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EOSINOPHYLLIC ESOPHAGITIS

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What is EOE?

- **EOE** is "a chronic, immune/antigen-mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation".

What is EOE?

- **EOE** were once considered to be a hallmark of GERD.
- But esophagus, is normally devoid of eosinophils, is an immunologically active organ that is capable of recruiting eosinophils in response to a variety of stimuli.
- When the GI eosinophilia is limited to the esophagus, is accompanied by characteristic symptoms, and other causes of esophageal eosinophilia have been ruled out, it is termed **EOE**.

What is Eosinophilic Esophagitis (EoE)?

- 2nd most common cause of chronic esophagitis (after GERD)
- Leading cause of dysphagia and food impaction in children
- Chronic, antigen-mediated (food)
- TH-2 pathway, non IgE mediated
- First defined in early 1990s
- Evolving definition

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What is EoE?

- **Requires both of the following:**
- Clinical
  - Esophageal dysfunction
    - Dysphagia, vomiting, feeding difficulties, abdominal pain
- Histological
  - Eosinophil-predominant inflammation (>15 eosinophils per field) isolated to the esophagus
    - Need to exclude other causes of esophageal eosinophilia
    - Persists after a high dose Proton Pump Inhibitor (PPI) trial

Subtypes

- **EoEe1 – A mild subtype with normal-appearing esophagus, and mild histological, endoscopic, and molecular changes.**
- **EoEe2 – An inflammatory endotype with highest expression of inflammatory cytokines and steroid-responding genes and a steroid refractory phenotype.**
- **EoEe3 – A fibrostenotic endotype associated with a narrow-caliber esophagus, and highest degree of endoscopic and histological severity and the lowest expression of epithelial differentiation genes.**

Eosinophils and acid in the esophagus

Intraepithelial eosinophils: a new diagnostic criterion **for reflux esophagitis** (Winter, 1982)

Esophageal eosinophilia with dysphagia. A **distinct clinicopathologic disorder**. (Attwood, 1993)

Correlation between number of eosinophils and reflux index on same day esophageal biopsy and 24 hour esophageal pH monitoring (Steiner, 2004)

"In EE… The esophageal abnormalities **do not respond** to treatment with **high-dose proton pump inhibitor** therapy" (Consensus Recommendations, Furuta, 2007)

"Therapeutic/basic studies and clinical experience have identified a **potential antiinflammatory or barrier-healing role** for proton pump inhibition in patients with esophageal eosinophilia"

(Updated Consensus Recommendations, Liacouras, 2011)

Other Causes of Esophageal Eosinophilia

- **GERD**
- **PPI-responsive esophageal eosinophilia**
- Eosinophilic gastrointestinal diseases
- Celiac Disease
- Crohn disease
- Infectious esophagitis
- Hypereosinophilic syndrome
- Achalasia
- Drug hypersensitivity
- Vasculitis
- Connective tissue disease
- Graft-versus-host disease

Epidemiology

- Prevalence in US: 56.7/100,000 (Dellon, 2014)
- Risk factors:
  - Male predominance (2-3x)
  - Personal or family history of atopy
- More common in non-Hispanic whites, but occurs in all racial / ethnic groups

Clinical Presentation

- Age-dependent
  - Infants / toddlers:
    - Persistent reflux symptoms
    - Vomiting
    - Feeding difficulties
    - Refusal to eat
  - School-age:
    - Vomiting
    - Abdominal pain

www.webmd.com

Clinical Presentation

- Adolescents and adults:
  - **Dysphagia (solids)**
  - **Food impactions**
  - Chest pain
  - Globus sensation
  - Throat-clearing

www.medscape.com

ENT symptoms?

True or False?

- All patients with dysphagia have EoE.
  - FALSE

- All patients with EoE have dysphagia.
  - FALSE

Compensating Behaviors

- Adaptations to esophageal dysfunction:
  - Drinking plenty of liquids with all meals
  - Prolonged chewing
  - Avoiding bulky foods, meats, breads
  - Slow or picky eaters
  - Parents cut food into very small pieces
- High index of suspicion needed!
- May diagnose other family members

Physical Exam

- Non-diagnostic for EoE
- Growth parameters can be low, normal, or high
- Find co-morbid allergic diseases
  - Allergic shiners
  - Rhinorrhea with pale boggy turbinates
  - Eczema, urticaria
  - Wheezing, prolonged expiration

DIAGNOSIS

EOE. DX.

