Food Allergy and Recent Evidence in Chronic Rhinosinusitis

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Disclosures

• This speaker has no commercial relationships to disclose.

Learning Objectives

• Provide an overview of the epidemiology of food allergy.
• Describe the types of food reactions, with emphasis on non-IgE mediated reactions.
• Review the current evidence on allergy in chronic rhinosinusitis.
• Discuss the role of food allergy specifically in chronic inflammation.
Food “allergy” and CRS: Is There a Correlation?

- CRS is multifactorial inflammatory disorder
- Up to 16% of the US population with associated health care costs of $6 billion/year
- Etiology and pathophysiology of CRS remain unknown
  - Innate and adaptive immune system deficiencies
  - Biofilm, fungal, viral triggers
  - Barrier defects
  - Allergy

- Nasal polyposis 4% lifetime prevalence
- Allergy (IgE mediated), Hypersensitivity (includes non-IgE mechanisms) vs. intolerance
- In US ~25% population believe they have food allergy

Is there a correlation between inhalant allergy and chronic rhinosinusitis?

A. In CRS without NP
B. In CRS with NP
C. In CRS regardless of NP
D. Definitely not
E. Don’t know
Is there a correlation between food allergy and CRS?
A. In CRS without NP
B. In CRS with NP
C. In CRS regardless of NP
D. Definitely not
E. Don’t know

The Role of Allergy Therapy in Chronic Rhinosinusitis: A Systematic Review

- Twenty-one articles supported a role of atopy in CRS, 16 papers showed no association
- Prevalence of atopy 16-85% for inhalant allergens and 12-81% for food allergens
- Dust mite and mold sensitivities as well as food sensitization more common in controlled studies suggesting a role for atopy
Milk allergy is frequent in patients with chronic sinusitis and nasal polyps

Claudia LEI, MD,1 Benjamin Louden, MD,1 Eshel Sporton, MD,1 Michaela Zverevskal, MD,1 Markos Brouner, MD,1 Gregory Biedermann, MD,1,2 and Herbert Thames, MD, PhD1

- 50 patients with CRS compared to 50 healthy controls
- In vitro testing performed
- 14% of CRS patients exhibited milk allergy compared to 0% controls (p=0.0125)
  - Of 5 patients, 4 had class 1 to milk, 1 patient had class 3 to milk
- 14% of CRS patients had wheat allergy compared to 14% controls
- Milk allergy may play a role in the pathogenesis of nasal polyps

Nasal polyps: Prevalence of positive food and inhalant skin tests

Melanie M. Collins, FRCS, ORL-HNS, Sean Lougahan, FRCS, ORL-HNS, Pauline Davidson, SRN, and Janet A. Wilson, MD, Salisbury, Manchester, and Newcastle-upon-Tyne, UK

- 40 patients with refractory CRS compared to 21 healthy controls
- IDT to panel of 16 foods, food diary completed for 2 weeks
- SPT to panel of 12 inhalants
- 70% of patients with nasal polyps had positive skin tests to an average of four foods compared to 34% of controls (p=0.0006).
- 35% of nasal polyp patients had positive inhalant skin tests
- Prevalence of positive inhalant skin tests similar to controls

What foods most commonly cause CRS symptoms

A. Melons and foods that cross react with ragweed "concomitant food allergy"
B. Wheat
C. Dairy
D. Nuts
Food vs. Inhalant Sensitivities

• 34 patients with nasal polyposis compared to 20 healthy controls
• SPT performed to 48 commonly consumed foods in Turkey
• 73.5% polyp patients exhibited food allergy compared to 15% controls (p < 0.001)
• Commonly found sensitivities include: buckwheat, oat, onion, grapefruit, plum, apple
• Note: did not test for dairy or wheat

