

# Food Allergy & Immunotherapy

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# Definitions, Prevalence, Natural History and Diagnosis

# 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.

# 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)

# 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)

# Prevalence of Food Allergy

- 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 include: asthma (39-48%)<sup>3,4</sup>, 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

<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.

# Estimated Prevalence of Food Allergy

Food	<u>Children (%)</u> <sup>1</sup>	Adults (%) <sup>2</sup>
Cow's milk	1.9	1.9
Egg	0.9	0.8
Wheat	0.5	0.8
Soy	0.5	0.6
Peanut	2.2	1.8
Sesame	0.2	0.2
Tree nut	1.2	1.2
Shellfish	1.3	2.9
Fish	0.6	0.9
Overall	7.6	10.8

# Natural History

- Allergies to peanut, tree nuts, fish, shellfish more frequently persist into adulthood<sup>1</sup>
- Allergies to milk, egg, wheat, and soy are more likely to be outgrown<sup>1</sup>
- 43-86% of food allergic children are allergic to multiple foods<sup>2</sup>
- Non-IgE-mediated GI allergy[e.g., FPIAP, FPIES]: Infant forms resolve in 1-3 years; toddler/adult forms more persistent<sup>1</sup>
  - EoE and PFAS tend to persist into adulthood

# Diagnosis of IgE Mediated Food Allergy: History & Physical Exam

History of symptoms, timing, amount, raw vs. cooked food, reproducibility, treatment, and outcome

- Cofactors: Concurrent exercise, medications, alcohol
- Diet details / symptom diary

Physical exam: assess for other atopic disorders

# Diagnosis of IgE Mediated Food Allergy: Tests

Skin prick tests (SPT) with extracts or fresh food (for suspected pollen food syndrome)

Blood test for food specific IgE (sIgE) and food components

- Larger skin tests/higher sIgE levels correlate with increased likelihood of reaction, but not severity
- Testing NOT recommended if low chance of food allergy. **Panel tests are NOT recommended**
  - 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)

# Diagnosis of IgE Mediated Food Allergy: Tests Continued

Additional blood tests

- Basophil activation test
- Bead based epitope assay

Oral food challenges

# Mixed IgE/ Non-IgE-Mediated Food Allergy

## Eosinophilic Esophagitis, Gastritis, Gastroenteritis

- Primary eosinophilic gastrointestinal disorders (EGIDs) are characterized by eosinophilic infiltrate into the gastrointestinal tissue in the absence of another demonstrable cause
- The manifestations of EGID vary based on the anatomical location within the gastrointestinal tract and can vary by age:
  - Young children: vomiting, nausea, abdominal pain, failure to thrive
  - Older patients: weight loss, dysphagia, food impaction

# Mixed IgE/ Non-IgE-Mediated Food Allergy

Diagnostic criteria — The diagnosis of EoE requires all of the following:

- Symptoms related to esophageal dysfunction.
- Eosinophil-predominant inflammation on esophageal biopsy, characteristically consisting of a peak value of  $\geq 15$  eosinophils per high power field (HPF) (or 60 eosinophils per  $\text{mm}^2$ ).
- Exclusion of other causes that may be responsible for or contributing to symptoms and esophageal eosinophilia

# Non IgE-Mediated Food Allergy

## Food Protein-Induced Allergic Proctitis/Proctocolitis

- Gross blood in stool ± other symptoms, usually well-appearing infant

## Food Protein-Induced Enteropathy

- Recurrent abdominal pain and chronic malabsorptive diarrhea, which may progress to weight loss and growth failure

## Food Protein-Induced Enterocolitis Syndrome (FPIES)

- Delayed (1-4 hours after ingestion): repetitive projectile vomiting +/- diarrhea that can lead to severe dehydration, onset usually in the 1<sup>st</sup> year of life

# Diagnostic Criteria for FPIES

## Major Criterion

- Repetitive Vomiting 1-4 hours after eating suspect food

## Minor Criteria

- A second (or more) episode of repetitive vomiting after eating the same suspect food
- Repetitive vomiting episode 1-4 hours after eating a different food
- Extreme lethargy with any suspected reaction
- Marked pallor with any suspected reaction
- Need for emergency room visit with any suspected reaction
- Diarrhea

*The diagnosis of FPIES requires that a patient meets the major criterion and at least 3 minor criteria*

# Key points on FPIES

- FPIES is a clinical diagnosis (no testing is helpful).
- Repetitive vomiting plus lethargy/pallor are the main clinical features
- Treatment is different from IgE-mediated food allergy
- Fluids are used to treat dehydration.
- Epinephrine is not indicated.