- Based upon symptoms, endoscopic appearance, and histological findings.
- EoE should be suspected in patients with chronic symptoms of esophageal dysfunction (eg, dysphagia, food impaction, food refusal, abdominal pain, heartburn, regurgitation, chest pain, odynophagia).
- A history of atopic comorbidities (eg, asthma, atopic dermatitis, allergic rhinitis, or immediate food-type allergies) and FHX.of EoE.
- Hx. of esophageal perforation or severe pain after dilation of a stricture .

EOE. DX.

- Since the symptoms are not specific, the dx. may be missed. (median delay in dx. may be more than 6/y!!)
- Increasing duration of delay in the dx. is associated with an increase in the prevalence of fibrotic features of EoE on biopsy and esophageal strictures.

EOE. DX.

- **Diagnostic criteria :**
  - Symptoms related to esophageal dysfunction.
  - Eosinophil-predominant inflammation on esophageal biopsy, characteristically consisting of a peak value of ≥15 eosinophils per HPF or 60 eosinophils per mm2.
  - Exclusion of other causes.

EOE. DX.

- **Radiology —**

  Barium studies are not sensitive, but can help characterize anatomic abnormalities and provide information on the length and diameter of strictures .

- **Findings of barium studies include strictures and a ringed esophagus .**
- **In addition, other causes for symptoms can be ruled out (eg, malrotation as a cause for vomiting).**
- **Barium studies can help to assess luminal narrowing that is not evident at endoscopy .**

EOE. DX.

- **Laboratory tests —**

  Elevated serum IgE levels (>114,000 units/L) in 50-60%

- Mild peripheral eosinophilia in 40 – 50%

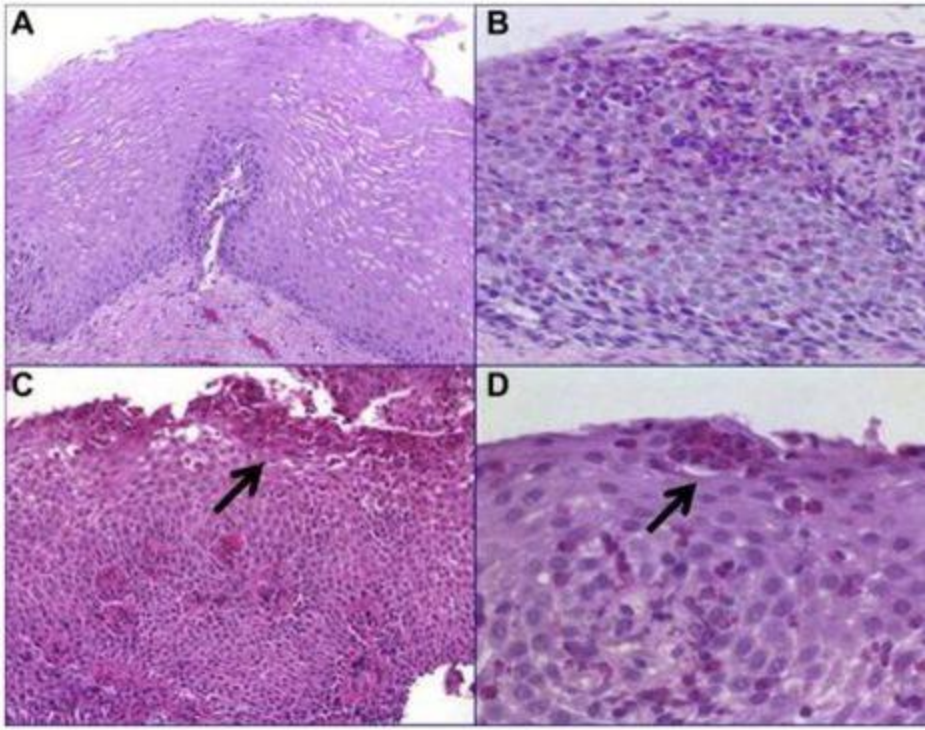
EOE. DX.

- **Evaluation for allergies —**

  Because of the strong association of EoE with allergies, we suggest that evaluate by an allergist. Children are often treated with dietary therapy, and the information gained from allergy testing may help guide therapy. Allergy testing may also help with the management of concomitant atopic disease, which is common in patients with EoE.

