Atopic Dermatitis and Food Allergy

Pediatric Health Network

Children's National

Future of Pediatrics

Ammara Ahmed, DO/MHS

Mansi Kotwal, MD/MPH

Priyanka Seshadri, MD

Pediatric Health Network

Children's National

- No disclosures

Learning Objectives

- Describe the pathophysiology of atopic dermatitis and food allergy
- Describe the relationship between atopic dermatitis and food allergy
- Review the LEAP study and evidence supporting early allergen introduction
- Identify when allergy testing is indicated
- Recognize the limitations and potential harms of indiscriminate allergy testing

Why this Matters

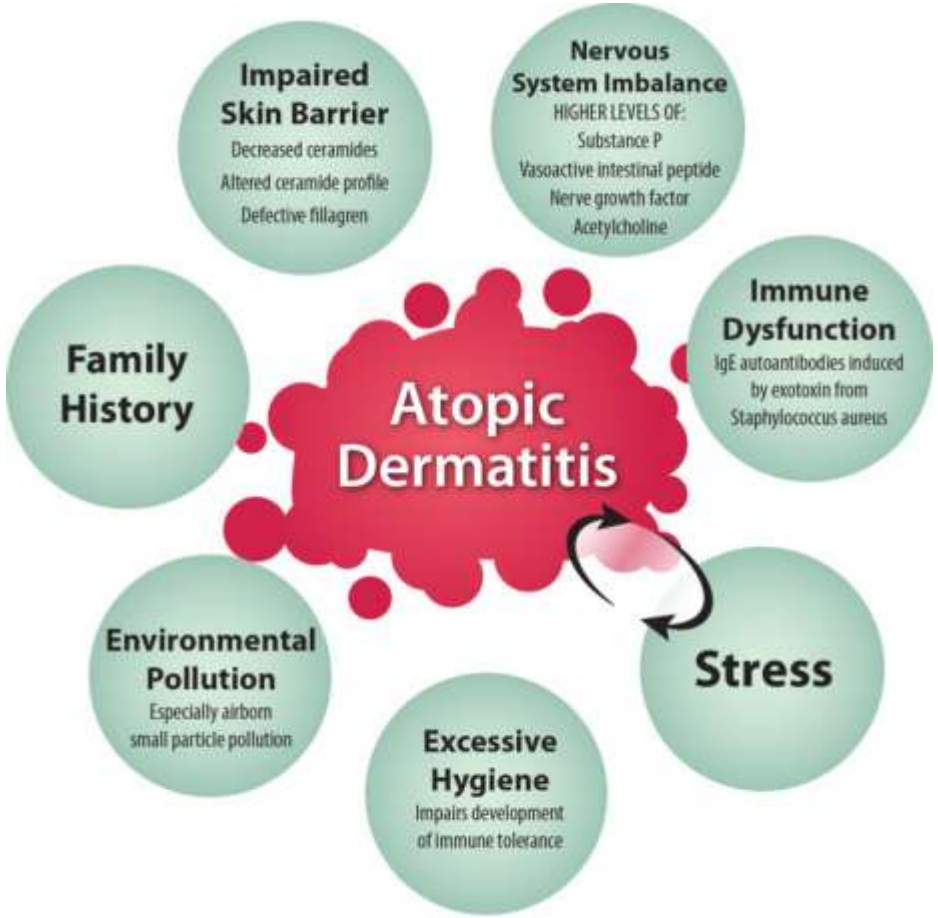
- Atopic Dermatitis affects up to 20% of children
- Both Atopic Dermatitis and Food Allergy prevalence continues to rise
- Infants with moderate-severe atopic dermatitis are at the highest risk for food allergy (up to 30-40%!)
- Testing for food allergy assesses for **IgE mediated** food allergy
- Testing when not indicated can lead to a variety of negative consequences (unnecessary food avoidance leading to nutritional/medical problems, psychologic, and financial)

Atopic Dermatitis

- A chronic inflammatory skin disease that often follows a relapsing/remitting course
- Common in infancy and childhood, often improves over time
- Affects up to 20% of children
- Characterized by:
  - Pruritus
  - Xerosis
  - Relapsing eczematous lesions

Atopic Dermatitis

- Multifactorial Disease:
- - Skin barrier dysfunction
- - Immune dysregulation
- - Environmental factors
- - Genetics
- Triggers: illnesses/infections, stress, weather changes, aeroallergens, food



atopic-dermatitis-768x774.jpg (768×774)

