

IgE



Gastrointestinal Hypersensitivity Disorders

Pollen-Food Allergy Syndrome Immediate GI Hypersensitivity

Eosinophilic Esophagitis Eosinophilic Gastritis Eosinophilic Gastroenteritis

Dietary Protein Enterocolitis Dietary Protein Proctitis Dietary Protein Enteropathy (Celiac Disease)

Cutaneous Hypersensitivity Disorders

Acute Urticaria & Angioedema
Acute Contact Urticaria

Atopic Dermatitis

Dermatitis Herpetiformis

Respiratory Hypersensitivity Disorders

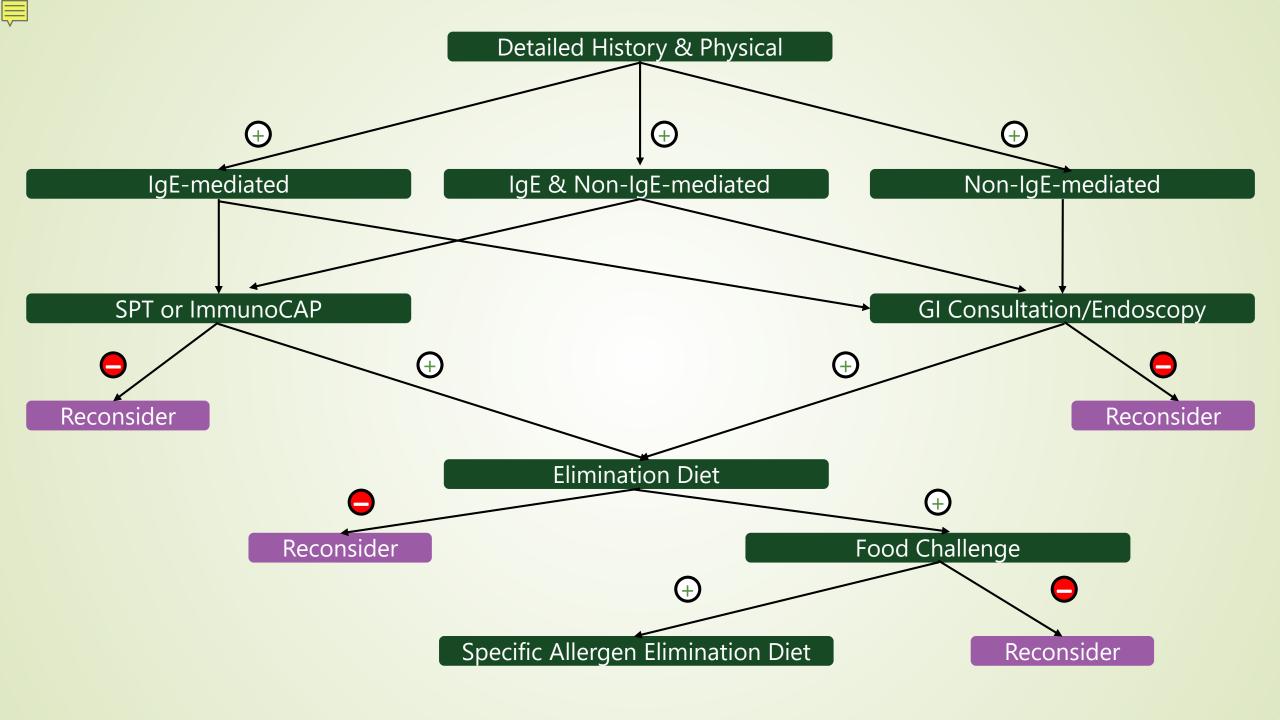
Allergic Rhinitis
Acute Bronchospasm

Asthma

Food-induced Pulmonary Hemosiderosis (Heiner Syndrome)