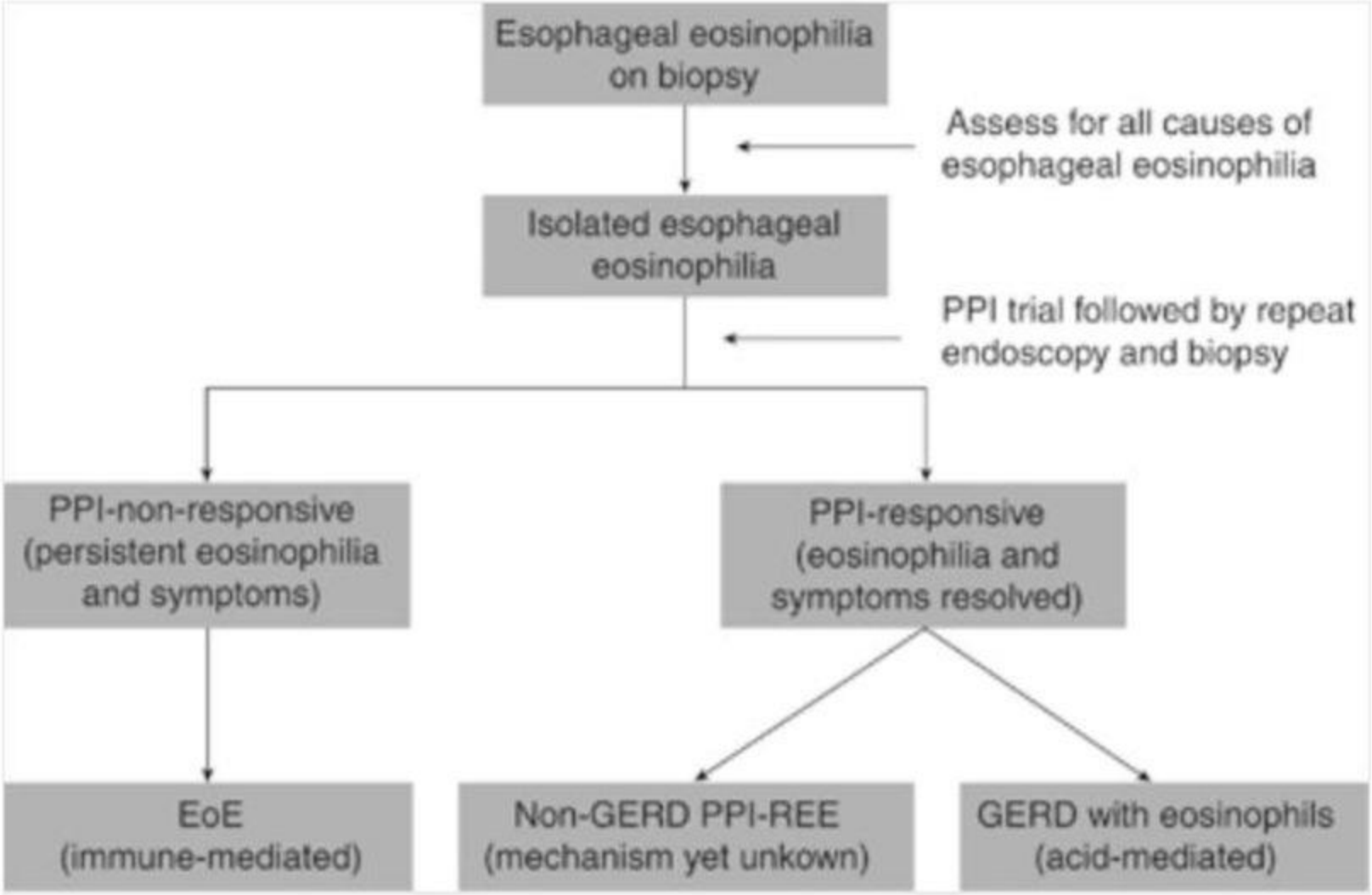
Histology

- ≥15 eosinophils per field in esophageal biopsy specimen after a PPI trial
- Isolated to the esophagus
- Other findings:
  - Eosinophilic microabscesses
  - Surface layering of eosinophils
  - Eosinophil degranulation
  - Basal cell hyperplasia
  - Lamina propria fibrosis
- Other causes ruled out.



