





Eosinophilic Esophagitis Diagnosis and Management

Jonathan M. Spergel, MD, PhD
Division of Allergy and Immunology
The Children's Hospital of Philadelphia
Perelman School of Medicine at Univ. of Pennsylvania

Disclosure



- Grants
 - Ception/Cephalon, **APFED**, **DOD**, NIH, Nutricia
- Consultant
 - DBV

Eosinophilic Esophagitis (EoE)

- *Eosinophilic esophagitis represents a chronic, immune / antigen mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation.*
- Diagnosed is based on clinical-pathologic findings on biopsy with greater than 15 eosinophils/HPF
 - Exclude other causes of esophageal eosinophilia
 - GERD, Celiac, IBD, Allergic Rhinitis
- EoE is a lifelong chronic condition

Liacouras, JACI 2011; Spergel et al J Pediatr Gastroenterol Nutr 2009

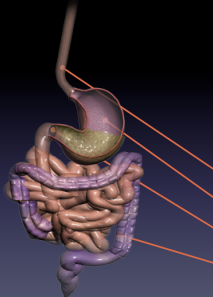



World Map of EoE







Gastrointestinal Eosinophils




Normal values, per 400x microscopic field:

- Esophagus (0)
- Gastric antrum (2-20)
- Duodenum (2-20)
- Colon (10- 50)





Review of EoE



Endoscopic findings

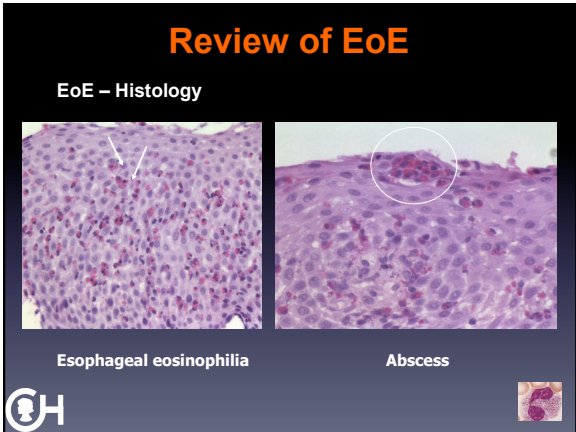
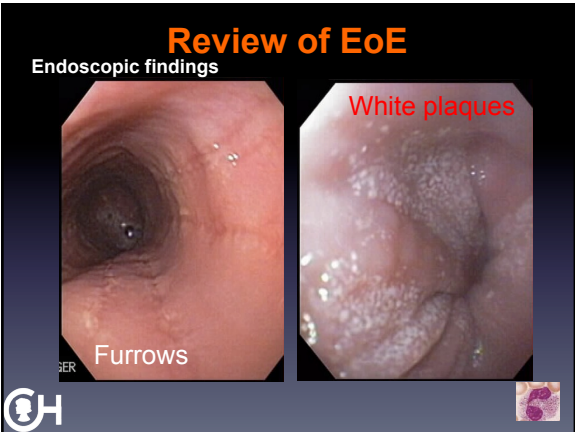