Asymptomatic IgE Mediated Food Hypersensitivity in Patients with Nasal Polyps

• 34 patients with nasal polyposis compared to 20 healthy controls
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Food Sensitivities in Turkish Patients
• 80 patients with nasal polyposis compared to 36 healthy controls
• IDT performed to 16 foods
• 81% polyp patients exhibited food allergy compared to 11% controls (p <0.001)
• Commonly found sensitivities include: wheat, potato, tomato
• Other reactions seen: milk, corn, egg, chicken, pork, pea, and orange
• Food hypersensitivities may be underestimated

Do you do food allergy testing?
A. Yes, in the majority of patients with nasal symptoms
B. No, not at all
C. In patients who have irritable bowel symptoms
D. In patients with nasal polyposis

How do you test for food allergies?
A. Skin prick testing
B. Intradermal dilutional testing
C. In vitro testing
D. Elimination challenge food diet
E. All of the above
Hypersensitivity Types

- Type I: Immediate (AR, asthma, food)
- Type II: Cytotoxic (Graves’ Disease)
- Type III: Immune complex (serum sickness)
- Type IV: Delayed, cell-mediated (TB, poison ivy)

Mechanisms of Food Allergy

- Pathophysiology remains unclear with type II, III, and IV delayed hypersensitivity reaction proposed
- IDT to food allergens shown to be more sensitive than SPT for detecting atopy
- Majority of study patients did not report a history of food hypersensitivity

IgE vs. Non-IgE-Mediated Food Allergy

- Symptoms worsen with cumulative exposure
- Anaphylaxis can occur
- Fixed
- Testing via in vitro or skin testing methods

- Symptoms may vary with dose and timing
- Tolerance can occur
- Mechanisms not fully understood
- Testing not established
Food Allergy and Anaphylaxis

- Immediate type reactions 5% of food allergy reactions
- Food is leading cause of anaphylaxis in outpatient setting
- Symptoms vary
  - 80% cutaneous
  - Urticaria
  - Angioedema
  - Dyspnea/wheezing
  - Hypotension

Adverse Food Reaction

- Immune mediated (Food allergy and celiac)
- Non-immune mediated (Primarily food intolerance)

- IgE mediated
- Non-IgE mediated
- Mixed IgE and non-IgE
- Cell Mediated
- Metabolic
- Meds
- Toxic
- Other/Idiopathic


Food Reactions

- Children vs. Adults
  - Young Child
    - Cow’s milk 2.5%
    - Egg 1.6%
    - Peanut 0.8%
    - Wheat 0.4%
    - Soy 0.4%
    - Tree Nuts 0.2%
    - Fish 0.1%
    - Shellfish 0.1%
  - Adults
    - Shellfish 2%
    - Peanut 0.6%
    - Tree nut 0.6%
    - Fish 0.4%

Development of tolerance

- Egg (66% by age 7)
- Cow’s milk (80% by age 5)
- Wheat (56% by age 8)

- Changes in skin tests in association with resolution of food allergy are less well defined – skin tests can remain positive long after tolerance to the food has developed
- A decrease in sIgE may be a marker of the onset of tolerance but not always


Peanut Allergy

- 1.4% children, 0.6% adults (incidence tripled in last 10 years)
- 8 foods account for 90% of IgE-mediated reactions (milk, eggs, fish, shellfish, tree nuts, peanuts, wheat, soybeans)
- Resolution in 20% by 5 years of age
- 90% severe anaphylactic food reactions involve peanuts or tree nuts

Peanut Allergy

- Sensitization: cutaneous, oral, lactational, in utero?
- Emerging evidence to dispute postponing early peanut exposure reflected in 2008 AAP recommendations
- LEAP (“Learning Early About Peanut Allergy”) study
  - Enrolled 640 high-risk children age 4-10 months
  - 2 arms: avoidance until age 3 vs. early, measured exposures
  - Risk factors for peanut sensitization were egg allergy (OR=2.31) and severe eczema (OR=2.47)

Can Nut Allergy be Prevented?