Liacouras, 2011

PPI-Responsive Esophageal Eosinophilia



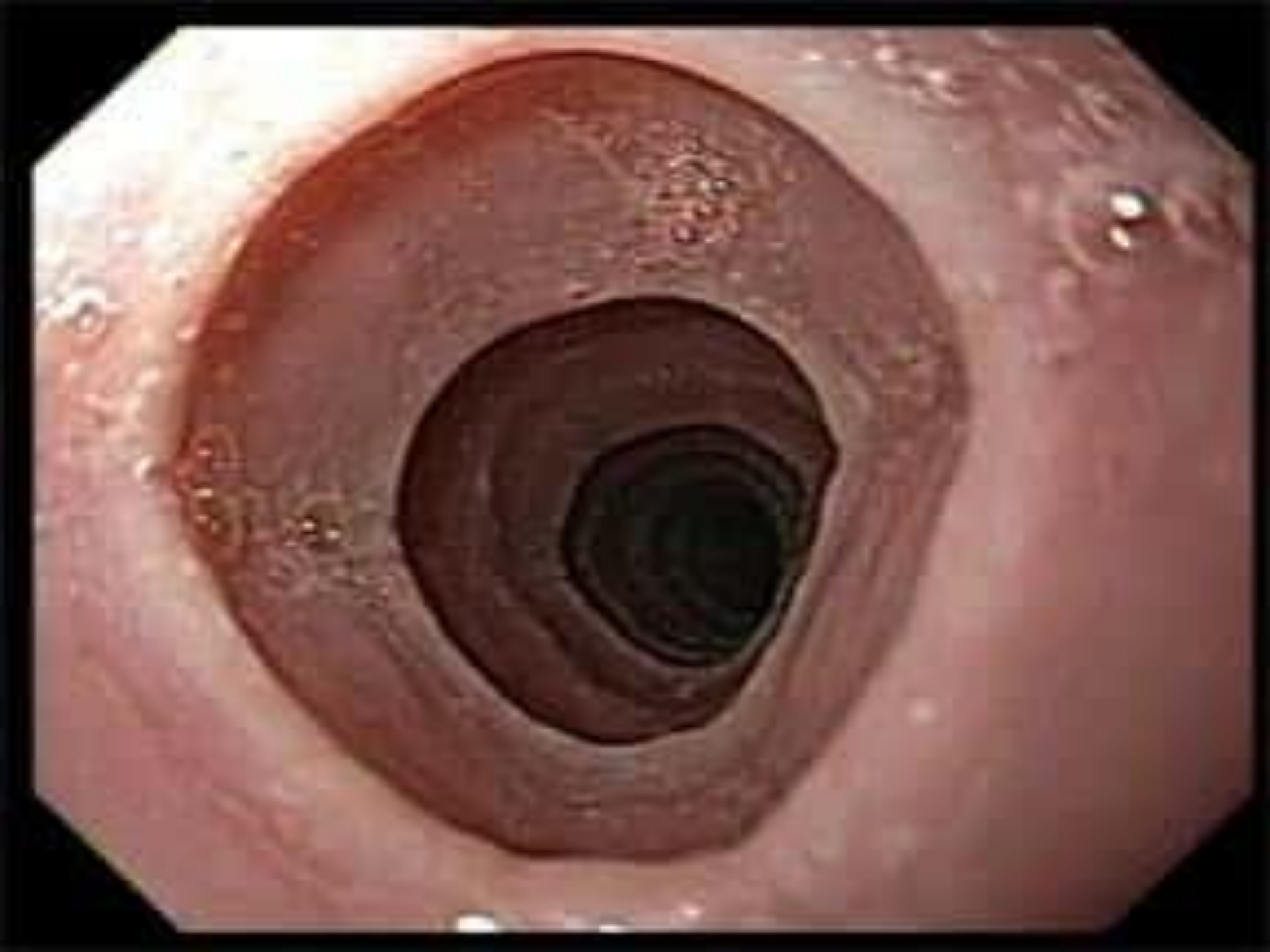
Endoscopy

- A scoring system that relies on the assessment of Exudate, Rings, Edema, Furrows and Strictures has been developed and validated in children and adults.