Normal

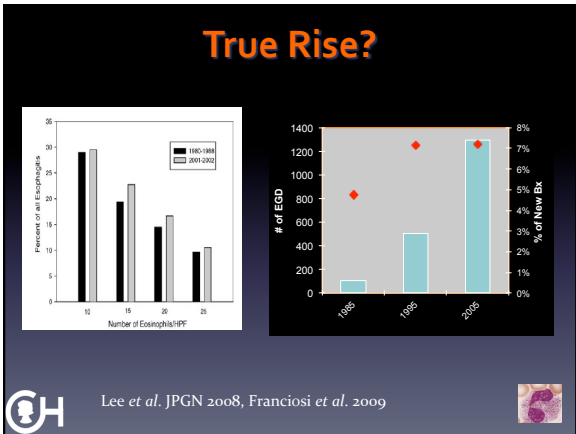
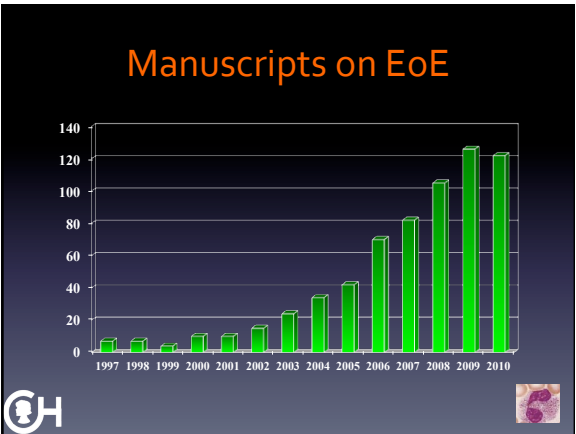
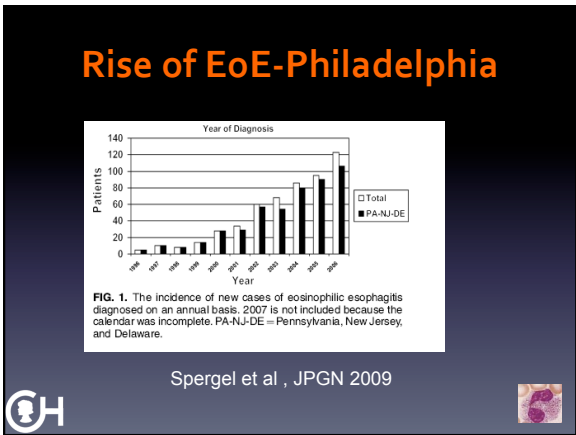


Rings

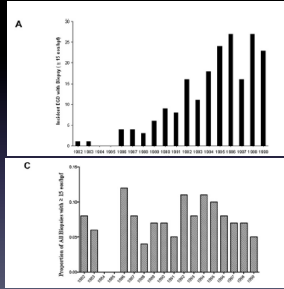





- ### Other Causes of Eosinophilia
- GERD
 - Celiac
 - IBD
 - Fungal Infection
 - Allergic Rhinitis
 - Drug Allergy
-



Is more endoscopy or more disease?



Debrosse et al, J Allergy Clin Immunol 2010; 120:112-9.



EoE Estimates in Europe and US

- ◆ Ronkainen and colleagues – performed EGD in random sample of adult Swedish population (no indication!)
 - ◆ 4/1,000 subjects with ≥ 20 eos/HPF
 - ◆ 11/1,000 subjects with ≥ 15 eos/HPF
 - ◆ Prevalence of 110/10,000
- ◆ Estimates based on community prevalence
 - ◆ 50/100,000 in Cincinnati, OH and Rochester, MN
- ◆ Estimates based on questionnaire
 - ◆ 52.2/100,000 in the US



Ronkainen et al. Gut 2007; Dalby et al. J. Pediatr Gastroenterol Nutr 2010; Spergel et al, J Pediatr Gastroenterol Nutr 2011



Management

- Serial Endoscopies
- Clinical Follow
 - Barium Swallow



Symptoms of EoE

EoE – Clinical manifestations

- Symptoms similar to those of GERD
 - Histology does not respond to PPI's.
- Age related differences in symptoms
- Symptoms may be intermittent
- Male > Female
- May progress to esophageal fibrosis and esophageal dysfunction if not managed appropriately.

EoE patient	Common Symptoms
Infant	Food refusal, FTT, feeding intolerances/aversions
Children	Vomiting, dysphagia, abdominal pain, heartburn, regurgitation, feeding refusal/feeding aversions
Adult	Dysphagia, food impaction, heartburn, reflux



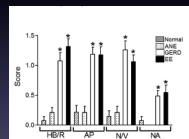
Furuta et al. Gastroenterology 2007
Spergel et al J Pediatr Gastroenterol Nutr 2009



