

GI Manifestations of Food Allergy

Hugh A. Sampson, M.D.

Professor of Pediatrics & Immunology
 Dean for Translational Biomedical Research
 Director, Jaffe Food Allergy Institute
 Mount Sinai School of Medicine
 New York, NY



WISC 2012 Hyderabad

Faculty Disclosures

FINANCIAL INTERESTS

I have disclosed below information about all organizations and commercial interests, other than my employer, from which I or a member of my immediate family or household receive remuneration in any amount

Name of Organization	Nature of Relationship
Allertin Therapeutics, LLC	Consultant, Minority Stockholder
University of Nebraska	Consultant
Food Allergy Initiative	Scientific Advisor
Danone Scientific Advisory Board	Scientific Advisor

RESEARCH INTERESTS

I have disclosed below information about all organizations which support research projects for which I or a member of my immediate family or household serve as an investigator.

Name of Organization	Nature of Relationship
National Institutes of Health	Grantee
Food Allergy Initiative	Grantee

- Patents – EMP-123 (recombinant protein vaccine) & FAHF-2 (herbal product)

Gastrointestinal Hypersensitivities



Oral Allergy
 Immediate
 GI Hyper-
 sensitivity

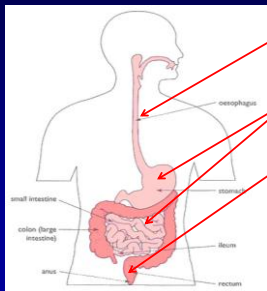
AEE
 AEG

Enterocolitis
 Enteropathy
 - Celiac
 Disease
 Proctocolitis

Immediate Gastrointestinal Hypersensitivity

- Onset - infancy & childhood
- Symptoms - nausea, abdominal cramping, vomiting within mins - 2 hrs; & /or diarrhea within 2 - 6 hrs; frequently involves other target organ, e.g. skin
 - freq ingestion may → “malabsorption” picture
- Foods implicated - milk, egg, peanut, soy, wheat
- Diagnosis - food-specific IgE Abs; challenge → “immediate” vomiting

Eosinophilic Esophagitis, Gastroenterocolitis & Proctocolitis



Eosinophilic Esophagitis (EoE)

Eosinophilic Gastroenteritis (EG)

Eosinophilic Proctocolitis

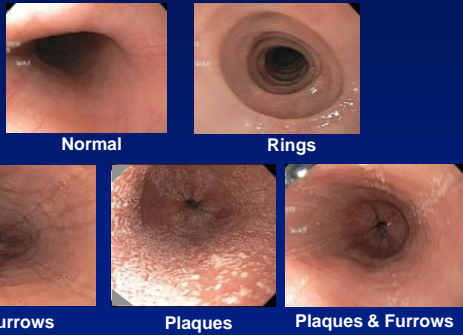
Diagnosis based on history, endoscopy & biopsy, and response to therapy

Eosinophilic Esophagitis Clinical Picture

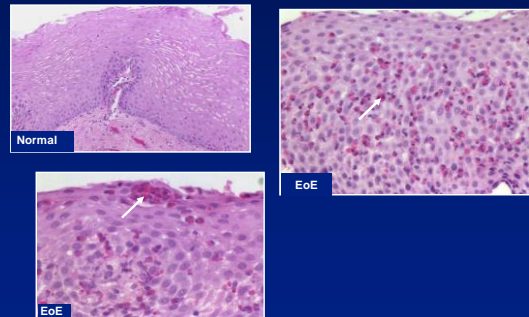
- Etiology
 - Multiple food allergens (*Kelly 1995*)
 - Airway/cutaneous priming? (*Mishra 2001; Akei 2005*)
- Clinical manifestations
 - Adolescents/adults: dysphagia, chest pain, globus, food impaction
 - Younger children: Reflux symptoms (emesis, spitting up, irritability, food refusal), abdominal pain, and/or failure to thrive
- Affects males > females
- Age at onset: infant to adult
- Personal and/or family history of atopy in >50% cases

Furuta GT et al. *Gastroenterology* 2007; 133:1342-1363

EoE: Endoscopic Diagnosis



EoE: Histological Diagnosis



Eosinophilic Esophagitis Diagnosis

- Food allergies
 - Food-specific IgE levels not always elevated
 - Prick skin tests not always positive
 - Combination: Prick skin tests and patch tests?