Systemic Hypersensitivity Disorders

Generalized Anaphylaxis Food-associated Exercise-induced Anaphylaxis



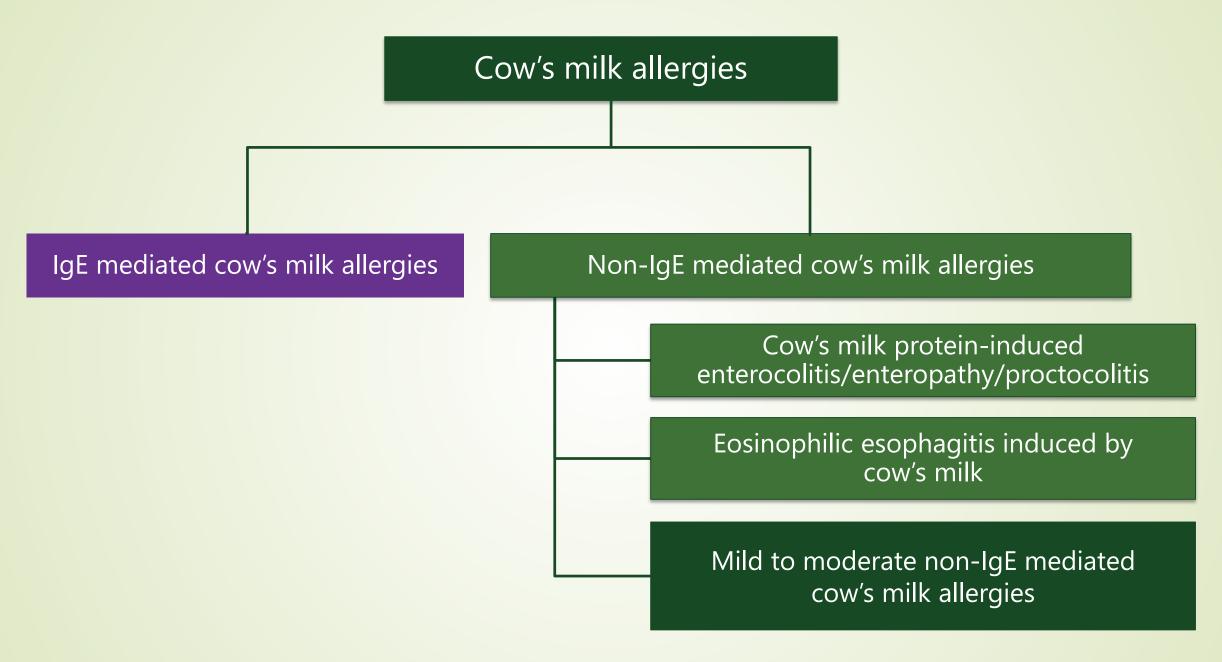


IgE-mediated vs non-lgE-mediated Reactions

Important to differentiate clinically between IgE-mediated and non-IgE-mediated characteristics.

Characteristic	IgE-mediated	Non-IgE-mediated
Time from exposure to reaction	Immediate onset— minutes to 2 hours	Delayed onset; usually ≥ 2 hours
Severity	Mild to anaphylaxis	Mild to moderate More severe presentations
Duration	Usually persist beyond 1 year of age	Often persist beyond 1 year of age
Diagnosis	Clinical history Specific serum IgE, skin-prick test Oral challenge	Clinical history Elimination diet Oral food challenge when indicated





Pathophysiology of Cow's Milk Allergy

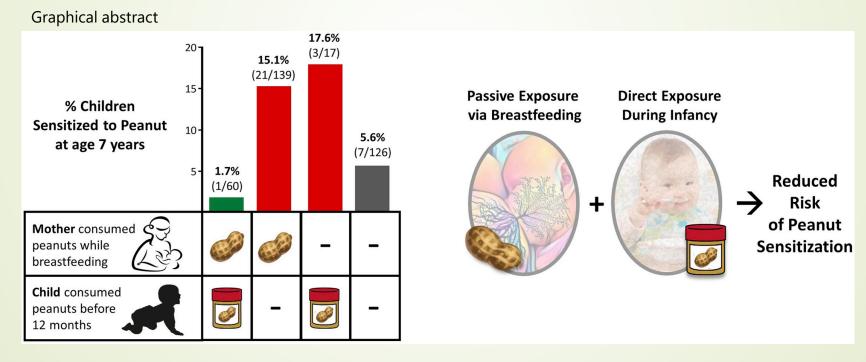
- Triggers—Principal cow's milk allergens
 - Casein fraction of proteins (α s1-, α s2-, β -, and κ -casein)
 - Whey proteins (α -lactalbumin and β -lactoglobulin)
- Complex interplay
 - Epithelial barrier
 - Mucosal and systemic immune response
 - Route of exposure
 - Microbiome and other influences resulting in allergy or tolerance



Breast Milk and What it Provides

Tolerance

- Support the infant's developing immune system
- Tolerance to potential food allergens?