Correlation between Symptoms and Endoscopy

- Symptoms can differentiate between normals and EE, but overlap with GERD

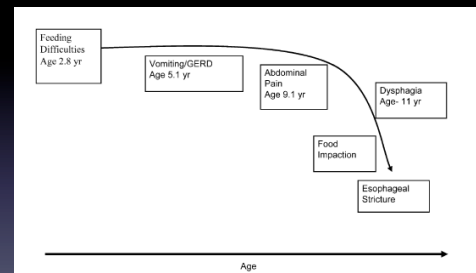
1. Has your child ever had a choking episode or been "choked"?
 Has your child ever had food coming back up into his or her mouth?
 2. Has your child ever had the "cereal-paste" vomit?
 3. Has your child ever had a cough or wheeze (any season) in the past?
 4. How often has your child coughed after eating/drinking?
 How often has your child been sick?
 5. How often has your child had a fever or had a sore throat?
 6. How often has your child had a fever or had a sore throat?
 7. How often has your child had a fever or had a sore throat?
 8. How often has your child had a fever or had a sore throat?
 9. How often has your child had a fever or had a sore throat?
 10. How often has your child had a fever or had a sore throat?
 Please indicate how often your child has had each of these symptoms.
 Legend: 1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Often, 5 = Always



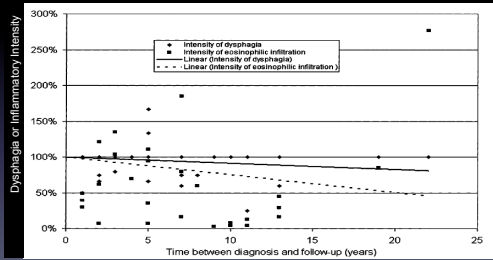
Aceves et al, Ann Allergy Asthma Immunol 2009; 103:401-6.



Symptom Progression in EoE

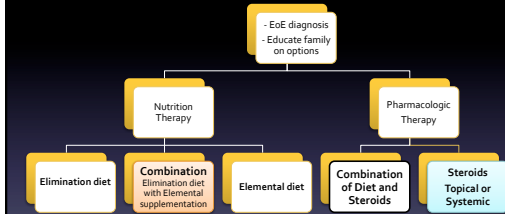


Chronic EoE: Adults



Straumann et al. Gastroenterology 2003

Treatment Options



Pharmacologic Therapy

Systemic Steroids – effective at improving symptoms and histology of EoE in 95% of pts

- Upon discontinuation, 90% had recurrence of symptoms
- (Long term use) Side effects: bone abnormalities, poor growth, adrenal suppression
- May be needed short term for extreme cases

Topical/swallowed Steroids – less toxic to pt while still 50-85% effective

- A mainstay of EoE treatment in adults and children.
- Upon discontinuation almost all patients have a recurrence of symptoms
- Often, large doses needed
- Side effects: esophageal candidiasis

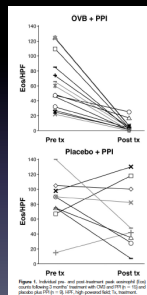
Liacouras et al. Clin Gastroenterol Hepatol 2005
Furuta et al. Gastroenterology 2007

Corticosteroid Therapy

Liacouras	Oral steroids	100% Response
Teitelbaum et al, Gastroenterol 2002	Topical Fluticasone Open label Pediatric	85% Response
Remedios et al, Gastroint Endos 2006	Topical Fluticasone Open label Pediatric	95% Response
Konikoff et al, Gastroenterol 2006	Topical Fluticasone Randomized, Controlled Trial	50% Response
Aceves et al, Am J Gastro 2007 Dohil et al Gastro 2010	Topical Budesonide Retrospective, Randomized PC	80-87% Response

Budesonide Study

- DBPC trial:
 - 15 OVB
 - 9 placebo patients
 - 1 mg BID (Children <5ft) and 2 mg BID (>5ft)
- Significant improvement in Symptoms and bx
- 85% response rate