Prick Skin Test



Atopy Patch Test



EoE: Food Allergens

- IgE-mediated food allergy is present in ~15% of EoE
- Sensitization to multiple foods is common in EoE
- SPT and APT are not predictive of EoE triggers

	SPT	APT
	PPV (%)	PPV (%)
Milk	96	83
Egg	85	78
Soy	70	67
Wheat	78	74
Peanut	78	75
Beef	82	94
Corn	57	66
Chicken	50	67
Rice	50	59
Potato	60	54
Oat	33	47
Barley	43	90

Spergel et al, JACI 2007

EoE: Dietary therapy

- Elemental diet
- Test-directed elimination diet
- Empiric elimination diet

Eosinophilic Esophagitis Attributable to Gastroesophageal Reflux: Improvement with an Amino Acid-Based Formula

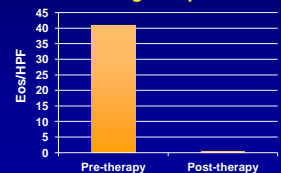
Kelly, Lazenby, Rowe, Yardley, Perman, Sampson

Gastroenterology 1995

10 children: amino acid formula ± corn and apple

Clinical response:
80% symptom resolution
20% symptom improvement

Histologic response:



Elemental Diet is an Effective Treatment for Eosinophilic Esophagitis in Children and Adolescents

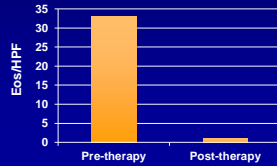
Markowitz, Spergel, Ruchelli, Liacouras

Am J Gastroenterol 2003

51 children: amino acid formula + grape or apple

Clinical response:
96% symptom resolution

Histologic response:



The Use of Skin Prick Tests and Patch Tests to Identify Causative Foods in Eosinophilic Esophagitis

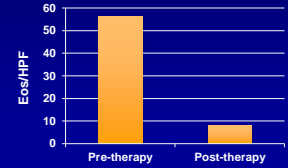
Spergel, Beausoleil, Mascarenhas, Liacouras

J Allergy Clin Immunol 2002

26 children: removal of foods that tested positive on SPT and APT

Clinical response:
69% symptom resolution
23% partial improvement

Histologic response:



Eosinophilic Esophagitis in Adults – No Clinical Relevance of Wheat and Rye Sensitizations

Simon, Straumann, Wenk, Spichtin, Simon, Braathen

Allergy 2006

• 6 adults (+SPT/IgE to grass, wheat, rye, -SPT/IgE to foods)

Removal of wheat, rye, barley

Clinical response:
17% partial improvement

Histologic response:
None

Effect of Six-Food Elimination Diet on Clinical and Histological Outcomes in Eosinophilic Esophagitis

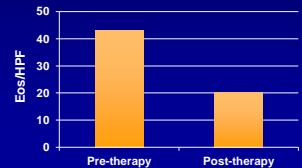
Kagalwalla, Sentongo, Ritz, Hess, Nelson, Emerick, Melin-Aldana, Li

Clin Gastroenterol Hepatol 2006

35 children: empiric removal of common food allergens (milk, egg, wheat, soy, nuts, seafood)

Clinical response:
74% improvement

Histologic response:



Elimination Diet Effectively Treats Eosinophilic Esophagitis in Adults; Food Reintroduction Identifies Causative Factors

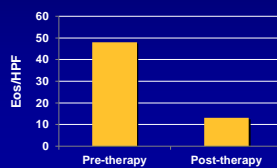
Gonsalves, Yang, Doerfler, Ritz, Ditto, Hirano