# Diagnostic Approach: Non-IgE-Mediated Disease or Those with Unclear Mechanism

- Elimination diets (may need elemental amino acid-based diet)
- Physician-supervised Oral Food Challenges
  - Timing/dose/approach individualized for disorder
    - FPIES reactions can induce shock
    - Eosinophilic gastroenteritis may need prolonged feedings before symptoms develop
  - Blinded challenges may be necessary
  - May require ancillary testing (endoscopy/biopsy)

# Pollen Food Allergy Syndrome (PFAS)

\*previously named 'oral allergy syndrome' or OAS

# Pollen Food Allergy 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
- Triggers include raw fruits and vegetables, tree nuts and legumes (usually peanuts or soy), which vary depending on the sensitizing pollen and variety of fruit or vegetable
- Management is avoidance of raw forms of the food trigger, but consumption of the cooked form is usually well-tolerated

# Triggers of PFAS

<b>Sensitizing Pollen</b>	<b>Potential Food Triggers</b>
Silver Birch	Apple, pear, stone fruit, strawberry, kiwi, hazelnut, walnut,, almond, Brazil nut, peanut, celery, carrot, potato, soy, fig, bean sprouts, mange tout
Grass	Melon, watermelon, orange, tomato, aubergine, pepper, potato, peanut, Swiss chard
Mugwort	Celery, celeriac, carrot, parsnip, dill, parsley, coriander, cumin, fennel, aniseed, sunflower seed, honey
Ragweed	Watermelon, melon, banana, courgette, cucumber, marrow, squash, pumpkin

# Food Allergy Therapies

# Oral Immunotherapy

- Involves 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%.
- In addition to avoidance, oral immunotherapy (OIT) for peanut is an option for children (4-17 yo).
- Indicated for use in IgE-mediated food allergy only
- FDA approved product for peanut OIT in 2020

Sampson HA. JACI-In Practice 2013;1:15-21.

Pouessel G, Lezmi G. World Allergy Organ J. 2023, 16(2):100747

<https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-treatment-peanut-allergy-children>

# Palforzia

- Peanut OIT product approved by the FDA in January 2020, following pivotal Phase 3 trial<sup>1</sup>
- Approved for the treatment of peanut allergic individuals age 1-17 years<sup>2</sup>
- Should be taken with initial dose and up dosing in a healthcare setting<sup>2</sup>
- Peanut should be avoided while taking Palforzia<sup>2</sup>
- Does not cure peanut allergy but reduces the risk of allergic reactions after accidental ingestion of peanut<sup>2</sup>

# Sublingual Immunotherapy

- Involves daily administration of allergen under the tongue to achieve desensitization.
- Has been investigated in clinical trials for the treatment of hazelnut, peach, apple, milk and peanut<sup>1</sup>
- SLIT for peanut allergy for 48 months allowed 70% of patients to tolerate 800 mg peanut<sup>2</sup>
  - Median reaction rate per dose of SLIT was 0.5%
  - Most reaction involved oropharyngeal pruritus (80%)
  - No participants required epinephrine

# Epicutaneous Immunotherapy

- 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>

# Epicutaneous Immunotherapy

- In the most recent phase 3 trial involving peanut allergic 1–3 year-olds, after EPIT for 12 months 67% of patients met the primary endpoint of tolerating either 300 or 1000 mg peanut depending on baseline reactivity<sup>2</sup>
  - 64.2% of patients tolerated at least 1000 mg peanut
- 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

# Biologics: 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 desensitization to single or multiple foods when used as an adjuvant to OIT<sup>1-3</sup>
  - Most common approach is to use a modified asthma-based dosing of omalizumab<sup>4</sup>
    - However, monthly dosing has been studied and shown to facilitate desensitization 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.

# OUtMATCH Study (NCT03881696)

- 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)

# FDA Approval of Omalizumab for Food Allergy

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

# A 7-year-old girl is the first Mainer to receive a new treatment for peanut allergies

Maine Public | By [Patty Wight](#)

Published December 19, 2022 at 1:35 PM EST



# ORAL IMMUNOTHERAPY

## BDN BANGOR DAILY NEWS

56 ° F

### First in Maine with peanut allergy treatment

by BDN Community  
December 16, 2022



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### MEDICATION FOR A PEANUT ALLERGY? NEWBURGH GIRL FINISHES FIRST PHASE OF NEW PROTOCOL