Dohil et al Gastroenterology 2010 139:418

Food Avoidance Therapy



Link Between Food Allergy and EoE

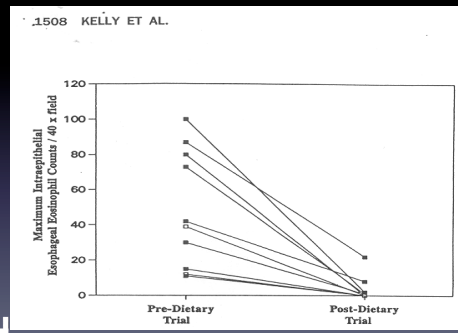
- Dobbins (1977): 51 yo with GERD, food allergy and esophageal eosinophilia
- Kelly and Sampson (1995)
 - 10 patients (5 yr range: 8 mo-12.5 yr)
 - Given amino-acid based formula (> 6 weeks)
 - Neocate® or Neocate 1+®
 - 6 prior Nissen fundoplication
 - Endoscopy pre- & post-trial



Dobbins et al. *Gastroenterology*, 1977;72:1312-1316.
 Kelly et al. *Gastroenterology*, 1995; 109: 1503-12.
 Van Rossum et al. *Am J Gastroenterol*, 1997;92:1054-1056.



Kelly, 1995 Results



Dietary Management Amino Acid-Based Formula

160 Patients	Pre-Diet	Post-Diet	P value
Eosinophils/HPF	38.7 ± 10.3	1.1 ± 0.6	<0.001
Dysphagia	30	1	<0.01
GERD Symptoms	134	3	<0.01

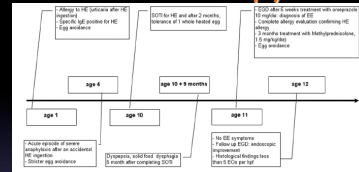
- 172 patients (128 nasogastric tubes, 32 oral, 4 failed, 8 noncompliant)
- Patients evaluated 4-6 weeks after starting diet



Liacouras et al. *Clin. Gastroenterol Hepatol* 2005



Oral Immunotherapy induces EoE



- Seen after egg, milk and peanut OIT
- Incidence about 5-20%
- Indicates foods causes EoE and it is not TH₂ mechanism



Ridolo et al, *Annals of Asthma Allergy Immunology* 2011:

Abstracts: 83, 87, 91, 94, 103

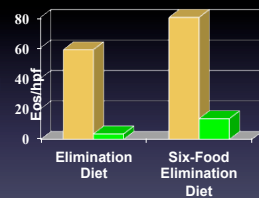


How to Select the foods?



Selective Diet: Guess

- 60 children
 - 35 children on elimination diet of milk, soy, wheat, egg, peanut and seafood
 - 25 children on elemental diet
- Repeat endoscopy-6 weeks later
- 74% of six-food diet had < 10 eos/hpf
- 88% of elemental diet had <10 eos/hpf



Kagalawa et al. *Clin Gastro Hepatol* 2006



SFED follow-up

- Single Food Reintroduction in 36 children
- 74% to milk
- 26% to wheat
- 17% to egg
- 10% to soy
- 6% to peanut
- Single food in 72%, 2 foods in 8% and 3 foods in 8%



Kagalwalla et al. JPGN 2011



Most Common Foods in EoE

Food	EoE by Bx	IgE Reactions	EoE by Symptoms	Total
Milk	168	25	145	338
Egg	43	44	81	168
Soy	41	10	74	125
Wheat	55	2	64	121
Peanuts	16	44	42	102
Beef	27	0	61	88
Corn	31	0	51	82
Chicken	25	1	51	72
Potato	19	0	33	52
Pork	16	0	30	46



Food Testing in EoE

- 74% Atopic (asthma, ARC, or AD)
- 1/3 have negative skin tests
- Most common foods were
 - Egg, soy, milk, peanuts, beef, chicken, wheat, corn, peas, and potato
- 1/4 have negative APT
 - 1/8 have both negative SPT and APT
 - Wheat, corn, soy, milk, beef, rice, chicken, egg, rye, oat, and potato