Gastroenterology 2012

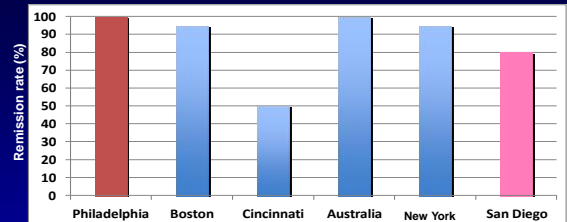
50 adults: empiric removal of common food allergens (milk, egg, wheat, soy, nuts, seafood)

Clinical response:
Dysphagia score - ↓ 94% patients

Histologic response:



EoE: Steroid Therapy

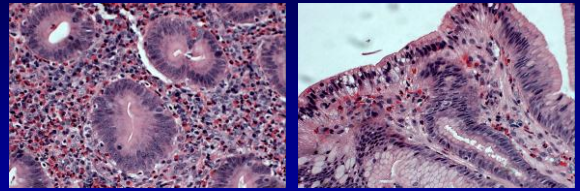


Liacouras et al, *J Pediatr Gastroenterol Nutr* 1998
Taitelbaum et al, *Gastroenterology* 2002
Konikoff et al, *Gastroenterology* 2006
Remedios et al, *Gastrointes Endosc* 2006
Chehade et al, unpublished data
Aceves et al, *Am J Gastroenterol* 2007

Eosinophilic Gastritis/Gastroenteritis

- **Epidemiology**
 - No data available
 - Less prevalent than EoE
- **Age at diagnosis**
 - Any age (infant to adult)
- **Atopic predisposition**
 - > 50% have asthma, allergic rhinitis, and/or AD
- **Clinical manifestations**
 - >50% have abdominal pain, emesis, early satiety, diarrhea
 - Failure to thrive in children
 - subset has edema & anemia 2° protein-losing enteropathy

EG: Histologic Diagnosis



Stomach

Duodenum

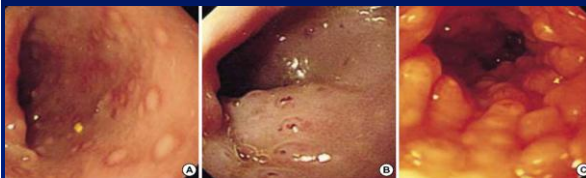
Eosinophilic Gastritis/Gastroenteritis

- **Etiology**
 - Subset related to multiple food allergens
 - PST and serum food-IgE not predictive of food triggers
- **Dietary**
 - Sometimes effective
 - Amino acid-based formula (*Sicherer 2001, Chehade 2005*)
 - Empiric food eliminations
- **Oral corticosteroids**
 - Effective but has long-term side effects
 - Prednisone (*Lee 1993*)

FOOD-INDUCED PROCTOCOLITIS SYNDROME

- Onset - generally in first 3 months of life
- Symptoms - blood streaked or Heme + stools
 - anemia rare; ± hypoalbuminemia
- Implicated protein - cow milk & soy protein
 - ~ 60% breast fed
 - egg, wheat, corn, fish, shellfish, and nuts
- Diagnosis - food challenge [0.3 - 0.6 g protein]
 - blood in stool within 6 - 72 hrs
 - Ag elimination: gross blood clears in 72 hrs

Sigmoidoscopy Findings



A. Nodular hyperplasia with circumscribed erosions

B. Nodular hyperplasia with central pit-like erosions

C. Nodular hyperplasia in endoscopically deflated state

Hwang JB et al, *J Korean Med Sci*, 2007

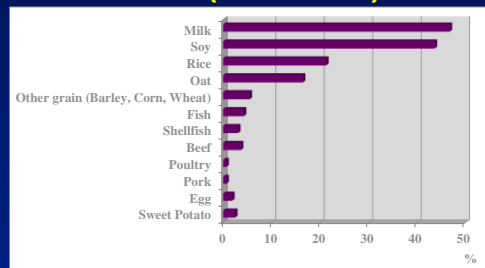
FOOD-INDUCED PROCTOCOLITIS SYNDROME

- Labs / Procedures -
 - CBC: normal or slightly decreased Hgb / Hct
 - significant anemia is rare
 - normal or slightly increased eos count
 - Stools neg for bacteria, virus, & parasites
 - Sigmoidoscopy: patchy injection → severe friability & aphthoid ulceration
 - Biopsy: eos. in crypts & lamina propria
- Natural Hx - symptoms usually clear in 1 - 2 yrs

