mechanism

PATHOGENESIS RELATED PROTEIN FAMILIES					STRUCTURAL PROTEINS
PR-2	PR-3&4	PR-5	PR-10	PR-14	PROFILINS
β-1,3-glucanases	Chitin binding proteins	Thaumatococcus-like proteins	Bet v 1 homologues	Lipid transfer proteins	
Hev b 2 (NRL) Mus a 5 (Banana) Ole e 9 (Olive)	Cas a 5 (Chestnut) Hev b 6 (NRL) Hev b 11(NRL) Mus a 2 (Banana) Pers a 1 (Avocado) Tri a 18 (Wheat) Vit v 5 (Grape)	Act d 2 (Kiwi) Cap a 1 (Bell pepper) Cry j 3 (Jap. cedar) Cup a 3 (Arizona cedar) Cup s 3 (Italian cedar) Jun a 3 (Mountain cedar) Jun r 3 (Temple juniper) Mal d 2 (Apple) Mus a 4 (Banana) Ole e 13 (Olive) Pru av 2 (Cherry) Pru d 2 (Plum) Pru p 2 (Peach) Pyr py 2 (Apple pear)	Act d 8 (Kiwi) Aln g 1 (Alder) Api g 1 (Celery) Ara h 8 (Peanut) Bet v 1 (Birch) Car b 1 (Hornbeam) Cas s 1(Chestnut) Cor a 1 (Hazelnut) Dau c 1 (Varrot) Fag s 1 (Eur. beech) Fra a 1 (Strawbrry) Gly m 4 (Soybean) Mal d 1 (Apple) Pru ar 1 (Apricot) Pru av 1 (Cherry) Pru p 1 (Peach) Pyr c 1 (Pear) Sola l 4 (Tomato) Vig r 1 (Mungbean)	Act d 10 (Kiwi) Amb a 6 (Ragweed) Api g 2 (Celery) Api g 6 (Celery) Ara h 9 (Peanut) Ara h 16 (Peanut) Ara h 17 (Peanut) Art v 3 (Mugwort) Cas s 3 (Cannabis sativa) Cit s 3 (Sweet orange) Cor a 8 (Hazelnut) Hev b 12 (NRL) Jug r 3 (Walnut) Mal d 3 (Apple) Mus a 3 (Banana) Ole e 7 (Olive) Par j 2 (Pellitory of the wall) Pla a 3 (London plane tree) Pru ar 3 (Apricot) Pru av 3 (Cherry) Pru p 3 (Peach) Pyr c 3 (Pear) Sola l 3 (Tomato) Sola l 6 (Tomato) Sola l 7 (Tomato) Tri a 14 (Wheat) Vit v 1 (Grape)	Act d 9 (Kiwi) Amb a 8 (Ragweed) Api g 4 (Celery) Ara h 5 (Peanut) Art v 4 (Mugwort) Bet v 2 (Birch) Cit s 2 (Sweet orange) Cor a 2 (Hazelnut) Cuc m 2 (Muskmelon) Dau c 4 (Carrot) Fra a 4 (Strawberry) Gly m 3 (Soybean) Hev b 8 (NRL) Mal d 4 (Apple) Mus a 1 (Banana) Ole e 2 (Olive) Phl p 12 (Timothy) Pla l 2 (London plane tree) Pru p 4 (Peach) Pyr c 4 (Pear) Sola l 1 (Tomato) Tri a 12 (Wheat)

legend of colors

Predominantly severe reactions

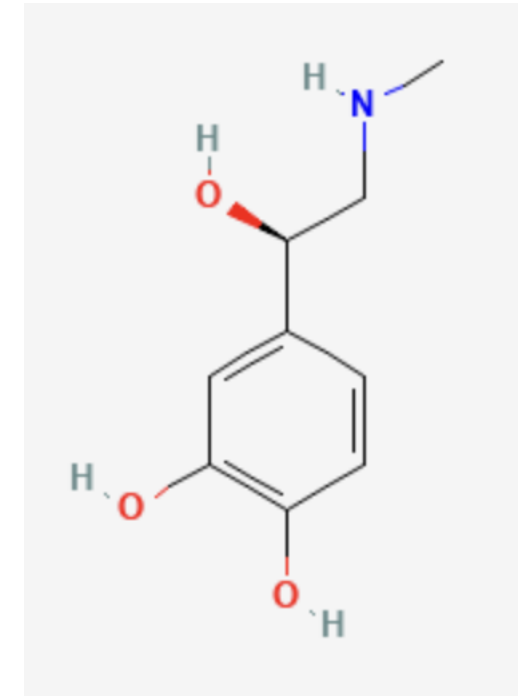
Both severe and mild reactions

Predominantly mild reactions



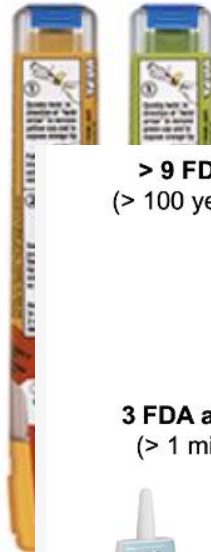
# EPINEPHRINE

THE TREATMENT FOR ANAPHYLAXIS... FULL STOP



# Epinephrine autoinjectors

## What epinephrine products are currently available in the U.S.?



> 9 FDA approvals in allergy  
(> 100 years of clinical experience)

3 FDA approvals  
(> 1 million Rx)



TOSYMRA®  
(sumatriptan)



VALTOCO®  
(diazepam)



OPVEE®  
(nalmeferene)

**Intravail®**  
dodecyl-maltoside: GRAS  
absorption enhancer



**Epinephrine**

**Spray**

7 FDA approvals  
(> 55 million Rx)



NARCAN®  
(naloxone)



VALTOCO®  
(diazepam)



NAYZILAM®  
(midazolam)



TOSYMRA®  
(sumatriptan)



OPVEE®  
(nalmeferene)



ZAVZPRET®  
(zavegepant)



IMITREX®  
(sumatriptan)





THANK  
YOU!