Predictive Values

- All pts had > 20 eos/hpf on GERD and AR medication and had
 - Removal of a single food leading to normal esophageal biopsy (0 eosinophils/HPF). And/or
 - Addition of a single food leading to increased esophageal eosinophils on biopsy after a previously normal biopsy.
- 104 Children
 - 64 male, 30 female
 - Age: 6.4 ± 4.2 (2 to 18 years)
- Redo the analysis currently on a larger n (200 patients)



Spiegel et al, JACI 2007



Predictive Values: Combination of SPT and APT

Food	Combined SPT and APT			
	PPV	NPV	Specificity	Sensitivity
Milk (n = 99)	93.0%	32.4%	84.6%	52.9%
Egg (n = 38)	65.5%	86.6%	86.7%	85.7%
Wheat (n=37)	73.7%	99.1%	80.8%	85.7%
Soy (n = 25)	43.2%	92.6%	75.9%	67.9%
Beef (n=21)	48.4%	96.2%	84.9%	65.2%
Chicken (n=20)	46.3%	99.0%	83.3%	84.0%
Corn (n=17)	62.5%	98.6%	81.7%	95.0%
Potato (n=12)	47.4%	98.2%	91.5%	81.8%
Rice (n=11)	32.3%	99.0%	82.5%	90.9%
Pork (n = 11)	38.5%	97.5%	93.1%	62.5%

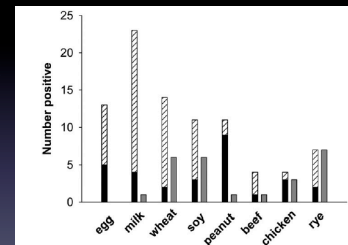


Spiegel et al, JACI 2007 and unpublished data



Specific IgE

- 53 adult patients
- 80% had positive sIgE to food or aeroallergens
- sIgE was most sensitive



Hatched (sIgE), Black (SPT), APT (Gray)



Erwin et al, J Allergy Clin Immunol 2010



What method is best?

Method	SPT/APT	MILK	Milk, Egg, Wheat	SFED	SPT/APT + Milk
Rate of Resolution	57%	30%	48%	60%	77%

- Retrospectively examined all patients with defined food identified
- Excluded patients on ICS or anti-IL5
- Examined which diet method lead to normalization of histology



Nutrition Therapy

Common Challenge - Diet Adherence Nutritional Balance



What have we learned in 28 years? Katz, Flores, Twarog SPR 1983

- Positive on Skin tests; highly atopic
- Response to Diet and Steroids
- pH probe negative
- Basal cell hyperplasia



Summary: Treatment in EoE

- **Pharmacologic therapy** has been shown effective but long term use and possible side effects must be considered
- **Elimination diet** is effective - keeping in mind nutrient deficiencies may occur
- **Elemental diet** is the most effective nutrition therapy. Compliance/cost may be an issue for some patients
- **Combination of diet and steroids** for difficult to treat patient
- **Combination of elimination diet with elemental supplementation** may be the best fit for patients and families dealing with EoE.

“Dietary therapy should be considered as an effective therapy in all children diagnosed with EoE.”

Furlis et al. Gastroenterology 2007
Feunling & Noel, Nutr Clin Pract 2010



Acknowledgements

- Allergy Section
 - Michele Shuker
 - Terri Brown-Whitehorn
 - Antonella Cianferoni
 - Rushani Saltzman
 - Mariel Boyd
 - Laura Gober
 - Kathy Pinzone
 - Jennifer Heimall
 - Mariel Boyd
 - Emily Dudek
 - Katie Ruymann
 - Malkora Maggadottir
- Center for Applied Genomics
 - Hakon Harkonson
 - Patrick Sleiman
- GI Division
 - Chris Liacouras
 - Joshua Friedman
 - Mel-Lin Wang
 - Ritu Verma
- Pathology/Vet
 - David Artis
 - Mark Sircusa
- HUP
 - Gary Falk
 - Benjamin Soule
- Collaborators
 - Seema Aceves
 - Glenn Furuta
 - Mark Rothenberg