Pathophysiology of Atopic Dermatitis

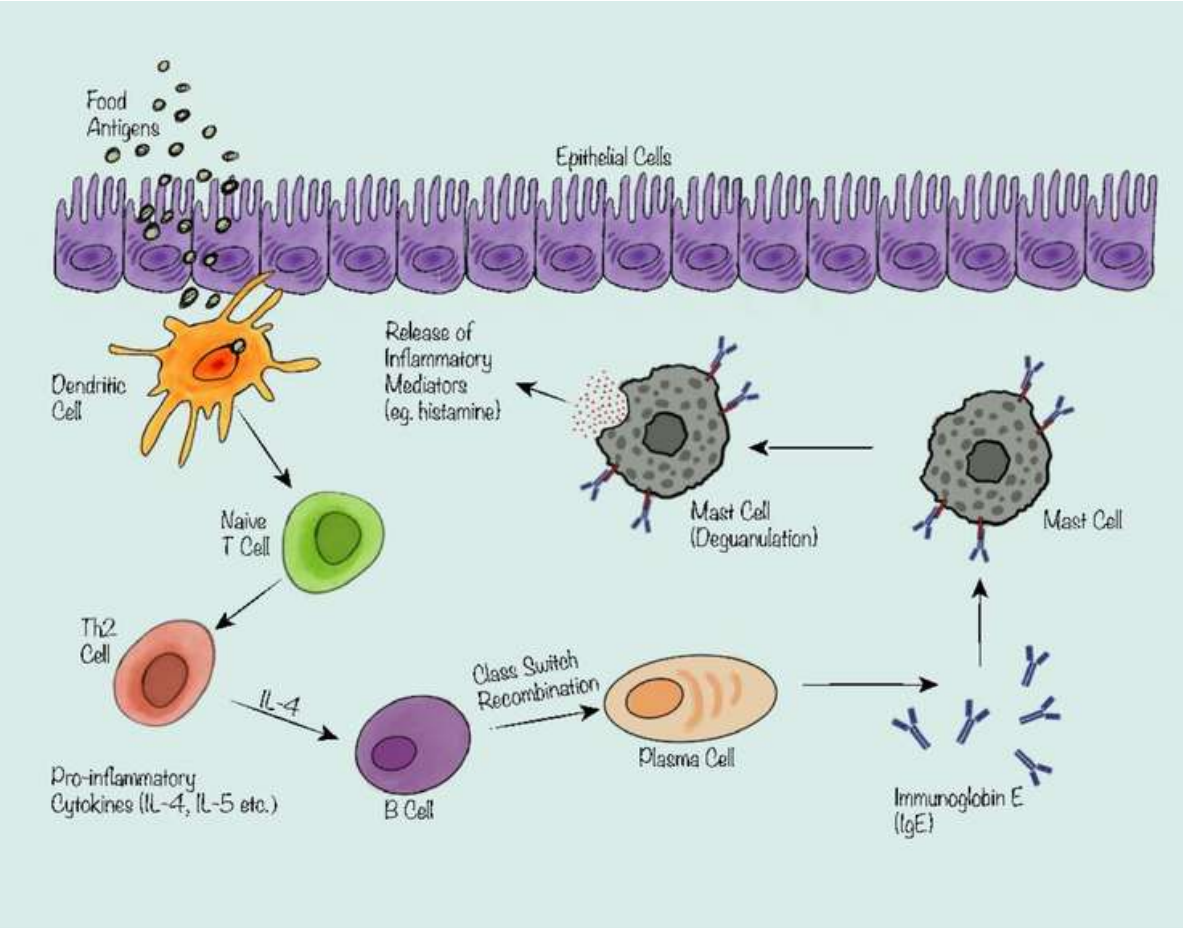
- Defective Skin Barrier
- - Increased transepidermal water loss
- - Easier penetration of allergens and microbes
- Filaggrin mutations associated with severe disease
- Immune activation
- - Th2-predominant inflammation
- - IL-4, IL-13, IL-31 involvement
- Skin microbiome alterations
- - Increased Staphylococcus aureus colonization

