Food Allergies

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9/26/15

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Overview

- Definition
- Prevalence Data
- Pathogenesis of Food Allergy
- Clinical Manifestations
- Diagnosis
- Management
- Treatments on the horizon

Definition

- **Food Allergy:** an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food.

1) Boyce JA, Jones SM, Rock L, et al. *Guidelines for the Diagnosis and Management of Food Allergy in the United States: Report of the NIAID-Sponsored Expert Panel*. Vol 126. Elsevier Ltd; 2010. doi:10.1016/j.jaci.2010.10.007.

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Definition

- **Food Allergy:** an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food.
- intended for human consumption
  - Includes:
    - Drinks
    - chewing gum
    - food additives
    - dietary supplements

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Prevalence

- 20-30% of population report food allergies
  - In reality:
    - 3-5% of the population

2) Branum AM, Lukacs SL. Food allergy among children in the United States. *Pediatrics*. 2009;124(6):1549-1555
3) Jackson KD, Howie LD, Akinbami LJ. Trends in Allergic Conditions Among Children : United States, 1997-2011. *NCHS Data Brief*. 2013;(121):1-8.

Prevalence

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  - In reality:
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    - Children
      - 3.4% (1997 - 1999)
      - 5.1% (2009 – 2011)
    - Adults
      - 3 - 4% (2009 – 2011)

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Adverse Response to Foods

- Immune Mediated:
  - IgE
  - Non-IgE
  - Mixed (both IgE and Non-IgE)
- Non-Immune Mediated:
  - Metabolic (eg. Lactose intolerance)
  - Pharmacological (eg. Caffeine in coffee)
  - Toxic (eg. Food poisoning)
  - Other

Common Food Allergies

Food

- Milk
- Egg
- Soybean
- Wheat
- Peanut
- Tree Nut
- Fish
- Shellfish

Common Food Allergies

Food	Children	Adults
Milk	**3.8%**	0.4-0.9%
Egg	**2%**	0.2%
Soybean	**1.4%**	0.7%
Wheat	0.5%	1.2%
Peanut	**1.9%**	0.7%
Tree Nut	1.1-1.6%	0.6-1.1%
Fish	0.2-0.5%	0.6%
Shellfish	0.5%	1.7-2.5%

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Got Milk?

- Protein allergen: Bos
- Cow's milk allergy
  - 90% allergic to goat's milk
  - 10% react to beef
  - 4% allergic to mare's milk
- 75% tolerate baked milk

4) Sicherer SH. Clinical implications of cross-reactive food allergens. *J Allergy Clin Immunol*. 2001;108(6):881-890.

Egg Allergy

- Egg white is more allergenic than egg yolk
- 70% tolerate baked egg products

5) Lemon-Mule H, Samspon HA, Sicherer SH, et al. Immunologic changes in children with egg allergy ingesting extensively heated egg. *J Allergy Clin Immunol* 2008;122:977-83.

Peanuts: Ara h

Including:

- Pressed peanut oil
- 5% cross reactivity to legumes

6) Sicherer SH. Munoz-Furlong A, Godbold JH, Sampson HA. US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. *J Allergy Clin Immunol* 2010;125:1322-6.

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* Highly refined peanut oil is okay*

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Tree nuts or seed fruit?

- Walnuts
- Pecan
- Hazelnut
- Cashews
- Pistachio
- Almonds
- Brazil nut
- Macademia nut

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7) Goetz, David W., Bonnie A. Whisman, and Andrew D. Goetz. "Cross-reactivity among edible nuts: double immunodiffusion, crossed immunoelectrophoresis, and human specific IgE serologic surveys." *Annals of Allergy, Asthma & Immunology* 95.1 (2005): 45-52.

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What Causes Food Allergies?

- Increased risk:
  - Genetics: eg. Peanut allergy
    - Monozygotic twins 64% vs Dizygotic Twins 7%
    - Parent or siblings with allergies = 7-fold increase
  - Eczema
    - Food allergies associated in 33-81% of children with eczema as an infant.

