

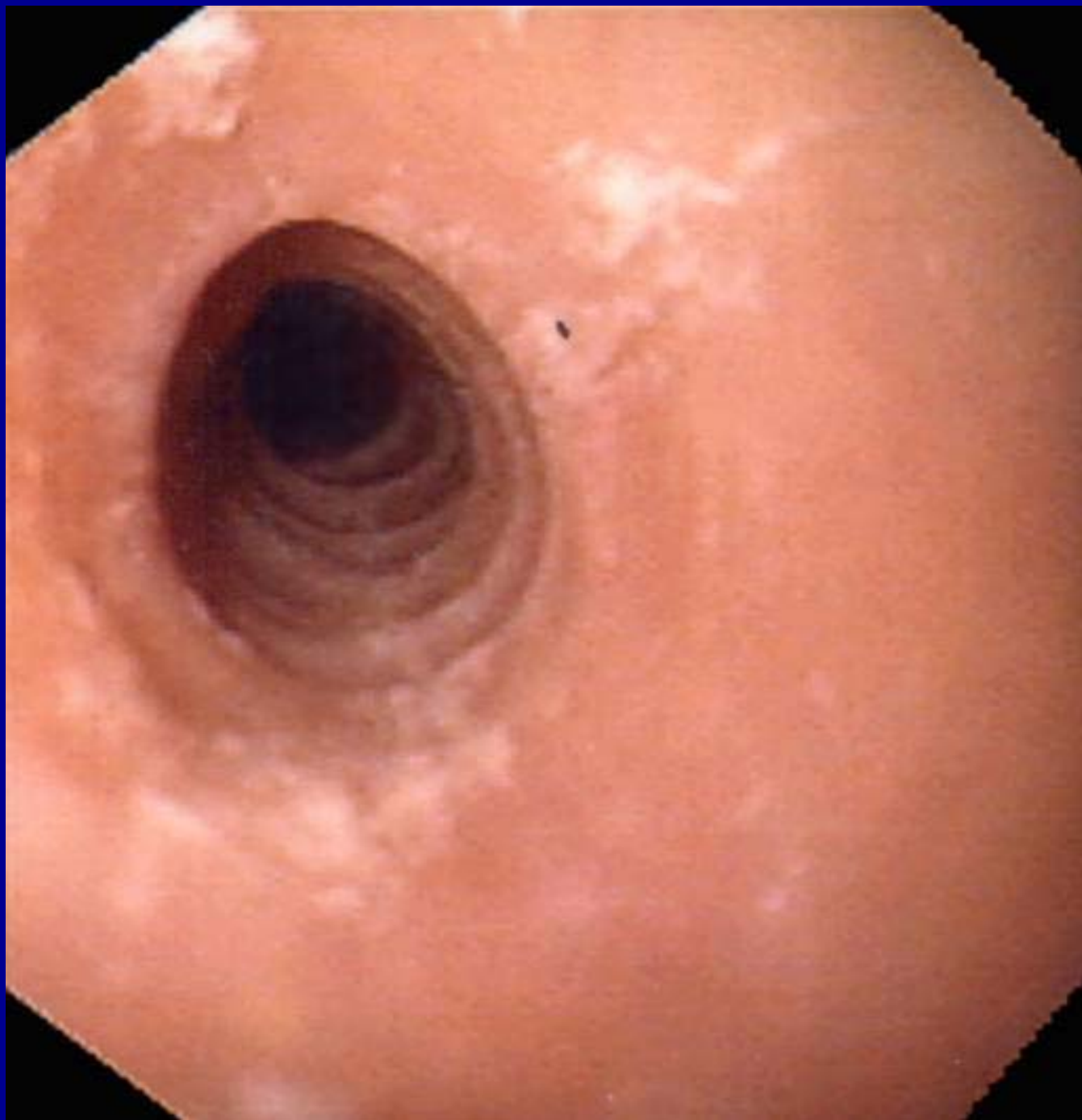
Eosinophilic Esophagitis

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February 2014

A Most Interesting Patient

36 year old self employed tree surgeon with long standing history of intermittent dysphagia and atypical GERD, NOT improved with H2RA's or PPI's. Has been seen and "scoped" by multiple gastroenterologists who tell him he has a narrow esophagus. Unsure of prior biopsy and no past dilation. Comes to you for second opinion