IgE mediated Food Allergies

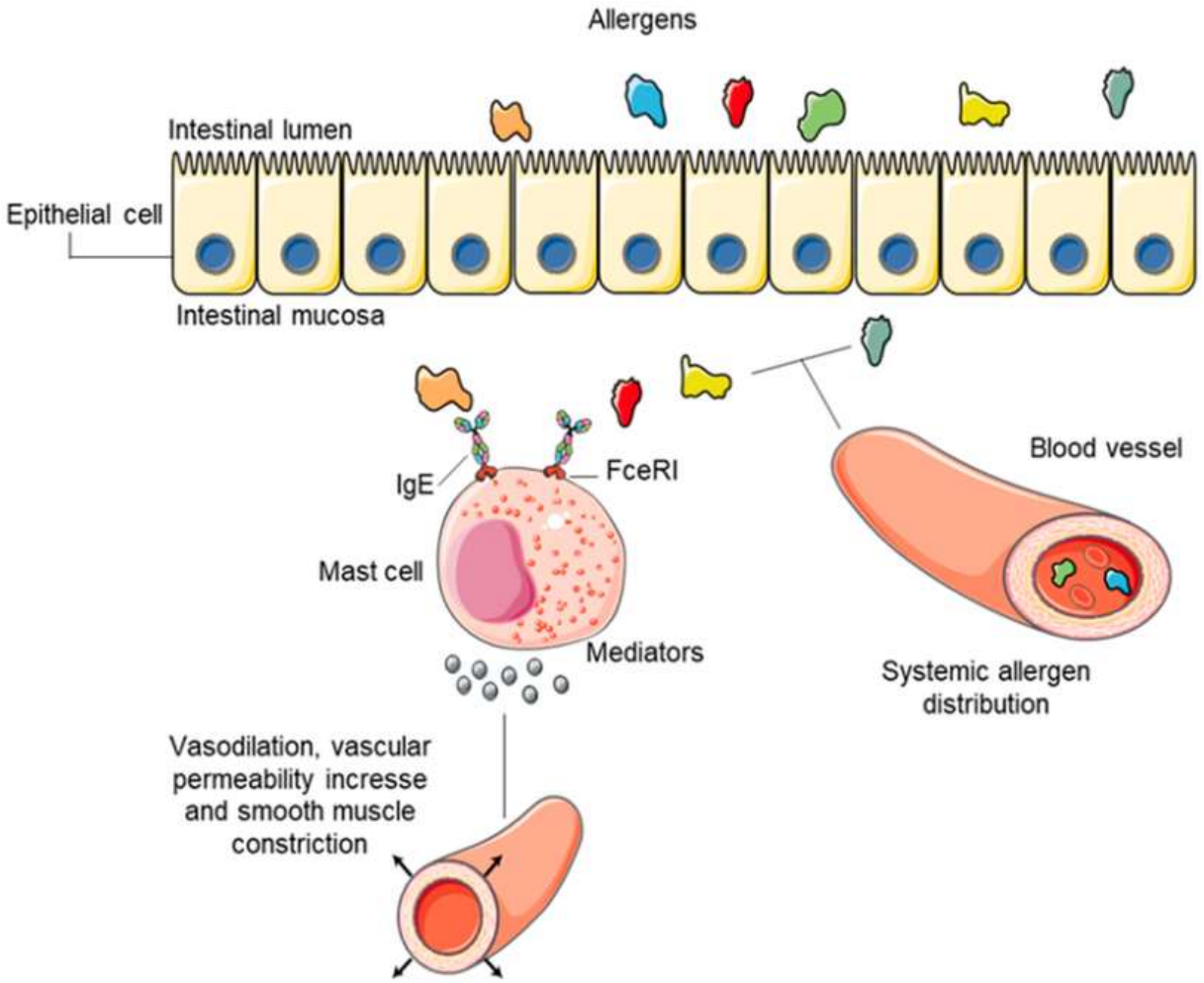
- Adverse immune response to a food protein that is driven by abnormal IGE production (as opposed to delayed T cell mediated pathology)
- Top Allergens:
  - Peanut
  - Tree Nuts
  - Egg
  - Cow's Milk/Dairy
  - Wheat
  - Sesame
  - Soy
  - Fish/Shellfish *

Pathophysiology of IgE-Mediated Food Allergy

- Sensitization phase:
- - Allergen exposure --> IgE production
- IgE binds to mast cells and basophils
- Re-exposure causes histamine release and acute allergic reaction symptoms
- Clinical manifestations:
- - Urticaria/Angioedema
- - Vomiting
- - Cough, Wheezing
- - Behavior change



Overview-of-the-mechanism-of-IgE-mediated-food-allergy-Antigen-presenting-cells-eg.tif (850×595)