8) Lack G. Epidemiologic risks for food allergy. *J Allergy Clin Immunol*. 2008;121(6):1331-1336

Other Predisposition Factors

- Newborns:
  - Lack IgA and IgM
  - Immature humoral immune system
  - Low basal gastric acid
  - Immature intestines – including microvilli
  - Exclusive Formula feeding

What makes one food more allergenic than another

- Resiliency of molecular structure
  - Protection from degradation
- Enhanced absorption
- Ability to stimulate the innate immune response
  - Protein glycosylation
- Protein structure vastly different than human homologs

8) Masilamani M, Commins S, Shreffler W. Determinants of food allergy. Immunol Allergy Clin North Am 2012;32:11-33.

Current Theories and hypothesis

- Hygiene: decreased exposure to infectious agents leaves individual more susceptible to allergic diseases.

Current Theories and hypothesis

- Hygiene: decreased exposure to infectious agents leaves individual more susceptible to allergic diseases.
- Dietary Fat
- Antioxidant
- Vitamin D
- Dual-allergen-exposure

Clinical Manifestations

- Cutaneous
  - Urticaria, angiodema, Eczema
- Lower Respiratory
  - Cough, wheezing, dyspnea
- Gastrointestinal
  - N/V/D, pain, reflux, oral pruritus, bloody stools
- Cardiovascular
  - Hypotension, brady/tachycardia

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- Ocular
  - Conjunctiva erythema, tearing
- Upper Respiratory
  - Sneezing, rhinorrhea, congestion, laryngeal edema/hoarseness
- Misc.
  - Sense of impending doom, Uterine contractions

Immune Mediated Gastrointestinal

IgE	IgE & Non-IgE	Non-IgE
Acute GI Hypersensitivity	Eosinophilic esophagitis	Allergic Proctocolitis
Oral allergy syndrome	Eosinophilic gastroenteritis	Food Protein-induced enterocolitis syndrome
		Dietary protein-induced enteropathy
		Celiac disease

Immune Mediated Cutaneous

IgE	IgE & Non-IgE	Non-IgE
Acute urticaria and angioedema	Atopic dermatitis	Contact dermatitis
Chronic urticaria and angioedema		Dermatitis herpetiformis

Immune Mediated Respiratory

IgE	IgE & NON-IgE	NON-IgE
Allergic rhinoconjunctivitis	Asthma	Pulmonary hemosiderosis (Heiner syndrome)
Acute bronchospasm		

Diagnosis

- History
- Skin Prick Testing
- Allergen-specific serum IgE
- Component Testing
- Oral Food Challenge

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- Skin Prick Testing
- Allergen-specific serum IgE
- Component Testing
- Oral Food Challenge
- Atopy patch testing and food elimination diets are not routinely recommended

History

- Symptoms
  - Timeline
  - Food
- Medical history
- Family history

Skin Prick Testing

- > 8mm for milk, egg and peanut → 95% predictive of clinical reactivity
- Negative skin tests → 95% predictive accuracy

9) Sporik R, Hill DJ, Hosking CS. Specificity of allergen skin testing in predicting positive open food challenges to milk, egg, and peanut in children. *Clin Exp Allergy* 2000;30:1540-6.

IgE Testing

Allergen	Level (kU_A/L)	Positive Predictive Value (%)
Egg white	7	98%
• Egg white ≤ 2 yr	2	95%
Milk	15	95%
• Milk ≤ 1 yr	5	95%
Peanuts	14	99%
Tree nuts	15	95%
Fish	20	99%
Soybean	30	73%
Wheat	26	74%

10) Sampson H a. Utility of food-specific IgE concentrations in predicting symptomatic food allergy. *J Allergy Clin Immunol*. 2001;107(5 SUPPL.):891-896.