Recommended Treatment of CMA

- Breastfed infants
 - May need to consider avoidance of cow's milk protein from maternal diet
 - May take up to 72 hrs to clear breast milk antigens
- Infants <6 months
 - Formulas extensively hydrolyzed protein or amino acid-based formula
- Infants > 6 months
 - Soy formula may be appropriate in IgE-mediated cases
 - Country specific: Not to be used in infants with food allergy <6 months of age



FPIES Clinical Phenotypes

- FPIES phenotype depends on dose and frequency of food allergen ingestion.
- Phenotype provides guidance for diagnosis and management.

Phenotypes influenced by		
Age of onset	early (<9 months)	late (>9 months)
Severity	mild-to-moderate	severe
Timing and duration of symptoms	acute (symptoms resolve in 24 hrs)	chronic (resolution may take days to weeks)
Associated IgE-mediated food allergy	IgE negative	IgE positive

FPIES Phenotypes (continued)

Acute	Chronic
Ingestion following a period of avoidance (at least several days)	Young infants fed continuously with milk or soy formulas
Onset of emesis: 1–4 hours	Watery diarrhea
Lethargy, limpness ("septic appearance")	Mucous, blood in stools
15% go into shock	Intermittent emesis
15% with methemoglobinemia	Low albumin and total protein
6–8 hours later: diarrhea	Failure to thrive, poor growth
Onset: usually under 12 months; Fish/Shellfish: children, adults	Onset: first 1–3 months of life
Symptoms resolve within 24 hrs	Symptoms resolve within days-weeks, may require TPN
Cow's milk, soy, rice, oat, vegetables	Cow's milk, soy

Distinguishing FPIES, FPIAP, and FPE

	Main clinical features
FPIES	Delayed repetitive vomiting, pallor, lethargy
FPIAP	Benign blood in stool, baby thriving Average age at onset lower: 2 months vs 4-6 months in FPIES, no acute symptoms upon food ingestion
FPE	Chronic diarrhea, malabsorption, low weight gain, no acute symptoms upon food ingestion

FPIAP, food protein-induced allergic proctocolitis; FPE, food protein-induced enteropathy.

Oral Food Challenge: What You Need to Know

- Oral food challenge (OFC) can confirm the diagnosis
- OFC is the only currently available diagnostic test
- FPIES diagnosis is based on consistent clinical features with improvement following withdrawal of suspected causal protein
- Physician-supervised OFC is necessary to evaluate for FPIES resolution
- Keep child away from food until challenge is done
- OFC is standardized

ER Letter—Individualized Allergy Action Plans

- Letter every parent should carry (see course downloads)
 - Provide letter to ER—What to do with accidental exposure
 - Letter includes:
 - Clinical features (it is this)
 - How this child is being treated for FPIES
 - Avoid medicine (eg, do not give antihistamine or epinephrine)
 - Foods this child has FPIES reaction(s) to
- How to Treat—Best treatment is rehydration in ER
 - Rehydration [with intravenous fluids]
 - Single dose of intravenous methylprednisone given in severe reactions
 - Ondansetron iv/im/po may be useful in mild-moderate reactions

Management While Breastfeeding

FPIES can happen in exclusively breastfed infants, although rarely

- Do not restrict maternal diet unless infant is symptomatic (acute or chronic), or is not thriving
- Majority are asymptomatic and thriving during breastfeeding
- Rarely have acute or chronic symptoms been reported in breastfed infants, attributed to foods in maternal diet
- Maternal dietary avoidance vs stopping
- Substitute for breast milk: Hypoallergenic formula
 - Extensively hydrolyzed casein or amino acid formula [up to 40%]



Selecting Safe Nutritional Alternatives

Ages and Stages	Lower-risk foods*	Moderate-risk foods*	Higher-risk foods*
 4 to 6 months (per AAP, CoN) If developmentally appropriate, and safe and nutritious foods are available: Begin with smooth, thin, purees and progress to thicker purees Choose foods that are high in iron Add vegetables and fruits 	Broccoli, cauliflower, parsnip, turnip, pumpkin	Squash, carrot, white potato, green bean (legume)	Sweet potato, green pea (legume)
 6 months (per WHO) Complementary feeding should begin no later than 6 months of age. In the breastfed infant, high-iron foods or supplemental iron (1 mg/kg/day) is suggested by 6 months of age. Continue to expand variety of fruits, vegetables, legumes, grains, meats, and other foods as tolerated. 	Blueberries, strawberries, plum, watermelon, peach, avocado	Apple, pear, orange	Banana

^{*}Risk assessment is based on the clinical experience and the published reports of FPIES triggers.