General-mechanisms-of-IgE-mediated-response-to-food-allergens-Interaction-between-food.tif (850×70

Relationship between AD and FA

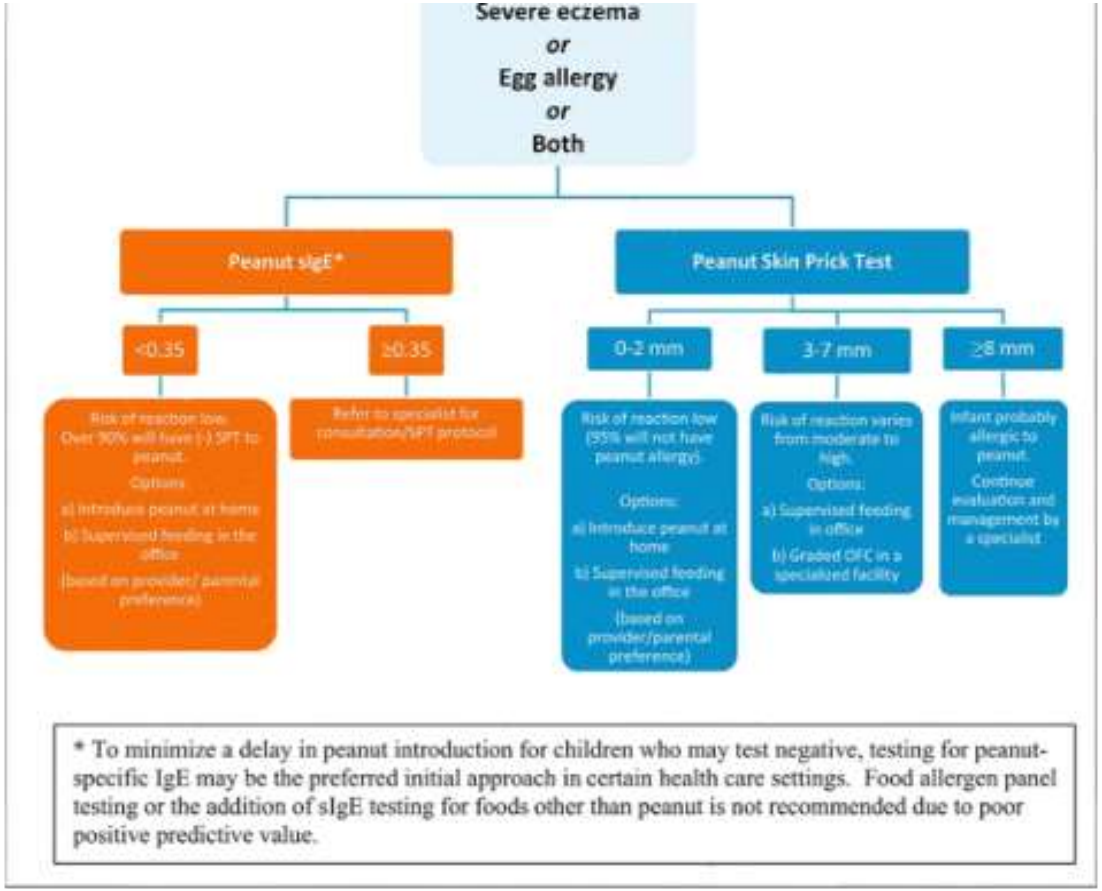
- Moderate to severe atopic dermatitis increases the risk of food allergy development (30-40%)
- Cutaneous exposure:
- - Allergens penetrate impaired skin barrier
- - Epicutaneous sensitization -> IgE production
- Oral exposure:
- - Early and consistent exposure promotes immune tolerance
- Avoiding foods without indication may increase risk of food allergy (i.e in the setting of eczema, reflux issues, etc.)

Relationship between AD and FA

- Most atopic dermatitis is NOT caused by food allergy
- Food allergy is rarely the sole driver of chronic atopic dermatitis (and even in cases where it may be exacerbating it, we no longer recommend avoidance due to risk of IgE sensitization)
- In infants with moderate to severe atopic dermatitis, early introduction and consistent exposure is more important for prevention of food allergy development

LEAP – Learning Early About Peanut Allergy

- LEAP Trial
  - High-risk infants between 4 and 11 months who had severe atopic dermatitis and/or egg allergy
  - Randomized to:
- - Peanut consumption
- - Peanut avoidance