Endoscopy

- Stacked circular rings ("feline" esophagus) : 44%
- Strictures (particularly proximal) : 21 %
- Attenuation of the subepithelial vascular pattern: 41 %
- Linear furrows : 48%

- Whitish specks (representing eosinophil microabscesses) : 27 percent
- Small caliber esophagus: 9 %



TREATMENT

Therapies

- Goals:
  - Reduced symptoms and improved histology
  - Prevent feeding dysfunction
  - Prevent fibrosis and stricture formation
- Food elimination diets:
  - Elemental
  - Empiric elimination
  - Allergy testing-based
- Topical steroids
- Prednisone for rapid improvement in symptoms
- Esophageal dilation

DIETARY THERAPY

- Effective first-line treatment in children and adults. Effective nonpharmacologic treatment.
- poses a risk of nutritional deprivation
- Can be difficult for patients and families (particularly if nasogastric feedings or gastrostomy tubes are required),
- Can lead to psychologic problems,
- May lead to unnecessary food aversion.

DIETARY THERAPY

- Costs! (often not borne by insurance providers),
- Inconvenience, ease of adherence,
- Relapse upon discontinuation of the diet is common.
- When used, elemental and elimination diets should be administered in consultation with a registered dietician.

Elemental Diet

- Amino-acid based formula[1]
- Up to 96% histologic remission rate[2]
- Disadvantages:
  - Poor tasting, expensive formula
  - Development of solid food aversion
  - NGT or GT
  - Long food reintroduction process, many endoscopies

1. Kelly, 1995
2. Henderson, 2012

Six-Food Elimination Diet (SFED)

- **W**heat
- **I**gnore
- **N**uts/peanuts

- **S**oy
- **F**ish/seafood
- **E**ggs
- **D**airy

Kagalwalla, 2006

4-Food Elimination Diet

- Milk
- Wheat
- Egg
- Soy




Milk Elimination Diet (65%)

Kagalwalla, 2012

Empiric Elimination + Meat

- Beef
- Chicken
- Pork
- Turkey

Allergy Testing Based Elimination

- Results similar to empiric food elimination
- Disadvantages:
  - Requires painful testing
    - Skin prick testing (IgE)
    - Atopy patch testing (non-IgE, high variability)

Allergy Dietician

- Prevent iatrogenic malnutrition
- Prevent contamination

PHARMACOLOGIC THERAPY

- **Acid suppression** — PPIs : among first line treatment options, together with dietary modification and topical glucocorticoids
- Initial treatment for 8wks.(full-dose once daily and, if symptoms fail to improve after 4wks increase the dose to twice daily.
- An alternative dosing regimen is to initiate PPI with a twice-daily dose.

PHARMACOLOGIC THERAPY

- Patients are assessed for symptomatic improvement following an 8 wk course of PPI .
- Endoscopy 8 wks after initiating therapy to assess for endoscopic and histologic improvement .
- For patients who respond, continue the PPI at the lowest dose successful at controlling symptoms.

PHARMACOLOGIC THERAPY

- For patients with persistent symptoms and/or esophageal eosinophilia, alternative therapy can be pursued (eg, dietary modification or topical glucocorticoid).

PHARMACOLOGIC THERAPY

- **Topical glucocorticoids -** Effective for achieving clinical and histologic improvement; Symptoms and histologic changes often recur when glucocorticoids are discontinued!!.
- **Fluticasone propionate** is sprayed into the patient's mouth and then swallowed. Patients should not inhale when the medication is being delivered and they should not eat or drink for 30 minutes following administration.

PHARMACOLOGIC THERAPY

- Children ages 1 -11 /y – 110 mcg/spray, 8 sprays daily in divided doses. 4-8 wks
- ≥12/y and adolescents – 220 mcg/spray, 8 sprays daily in divided doses. 4-8 wks
- ≥18/y– 220 mcg/spray, 4 sprays daily in divided doses. 4-8 wks
- Endoscopy 8 -12 wks after initiating therapy to assess for endoscopic and histologic improvement.

PHARMACOLOGIC THERAPY

- Frequently relapse when treatment is stopped, (14 - 91 percent . Thus, we lower the dose gradually after clinical remission has been achieved, and continue to monitor symptoms as the dose is gradually lowered to a maintenance level.
- For patients who do not respond to fluticasone, options include a higher dose of fluticasone, a change to oral viscous budesonide, a trial of PPI, or a dietary approach.