- Prospective cohort study 8,205 children with 308 cases of food allergy, 140 cases of peanut/tree (P/TN) nut allergy
- Incidence of allergy lower among children of mothers who consumed more P/TN in peri-pregnancy diet
- Early allergen exposure increases tolerance

Frazier AL et al. Prospective Study of Peripregnancy Consumption of Peanuts or Tree Nuts by Mothers and the Risk of Peanut or Tree Nut Allergy in Their Offspring. JAMA Pediatr. 2013 Dec;167.

Food Allergy and Atopic Dermatitis

- Role of food controversial
- Induction of urticarial lesions and itching after food ingestion
- More common in infancy and young children
- 33% of children with infantile eczema have IgE-mediated food allergy
- Eczema in first 6 months associated with peanut allergy

Crustaceans

- High cross reactivity between crustaceans
- Low cross reactivity with mollusks
- Tropomyosin muscle protein
- Not associated with anaphylactoid reaction from radio-contrast dye

Oral Allergy Syndrome

- Inhalant food cross-reactivity
- Raw foods
- OAS affect 50-70% of pollen sufferers
  - May peak during associated pollen season
- Symptoms limited to oropharynx
  - Tingling, pruritus, angioedema
  - Fast onset, IgE-mediated
- Improves with inhalant immunotherapy


Inhalant and Food Cross-reactivity

- Grasses and cereal grains
- Birch and carrot, cherries, apples, hazelnuts
- Ragweed and melons
- Mugwort and celery, coriander


If a patient has birch tree pollen allergy, what foods can cause oral allergy syndrome?
Non-IgE Mediated Mechanisms

- Food-specific IgG produced
- Antigen/antibody complexes are formed
- Complexes deposited in tissue and activate complement and macrophages
- Delayed reaction may last for several days to weeks
- No approved in vitro test for non-IgE mediated food allergy
  - IgG4 elevation only shows exposure to food

Non-IgE Mediated Food allergy in Inflammatory Diseases

- Chronic rhinosinusitis
- Asthma
- Rheumatoid arthritis
- Eczema
- IBS
- Ulcerative colitis
- Crohn’s disease
- Migraine headaches

Symptoms of Non-IgE Mediated Food Allergy

- Nasal congestion, rhinitis, postnasal drainage
- Muscle or joint pain
- Stomach cramps, bloating
- Headache
- Fatigue and sleep disorders
Food Protein-Induced Enterocolitis Syndrome

- Non-IgE-mediated
- Triggered by cow’s milk, soy, cereals
- Severe vomiting and diarrhea
- Oral food challenge usually needed
- Hydrolyzed or amino-acid based formula helpful
- Elimination diets can also help with resolution in 90% of patients
- Usually resolves by age of 3

Eosinophilic Esophagitis

- Combination of IgE-mediated and non-IgE-mediated mechanisms
- Chronic immune/antigen-mediated disease
- Usually presents in childhood or during 3rd-4th decade of life
- Male/female ratio, 3:1
- 95% Caucasian
- 15 eosinophils/hpf minimum threshold for diagnosis

Eosinophilic Esophagitis Symptoms

- Dysphagia (especially to solid foods)
- Abdominal pain
- Chest pain
- Food impaction in 33-54% adults
- Globus
- Nonspecific throat symptoms
- Vomiting
- Difficulty feeding, failure to thrive
**Eosinophilic Esophagitis**

- Eosinophilic plaques
- Trachealization of esophagus

**Eosinophilic Esophagitis and Allergy**

- Allergic rhinitis 40-75% with documented rates of 71-93% SPT positivity to aeroallergens
- Asthma 14-70%
- Eczema 4-60%
- In experimental models, perennial allergens induce esophageal eosinophilia
- Increased levels of esophageal mast cells, IgE, IL-5, IL-13, TGF-β
- Esophageal remodeling similar to pathologic process in asthma