Selecting Safe Nutritional Alternatives

Ages and Stages	Lower-risk foods*	Moderate-risk foods*	Higher-risk foods*
 8 months of age or when developmentally appropriate Offer soft-cooked and bite-and-dissolve textures around 8 months of age or as tolerated by infant. 	Lamb, fortified quinoa cereal, millet	Beef, fortified grits and corn cereal, wheat (whole wheat and fortified), fortified barley cereal	Higher iron foods: Fortified, infant rice and oat cereals.
 12 months of age or when developmentally appropriate Offer modified tolerated foods from the family table: chopped meats, soft cooked vegetables, grains, and fruits. 	Tree nuts and seed butters* (sesame, sunflower, etc)	Peanut, other legumes (other than green pea)	Milk, soy, poultry, egg, fish

^{*}Risk assessment is based on the clinical experience and the published reports of FPIES triggers.

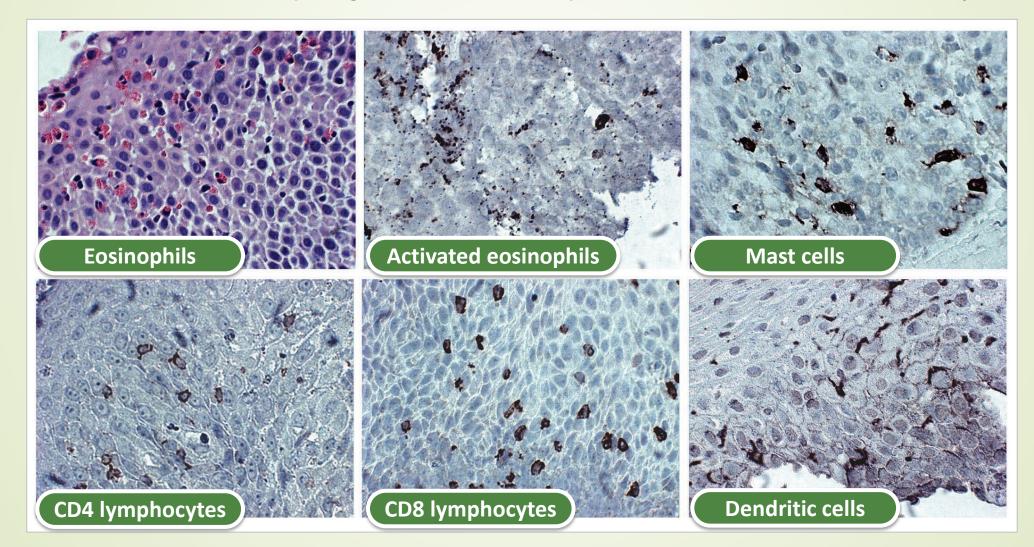
FPIES Resources

- FPIES.org https://www.fpies.org
- FPIES Guidelines https://www.fpies.org/fpies-guidelines/
- FPIES Emergency Room Letter example
 https://www.fpies.org/wp-content/uploads/2017/12/IFPIES-ER-Letter.pdf
- Help track frequency of FPIES occurrence
 - o ICD-10 code: K52.2

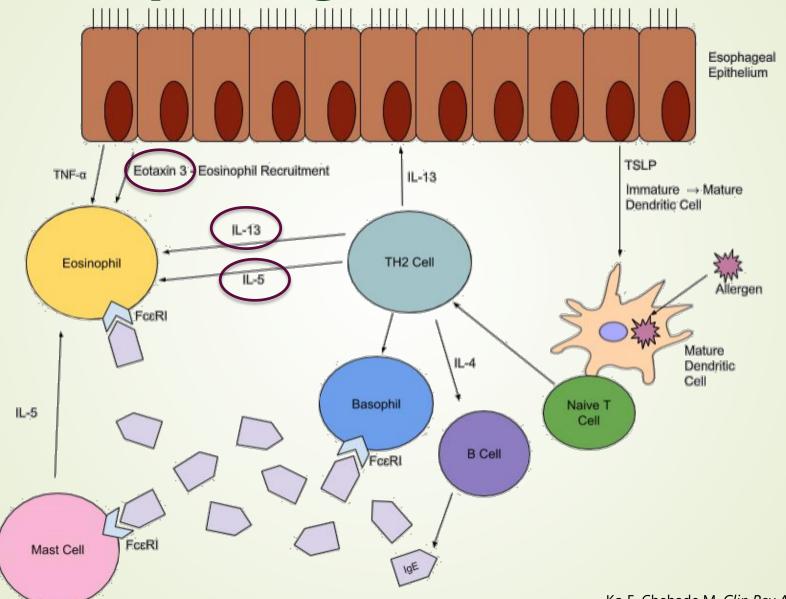
https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20Management/finances-coding/FPIES-Codes-ICD-10.pdf