# Who Might be a Good Treatment Candidate?

## II. Caregiver / Family



# Caregiver Requirements: Amateur Nursing

- Remember that 99% of OIT dosing happens at home
- Caregivers must shift mindset from “threat” to “medicine” and:
  1. Determine if the child is fit to receive a dose and ensure appropriate conditions are maintained (no activity / exercise; supervision);
  2. Prepare the dose properly;
  3. Administer the dose;
  4. Assess for any adverse events;
  5. If adverse events, determine if a rescue medication is needed and which one;
  6. Determine next steps: call to office? ED? EMS?;
  7. Record dose / log adverse events into a data capture system;
  8. Take off work / attend regular in-office appointments

Daily

Biweekly/Monthly/PRN

Indefinitely

# Interactions with Families Are Critical in Running an OIT Practice

## Caregiver Characteristics

- Adherent to the practice's instructions
- Some level of risk tolerance
- Good communicator – knows when to call and when not to call
- Unafraid to give epinephrine: *you will advise its liberal use*
- Engaged with child, esp. as pre-teens & teens develop independence

## Office Characteristics (not exhaustive list)

- Must provide clear, evidence-based instructions for OIT program
- Must have 24/7 coverage and know how to handle secondhand info from nervous parents
- Must think carefully about patient selection vs. volume
- Ideally has flexible hours / staffing / physical facility
- REMS Certification for Palforzia – office/nurse manager to take lead

# Getting Started

## **I. The Patient Journey**

# The PALFORZIA Treatment Pathway



\*These appointments occur based on the healthcare provider's discretion.

# PALFORZIA Missed Doses

## **Dose Modification**

Dose modifications are not appropriate during Initial Dose Escalation.

Temporary dose modification of PALFORZIA may be required for patients who experience allergic reactions during Up-Dosing or Maintenance, for patients who miss doses, or for practical reasons of patient management. Allergic reactions, including gastrointestinal reactions, that are severe, recurrent, bothersome, or last longer than 90 minutes during Up-Dosing or Maintenance should be actively managed with dose modifications. Use clinical judgment to determine the best course of action, which can include maintaining the dose level for longer than 2 weeks, reducing, withholding, or discontinuing PALFORZIA doses.

## **Management of Consecutive Missed Doses**

Following 1 to 2 consecutive days of missed doses, patients may resume PALFORZIA at the same dose level. Data are insufficient to inform resumption of PALFORZIA following 3 or more consecutive days of missed doses. Patients who miss 3 or more consecutive days of PALFORZIA should consult their healthcare providers; resumption of PALFORZIA should be done under medical supervision.

# With Palforzia® Ending, What's Next for Peanut Allergy Patients?

- Palforzia was developed by Aimmune Therapeutics, acquired by Nestlé Health Science, and subsequently divested to Stallergenes Greer.
- Stallergenes Greer is discontinuing Palforzia, the only FDA-approved peanut allergy immunotherapy, on **July 31, 2026**.
- This voluntary decision stems from low adoption and commercial challenges, not safety or efficacy issues.
- Manufacturer set the list price at **\$890 per month**, which amounts to approximately **\$10,680 to \$11,000 per year**

# Key Next Steps and Alternatives for Patients:

- **Transition to Custom OIT:** Many allergists are transitioning patients to custom, private-practice OIT programs that use standardized peanut flour rather than the branded Palforzia powder.
- **Biologic Therapy (Xolair):** Xolair (omalizumab), approved in 2024, is used to increase the threshold for allergic reactions to peanuts (and other foods) in adults and children 1 year and older. It is often considered more convenient as it is administered via injection every 2-4 weeks.
- **Future Treatments (Viaskin Peanut):** The "peanut patch" (Viaskin) is moving toward potential FDA approval, providing a new option for allergy desensitization through the skin.
- **Strict Avoidance and Emergency Prep:** Patients must return to strict avoidance of peanuts and ensure they carry epinephrine auto-injectors

# Early Food Introduction and Prevention

# Early Introduction Is Safe and Effective

- Before 2016, no country endorsed early introduction to prevent food allergy.
- Since 2017, multiple countries advocate this strategy to reduce the risk of developing specific food allergies, vs. deliberately delaying introduction
  - Approaches differ by country for which risk population and what foods are prioritized, and if screening is recommended. US data have suggested screening is not cost-effective.
  - There are limited data regarding the optimal time for introduction during the first year of life

# Early Introduction Is Safe and Effective

- Australian data suggest that early peanut and egg introduction can be accomplished with high uptake across all populations safely (~4% risk of severe reactions), without screening