Historical Perspectives

- EoE is currently defined as a chronic immune-mediated condition with infiltration of eosinophils into the esophageal mucosa leading to symptoms of esophageal dysfunction
- Symptoms invariably include dysphagia more often than heartburn, though often coexist

EoE Demographics

- Incidence and prevalence are increasing rapidly
- 6-15% children and adults undergoing EGD
- 43-52/100,000, approaching the prevalence of IBD
- Males are 2-4x more likely than Females
- Highest in US and Western Europe, lowest in Japan and China
- Whites > non-Whites but seen in all ethnicities

Clinical Presentation

Infants and Toddlers

- Failure to thrive, poor growth
- Feeding intolerance
- Abd pain, nausea, vomiting
- Regurgitation, food aversion
- *up to 80% children diagnosed with EoE have atopy, supporting allergic etiology

Clinical Presentation in Adults

- Most often before age 40
- White Males comprise the majority
- Oftentimes with decades of symptoms
- **Most** have concomitant history of environmental allergies, allergic rhinitis, asthma, and/or food allergies
- Symptoms include food impaction (40%) dysphagia, heartburn, chest pain

Diagnosis

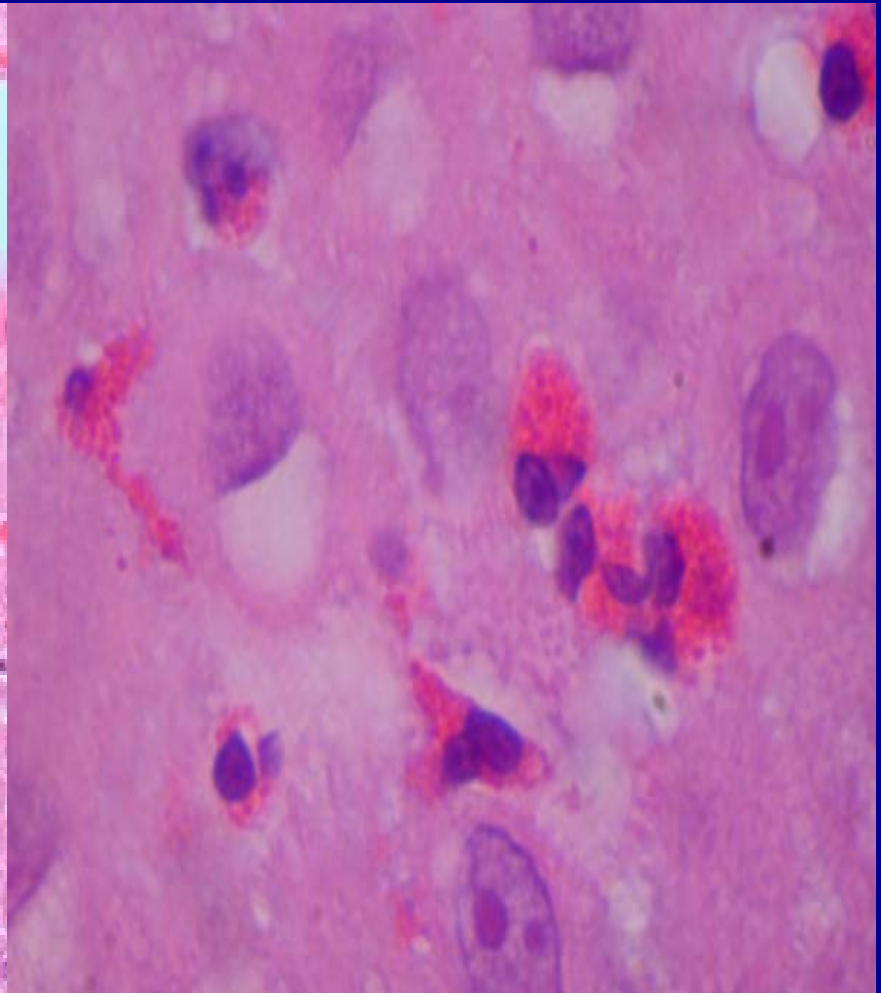
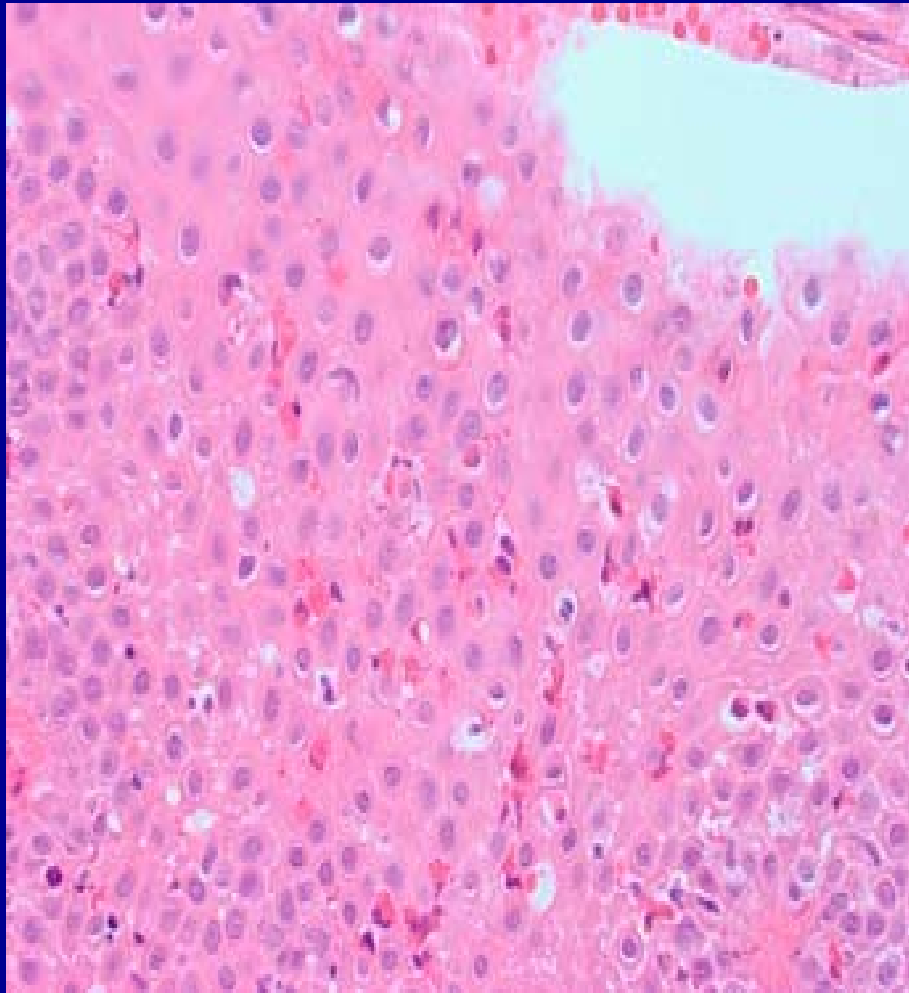
- EGD with biopsy: obtain 4 in proximal-mid and 4 in the distal esophagus (about 6cm proximal to GEJ)
- Because EoE is a patchy disease, multiple biopsies at multiple sites are recommended
- Endoscopic findings
 - Linear furrows
 - Concentric rings
 - White spots or exudates (can be confused with candidiasis)
 - Crepe-paper mucosa (manifestation of mucosal fragility)