PHARMACOLOGIC THERAPY

- **Budesonide** —For 12 wks: Administered as an oral viscous slurry (1 mg daily for children under the age of 10 years, and up to 2 mg twice daily for older children and adults; the total daily dose is often divided into twice daily) ; over 5 -10 min., and not eat or drink for 30 min. after taking the budesonide suspension.
- Endoscopy 8 -12 wks after initiating therapy to assess for endoscopic and histologic improvement.

PHARMACOLOGIC THERAPY

- **Ciclesonide,** a topical glucocorticoid with less systemic absorption than fluticasone, has been evaluated in small case series.
- Further studies are needed.
- **Mometasone furoate**, a topical glucocorticoid with limited systemic bioavailability (ie, approximately 1 percent), has been studied for treating children and adolescents with EoE.

PHARMACOLOGIC THERAPY

- **Maintenance therapy —with topical glucocorticoids and/or dietary restriction should be considered for all patients, but particularly in those with severe dysphagia or food impaction, high-grade esophageal stricture, and rapid symptomatic/histologic relapse following initial therapy .**
- **The lack of symptoms does not reliably predict the absence of disease activity**

PHARMACOLOGIC THERAPY

- Optimal approaches to maintenance therapy have not been well established. Thus, the approach should consider the clinical setting, patient preferences, and available resources.
- Long-term dietary restriction is effective in maintaining remission in patients in whom dietary triggers have been identified.

PHARMACOLOGIC THERAPY

- In patients unwilling to maintain a dietary approach and those in whom a trigger cannot be identified, topical glucocorticoids can be used at the lowest dose, and for pediatric patients, in endoscopic and histologic remission.

PHARMACOLOGIC THERAPY

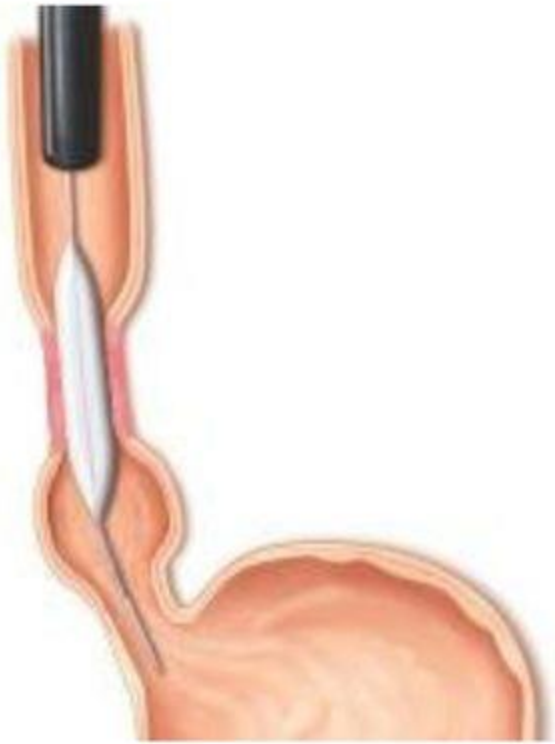
- **Dupilumab** —An IL-4 receptor alpha antagonist that blocks the shared receptor component for IL-4/IL-13. 300 mg weekly or every other week for 28 weeks
- Approved for use in the United States for the treatment of EoE in adults and in pediatric patients who are 12 years of age and older and weigh at least 40 kilograms.
- Treatment for a total of 52 weeks,: rates of histologic remission (defined as ≤6 eosinophils/HPF) were 85 %

Topical Steroids

- Not FDA-approved for EoE
- 50-80% histologic remission, common recurrence
- **Swallowed fluticasone:**
  - Metered dose inhaler without spacer
- **Oral viscous budesonide:**
  - 10 packets of Splenda per 2 respule (0.5 mg/2 ml)
  - Neocate Nutra ½ tsp per 2 respules
  - Small amount applesauce
- No drinking or eating for 30 minutes, then drink water
- Can swish and spit with water
- Possible adrenal insufficiency

Esophageal Dilations

- Mostly in adolescents and adults
- Treats strictures, but not underlying inflammation
- 3% risk for significant adverse effect same as non-EoE (Menard-Katcher, 2017)
  - 15% chest pain.



www.olympus.nl

Epinephrine injection and allergy shots are NOT part of EoE treatment.


متشکرم