# Food Allergy Prevention

1. Earlier introduction is generally associated with a reduced relative risk of developing IgE-mediated allergy vs. prolonged avoidance of introducing the food
2. The best evidence exists for egg and peanut early introduction, with no beneficial effect seen for milk or other foods, though also no harm seen either.
3. Harm was shown in studies of multiple simultaneous introductions with regards to risk withdrawal and difficult adherence.
4. The findings support the concept of using earlier allergenic food introduction to prevent food Allergy but highlight the need for more acceptable forms of multiple allergenic foods.
5. Most studies were initiated before 6 months of age and conducted in wealthy countries

# Guidelines for Early Food Introduction and Patterns of Food Allergy



## Maine allergist calls study on reducing peanut allergies 'encouraging'

Maine Public | By [Patty Wight](#)  
Published October 26, 2025 at 1:19 PM EDT



The New York Times

### *Peanut Allergies Have Plummeted in Children, Study Shows*

Doctors have long recommended that infants avoid peanut products. But in 2017, experts officially reversed that guidance, and food allergies decreased sharply.

A new study published in the Journal of Pediatrics has found that early exposure to peanuts has resulted in roughly 40,000 fewer allergies in U.S. children over the past decade.

Starting in 2017, guidance changed to recommend introducing peanuts to infants early instead of waiting until age three



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## New CHOP Study Shows Early Introduction Guidance Is Dramatically Reducing Peanut Allergies Nationwide

Pediatrics, 2025 Nov 1;156(5):e2024070516.

Guidelines for Early Food Introduction and Patterns of Food Allergy..

Stanislaw J Gabryszewski et al

# Shared Decision-Making in Food Allergy

# Preference Sensitive Decision-Making

- Role of Values Clarification: this is the process of helping patients consider the desirability of options and attributes of options within a specific decision context, to identify their preferences
  - The process is felt to help make treatment decisions more reflective of what a patient truly wants and values
  - What is important to one family may not be important to another
- Patients may still choose to deviate from evidence-based guidelines for many reasons, including quality-of-life concerns, cost considerations, lifestyle choices and family decisions.
  - We have to let go of our biases, which may be difficult. We make suggestions, they make decisions.

# Misinformation, Unproven Therapies and the Allergist's Role

# Misinformation & Unproven Testing/Therapies

- There are several areas in food allergy where strongly-held patient beliefs may be at odds with evidence.
- e.g., **IgG testing, provocation-neutralization**, hair analysis, applied kinesiology, & electrodermal testing
- Misinformation about food allergy diagnosis and management can be exacerbated by social media.
- A 'PEARLS' approach can help open communication channels.

Step	Example
Partnership	"Let's work together to find a plan that's right for you"
Empathy	"I'm listening, tell me your concerns"
Affirmation	"You are doing a great job of trying to seek out all the best evidence before making a decision"
Reflection	"These can be difficult things to discuss"
Legitimization of patient	"All this information can be confusing for patients" ( <i>this is <u>not</u> testing legitimization</i> )
Support and Education	"I want to help provide the best expertise and advice I can"

# Unproven Testing/Therapies & Patient Choices Arising From Misinformation

- NOT appropriate for shared decision-making, but does require compassion, clear patient education, and respect for patient autonomy
- Respect for patient autonomy is not the same as shared decision-making
- Shared decision-making is appropriate in instances of clinical equipoise (i.e., conditional medical recommendations)
- Clinical equipoise is absent in settings of unproven testing/therapies and misinformation

# Role of the Allergist

- Diagnose food allergy correctly (prevent over- and under-diagnosis)
- Identify food triggers, educate on avoidance, risk of anaphylaxis, signs and symptoms of allergic reactions and appropriate treatment
- Present all available management options to patients and engage in shared decision-making
- Ensure appropriate follow up and multi-disciplinary involvement, as required for each patient
- Promote awareness of food allergy and liaise with all stakeholders to optimize management
- Tackle misinformation on food allergy and offer evidence-based resources to patients

# Thank you!



The image shows a screenshot of a news website header. At the top, there is a dark blue navigation bar with links for "Half Off Deals", "Contests & Giveaway", "Pet of the Week", "Binge Watch News", and "Watch Last Newscast". Below this is a blue header bar containing the "FOX 22 WFVX BANGOR" logo, a large "7 abc" logo, a hamburger menu icon, a home icon, and navigation links for "NEWS", "SPORTS", "FEATURES", "WEATHER", "PROGRAMMING", and "CONTACT". On the right side of the blue bar, the weather is displayed as "6 AM", "36°", and a cloud icon. The main headline reads "Mainer becomes first to take part in peanut allergy treatment". Below the headline, it says "Dec 22, 2022 Updated Jul 14, 2025".