FOOD-INDUCED ENTEROCOLITIS SYNDROME

- Onset - generally in first 3 months of life
- Symptoms - recurrent projectile vomiting, diarrhea, abdominal distention, & FTT
 - Infants may present with dehydration &/or "septic-like" picture
 - Adults - severe vomiting ~ 2 hrs post-seafood ingestion
- Implicated protein - cow milk & soy, rice, poultry, cereal grains; Adults: shrimp & other shellfish
- Diagnosis - food challenge [0.3 - 0.6 g protein]
 - vomiting - 2 - 4 hrs; ~15% hypotensive
 - diarrhea - 5 - 10 hrs

Reported foods in 165 infants with FPIES (2001-2009)



Prevalence in Mt Sinai Pediatric Allergy Practice patient population -1-2%

Jarvinen K, et al JACI (abstract) 2010

FOOD PROTEIN-INDUCED ENTEROCOLITIS SYNDROME

- Labs / Procedures-
 - CBC: leukocytosis with left shift
 - Stools: Hgb +, PMN's & Eosinophils
 - Biopsy: flattened villi, edema, & increased lymphs, eos, & mast cells
 - Cell culture: Ag + PBMC's → ↑ TNF- α
- Natural Hx -
 - cow milk: with exclusion, 50% resolve in 1 yr, 90 % in 3 years
 - soy, cereal grains & other foods tend to be more persistent; adults with shellfish allergy - ?

Dietary Protein Enteropathy

- Onset - generally in first few months of life
- Symptoms - diarrhea, steatorrhea, malabsorption, FTT, vomiting, abdominal distention, anemia, hypoproteinemia, early satiety
- Implicated protein - cow milk, soy, cereal & egg
- Diagnosis - food challenge => vomiting &/or diarrhea in 40 - 72 hrs
 - may need to confirm patchy villous atrophy post-challenge

Dietary Protein Enteropathy

- Diagnostic lab procedures -
 - radiographic: small bowel edema
 - biopsy: patchy villous atrophy; prominent lymphocytic & minor eosinophilic infiltrate in epithelium & lamina propria
 - IgE, peripheral eos, α -endomysial Ab - neg.
- Natural Hx - most cases resolve in 2 - 3 yrs
 - elimination of Ag → symptomatic clearing in 3 - 21 days

CELIAC DISEASE

- Onset: variable; dependent upon when gluten is introduced into the diet
- Symptoms: diarrhea / steatorrhea, abdominal distention & flatulence, FTT or weight loss; oral ulcers; some asymptomatic ["silent"]
- Implicated protein - wheat, rye and barley [gliadin]
- Diagnosis: "classic" laboratory and endoscopic finding on & off diet
 - 90% assoc with HLA-DQ2 & 10% with DQ8 haplotype
- Incidence: US - 1:105 Sweden - 1:300

CELIAC DISEASE

- Labs / Procedures -
 - Biopsy: extensive villous atrophy; ↑ crypt length, ↑ intraepithelial lymphocytes [esp. γ/δ]
 - Radiographic: malabsorption pattern
 - IgA α -endomysium, α -tTGase & α -gliadin Abs.
- Mechanism - tTGase deamidates specific glutamines within gliadin → DQ2 (DQ8)-specific epitopes → activation of lymphocytes
- Natural Hx - life-long; ↑ GI malignancy [lymphoma]

GI Food Allergy: Summary

- Food allergies affect up to 8% of children < 3 yrs and ~ 3.5% of the US population; ~40% GI in infants
- Most GI allergic disorders are not IgE-mediated
- Diagnosis requires characteristic history, supporting lab studies, dietary elimination & often challenge
- Therapy consists of strict avoidance and use of corticosteroids in some cases
- EoE is growing problem in both children and adults
 - elimination diet is optimal, but often not practical
 - good symptomatic relief with topical steroids