EoE: Allergic Histopathology

Allergen exposure → Allergic inflammatory response → Infiltration of the esophagus with eosinophils and other inflammatory cells



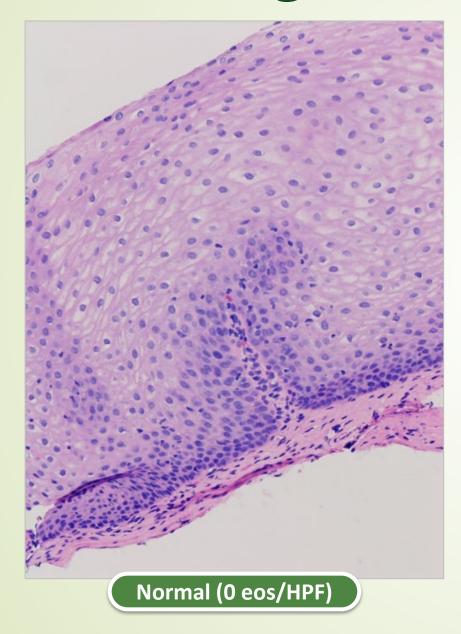
EoE: Immunopathogenesis

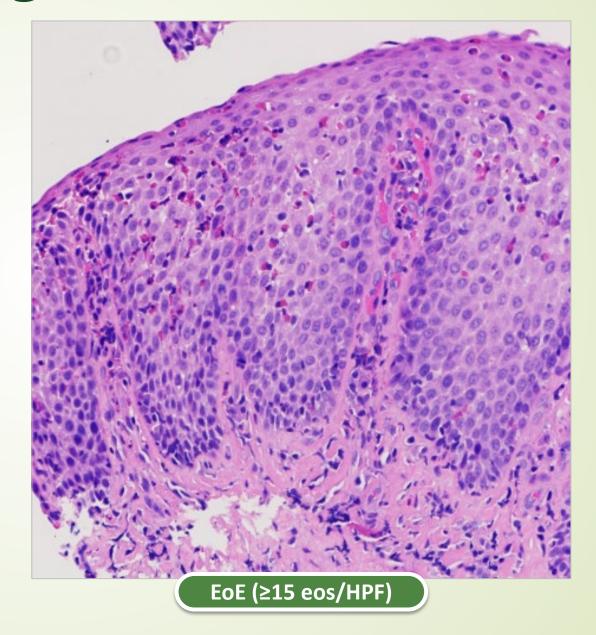


EoE: Endoscopic Diagnosis

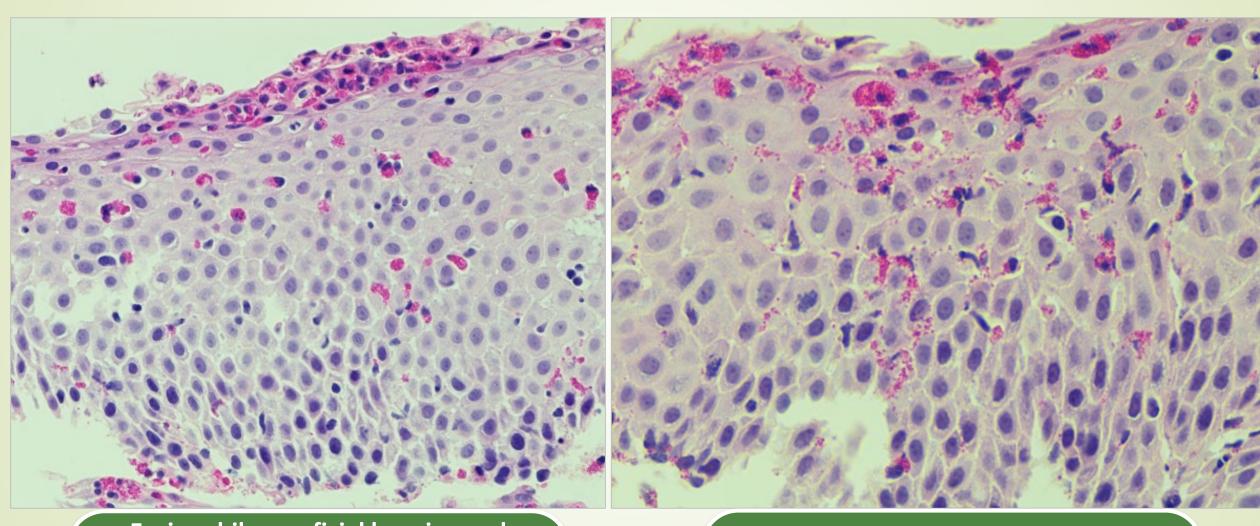


EoE: Histological Diagnosis





EoE: Histological Diagnosis

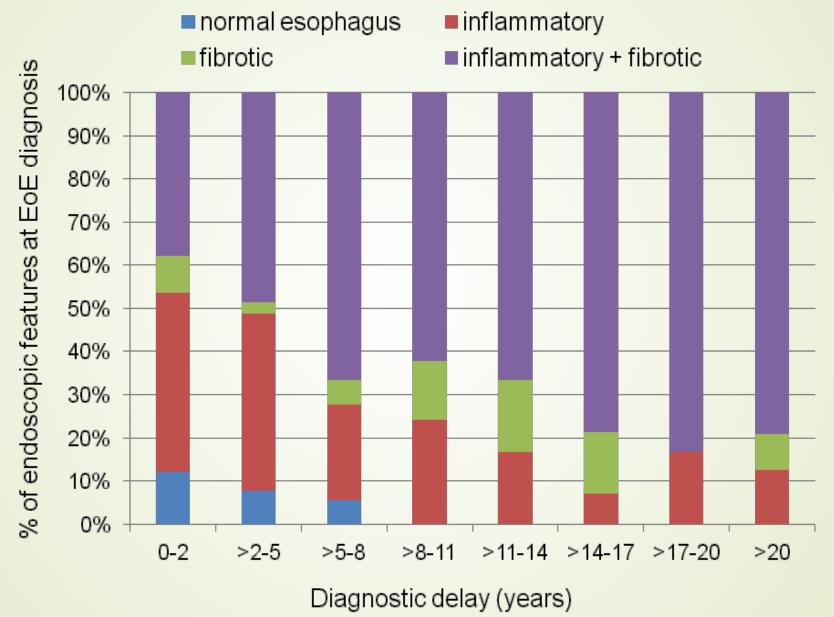


Eosinophil superficial layering and microabscesses

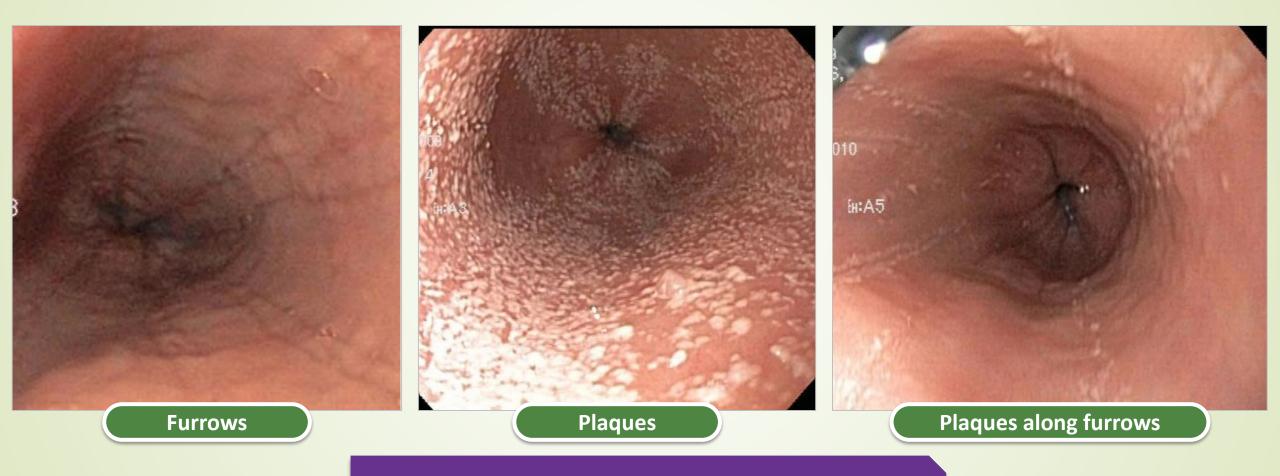