Oral Food Challenge

- Gold standard is double blinded placebo controlled oral food challenge
- In clinical setting
  - Open food challenge
  - Single-blinded challenge

Unproven Diagnostic Tests

- Provocation – neutralization
- Cytotoxic tests
- Applied kinesiology
- Hair analysis
- Serum specific food IgG levels
- Electrodermal testing

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Management

- Prevention:
  - Breastfeeding or formula feeding until 4-6 months of age
  - Introduce solids at 4-6 months of age
  - Maternal diet should not be restricted during pregnancy or while breastfeeding
    - In the past, advised to avoid milk for 1st year, eggs until 2nd year and tree nuts and fish until 3rd year
    - No evidence to support this
- Avoidance of known food allergens
- Treatment of Anaphylaxis
  - IM epinephrine (1:1,000)

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Medical Alert Bracelets

Future Directions

- Oral immunotherapy (OIT)
  - Oral immunotherapy + Xolair
  - Peanut, milk, egg
- Sublingual immunotherapy
- Epicutanous immunotherapy

Oral Immunotherapy - Peanuts

- n=24
- Treatment
  - 4000mg peanut protein for 3.98 years
- Results
  - 12/24 (50%) passed OFC after 1 month of stopping OIT

- n=24
- Treatment
  - 4000mg peanut protein for 24 months
- Results
  - 20/24 desensitized
  - 7/24 (29%) passed OFC after 3 months of stopping OIT

13) Vickery BP, Scurlock AM, Kulis M, et al. Sustained unresponsiveness to peanut n subjects who have completed peanut oral immunotherapy. J Allergy Clin Immunol 2014;133:468–75.e6.
14) Factor JM, Mendelson L, Lee J, et al. Effect of oral immunotherapy to peanut on food-specific quality of life. Ann Allergy Asthma Immunol 2012;109:348–52.e342.

Oral Immunotherapy – Egg

- n=55 (age 5-11 years old)
  - Placebo group 15, treatment group 40
- Treatment: consume 2 g of egg white powder per day
- Follow up:
  - Oral food challenge at 10 months, 22 months and 24 months
- Results:
  - 35 underwent OFC at 10 months → 22 passed
  - 34 underwent OFC at 22 months → 30 passed
  - 29 underwent OFC at 24 months → 11 passed
  - At 36 months → 10 had no symptoms (1 lost to follow up)

15) Burks a. W, Jones SM, Wood R a., et al. Oral Immunotherapy for Treatment of Egg Allergy in Children. *N Engl J Med*. 2012;367(3):233-243.

Sublingual Immunotherapy (SLIT)

- Clinical trials for:
  - milk, peanut, hazelnut and peach extracts

Epicutanous Immunotherapy

Peanut

- Arachild study
  - n=54
  - Treatment for 18 months of 100ug of peanut protein
  - 40% treatment response
- Phase III trial – ongoing

Milk

- Pilot study
  - n=19
  - Treatment for 3 months

Summary

- Most common allergenic foods in children: milk, egg, soy, peanut
- Diagnosis based on history, skin prick test, IgE and oral food challenge
- Management: prevention, avoidance, early epinephrine use and re-evaluation
- Future direction: oral immunotherapy, sublingual immunotherapy

Acknowledgements

- University Hospitals Regional Hospitals/LECOMT
- Mentors: Allergy and Immunology Associates
  - Dr. Hostoffer, DO (Program Director)
  - Dr. Tcheurekdjian, MD
  - Dr. Sher, MD
  - Dr. Jhevari, DO
- Colleagues in the Fellowship

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- *All of you!!!*

Resources

- FARE – Food Allergy Research & Education
  - https://www.foodallergy.org
- American Academy of Allergy Asthma & Immunology
  - http://www.aaaai.org/conditions-and-treatments/allergies/food-allergies.aspx
- American College of Allergy, Asthma & Immunology
  - http://acaai.org/allergies/types/food-allergies
- Kids with Food Allergies
  - http://www.kidswithfoodallergies.org/page/welcome.aspx