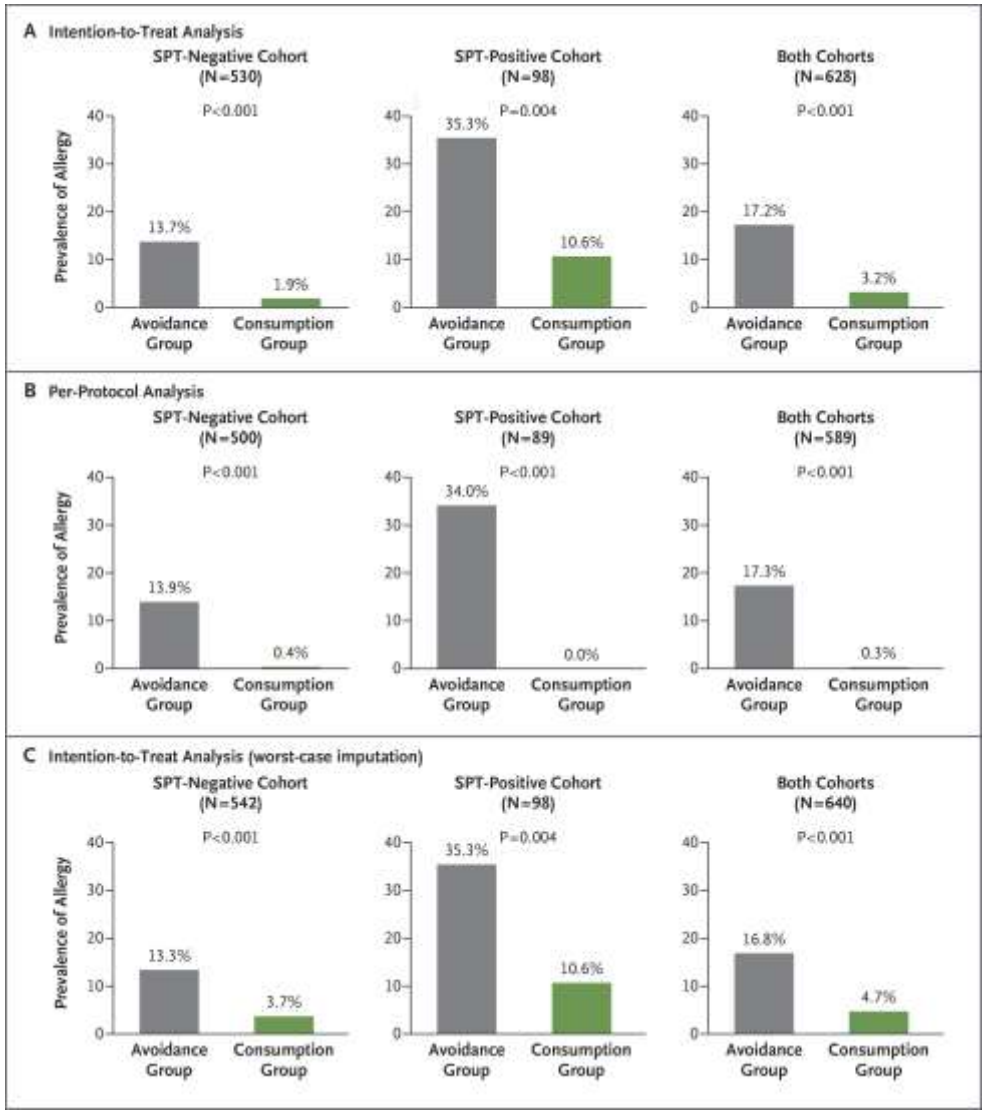
* To minimize a delay in peanut introduction for children who may test negative, testing for peanut-specific IgE may be the preferred initial approach in certain health care settings. Food allergen panel testing or the addition of sIgE testing for foods other than peanut is not recommended due to poor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

LEAP
Study Results

Shift paradigm from delayed introduction (in the past some clinicians would recommend avoidance of allergenic foods until about 2 years of age) to early introduction of allergens

Peanut – 2 gm protein 3x/per week

Findings: Early introduction and maintenance in diet reduced peanut allergy development by 80% at 5 years of age