Eosinophilic degranulation



EoE: Course With Increasing Duration of Symptoms

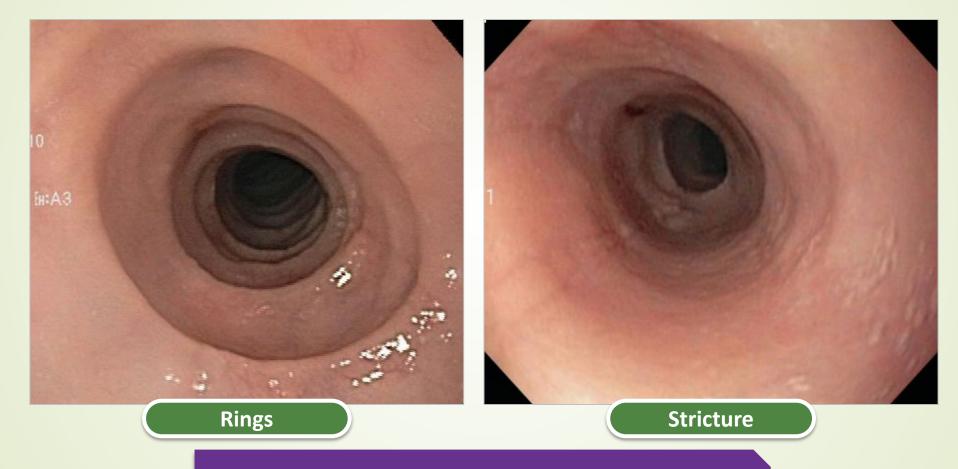


EoE: Inflammatory Phenotype



- Seen more often in early disease
- Seen more often in children

EoE: Fibrostenotic Phenotype



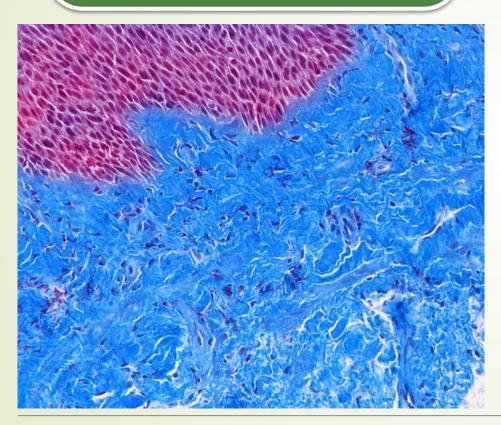
- Seen more often in late disease
- Seen more often in adults

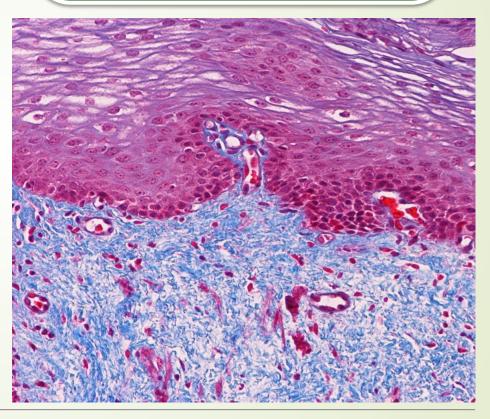


Pediatric EoE: Fibrosis can be reversed with diet or topical corticosteroids

EOE Patient Pre-treatment

EOE Patient Post-treatment





Trichrome stain

EoE: Histological response to topical corticosteroids in children

RCT	Konikoff Gastro 2006	Schaefer CGH 2008	Dohil Gastro 2010	Butz Gastro 2014
No. subjects	36	80	24	42
Drug	fluticasone	fluticasone	budesonide	fluticasone
μg/day	880	880/1760	1000/2000	1760
Control group	placebo	prednisone	placebo	placebo
Blinding	DB	open	DB	DB
Rx duration	12 weeks	4 weeks	12 weeks	12 weeks
Eos/HPF	70 60 50 40 30 20	70	80 70 60 50 40 30 20 10	80 70 60 50 40 30 20 10

DB, double-blind

EoE: Biologics