**EoE and Food Allergy**

- Among adult patients 50% with positive results to at least 1 food, higher rates in children reported
  - Peanut 38%
  - Egg 27%
  - Soy 23%
- SPT results to milk, egg, soy, wheat, corn, and beef
  - PPV 57-66%
  - NPV 58-75%
  - Sensitivity 90-98%, Specificity 14-65%

EoE Treatment

- Endoscopy with biopsy
- PPI therapy
- Topical steroids
- Oral steroids
- Dietary therapy (more effective in children)
  - Strict use of amino-acid based/elemental formula
  - Dietary restriction based on allergy testing
  - Dietary restriction based on elimination
- Control of atopic disease

Elimination Challenge Diet

- For 5-10 days eliminate food from diet and monitor response
- After this period, patients counseled to eat the food and 15 minutes-6 hours after ingesting the food, monitor response
- Patients are instructed to eliminate one food at a time:
  - Wheat
  - Corn
  - Soy
  - Dairy
  - Egg
- Symptoms: postnasal drainage, cough, facial pressure/pain, nasal congestion

Problematic Foods

- WHEAT: All bread products made from wheat, including pasta, pizza, cookies. If it says “gluten Free” it does NOT contain wheat
- DAIRY: Yogurt, “Lattes,” milk, cheese, cream, many baked goods and soups
- EGGS: May also be an ingredient in casseroles, cakes, baked goods
- SOY: Present in many processed foods as soy oil
- CORN: Present in many processed foods as “fructose”, corn syrup, corn oil
## Grains with and without Gluten

<table>
<thead>
<tr>
<th>Grains with Gluten</th>
<th>Gluten-free Grains</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheat, including varieties like spelt, kamut, farro and durum; and products like bulgur, semolina</td>
<td>Amaranth</td>
</tr>
<tr>
<td>Barley</td>
<td>Buckwheat</td>
</tr>
<tr>
<td>Rye</td>
<td>Corn</td>
</tr>
<tr>
<td>Triticale</td>
<td>Job’s Tears (or Hato Mugi)</td>
</tr>
<tr>
<td>Millet</td>
<td>Montina (Indian rice grass)</td>
</tr>
<tr>
<td>Oats</td>
<td>Quinoa</td>
</tr>
<tr>
<td>Rice</td>
<td>Ragi</td>
</tr>
<tr>
<td>Sorghum</td>
<td>Teff</td>
</tr>
</tbody>
</table>

## Which of the following are gluten free?

A. Semolina  
B. Rye  
C. Durum  
D. Barley  
E. Buckwheat

## Can Elimination Challenge Food Diets Help?
- Prospective collection of data on CRS patients undergoing ECFD  
- 43 Adults with CRS: 21 without nasal polyps, 22 without  
- Intervention: Completion of QoL surveys, nasal endoscopy, allergy testing, ECFD  
- 49% reported improvement in sinonasal symptoms  
- 22% reported increased energy, decreased abdominal symptoms
Can Elimination Challenge Diets Help?

- Most commonly reported food was wheat (43%) followed by dairy (28%), or both 14%.
- Endoscopic improvement in 24%.
- 33% of responders had positive allergy testing.
- Only 9% aware of food allergies prior to office visit.

Validated Symptom Survey

Weird Food Allergies

- Ticks that spread Red-Meat allergy.
- Only allergic if two foods to which hypersensitive are eaten.
- Only allergic if exercise and eats food.
Link Between Our Environment and Food Allergy?

Dichlorophenol-containing pesticides and allergies: results from the US National Health and Nutrition Examination Survey 2005-2006

- Sensitizations to 1 or more food allergens common in those with exposure to dichlorophenol metabolites
- High urine levels of dichlorophenols associated with sensitization to foods in US
- Where are chlorophenols found:
  - Pesticides
  - Chlorinated water
  - Deodorizers, moth balls

Emerging Treatments

- Probiotics
- Desensitization
- Development of tolerance
- Environmental considerations
- Peptide and plasmid-based vaccines

Thank you!

Alyssa Kanaan, MD
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John McCormick