Benefits of early initiation of food allergy treatments

- Early introduction also allows for early identification of food allergies
- Early initiation of treatment for food allergies has shown to have fewer rates of epinephrine use and potentially allows for higher chance of 'free eating"[1]
  - One study demonstrated a statistically significant trend that younger patients were more successful in completing peanut OIT [2]
  - Disease modifying: Brian Vickery found that early initiation of peanut OIT resulted in higher rates of sustained unresponsiveness at 4 weeks compared to placebo [3]
- Baby OIT at Childrens
  - •Total: ~30 patients
  - •Age Range: 7m-30m
  - •Foods: Peanut, Cashew, Walnut, sesame, and wheat
  - •Reaction History: Sensitization only, Hives/rash (most common), vomiting, and anaphylaxis.
  - •Outcomes: 1 in office reaction, cutaneous only, No reactions requiring treatment with anti-histamines or epinephrine during office dosing., No reactions requiring treatment with epinephrine during home dosing, Several patients (~7-10) have reacted with mild cutaneous reactions at home that required either treatment with cetirizine or dose reduction.

Pediatric Health Network

Children's National

To Test or not To Test?

- Appropriate when:
- - Immediate reactions after food ingestion concerning for an IgE-mediated allergy
- - If known food allergy leads to an increased risk for another food allergy (peanut and egg, peanut and tree nuts)
- May consider when:
- - Before Peanut introduction in select, high-risk infants *
  - Discuss risk v benefits in children with siblings with peanut allergy (7-8.5% risk)
  - "In an effort to expand diet" i.e. in families who likely will not introduce without testing
-

To Test or not To Test?

- Would **avoid** testing:
- - Delayed eczema flares without acute reaction history
- - Only concern is "family history" of a food allergy
- - Food is in the diet consistently
- - Chronic, non-specific symptoms (headaches, abdominal pain, bloating/gas, chronic hives with no identifiable cause)

What does an allergy test actually mean?

- *I*ndicates *sensitization,* not clinical allergy
- - Higher IgE or larger the SPT --> Increased likelihood of allergy, NOT severity

- High false positive rates (skin and serum testing, 40-50% and 30-40% respectively), high negative predictive value

- Gold standard of diagnosis is an oral food challenge (OFC)
- - Can delay introduction due to access of these in general and wait times for challenges

Potential Consequences of testing

- When not indicated, testing can lead to:
- - Delayed introduction
- - Unnecessary avoidance
- - Transition from sensitization to true, clinical allergy
- - Anxiety for family and patient
- - Nutritional deficiency
- - Reduced quality of life
- - Increased cost (to families and healthcare utilization)
- - Over referral

Key Takeaways

- Atopic Dermatitis and Food Allergy are linked through the skin barrier dysfunction and immune dysregulation
- Early oral allergen introduction promotes tolerance, i.e. reduces the risk of IgE-mediated food allergy development
- The LEAP study truly transformed prevention strategies and changed practice
- In addition, early food allergy treatments have also been shown to be more effective as well!
- Allergy testing should be targeted (no panel testing) and performed when clinically indicated
- Testing when not indicated can lead to a variety of consequences

Current treatment options and food allergy trials

- **Current Practice:**
  - Avoidance
  - Oral Immunotherapy (OIT), including Baby OIT protocol
  - Xolair for Food Allergy
- **Clinical Trials:**
  - COMFORT Toddler – 1-3 yo with peanut allergy; testing peanut patch
  - PrestIgE Study – 12 –21 yo with food allergies using a new biologic medication
  - Neffy Study – children scheduled for an oral food challenge may participate in a post-marketing study using Neffy (nasal epinephrine spray)

References

- Tit G, Roberts G, et al. "*Randomized Trial of Peanut Consumption in Infants at Risk for Peanut Allergy*" New England Journal of Medicine, February 2015; 372:803-813
- Jeimy S, Yu N, Chan ES, Cook V. Oral immunotherapy for treatment of food allergy in infants and preschoolers. CMAJ. 2024 Jun 16;196(23):E790-E791. doi: 10.1503/cmaj.231478. PMID: 38885980; PMCID: PMC11182680.
- DOI: 10.1111/pai.13449
- Vickery BP, Berglund JP, Burk CM, Fine JP, Kim EH, Kim JI, Keet CA, Kulis M, Orgel KG, Guo R, Steele PH, Virkud YV, Ye P, Wright BL, Wood RA, Burks AW. Early oral immunotherapy in peanut-allergic preschool children is safe and highly effective. J Allergy Clin Immunol. 2017 Jan;139(1):173-181.e8. doi: 10.1016/j.jaci.2016.05.027. Epub 2016 Aug 10. PMID: 27522159; PMCID: PMC5222765.