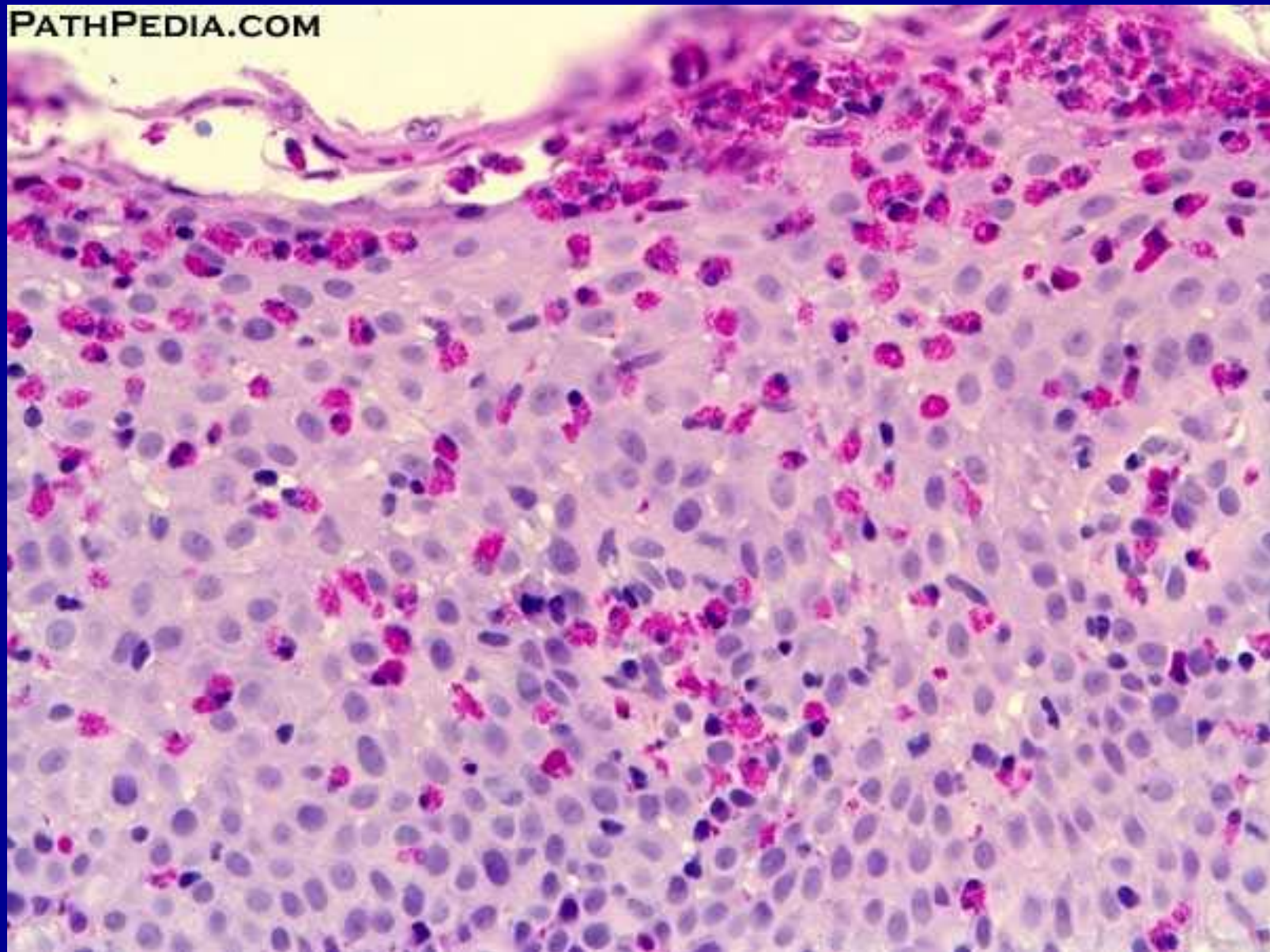
Histologic Features

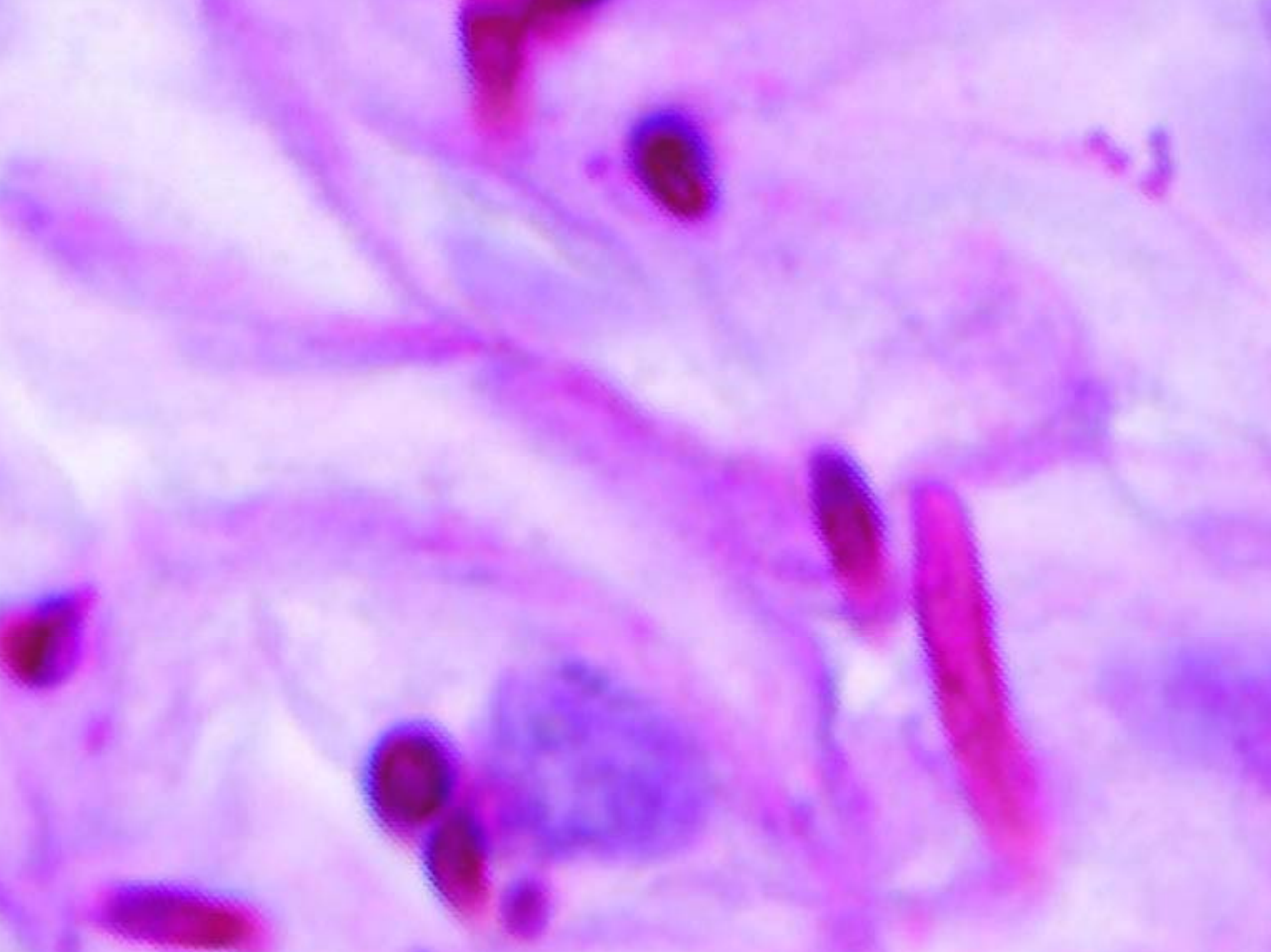
- >15 Eosinophils per high power field
- Eosinophilic micro abscesses
- Extracellular granular proteins
- Fibrosis in the lamina propria
- Basal layer hypertrophy and Rete PEG elongation

Pathophysiology

- IgE mediated and non-IgE (cell mediated) hypersensitivity response
- IL-5 (inducer of eosinophil proliferation and activation)
- Cysteine leukotrienes are known eosinophil chemoattractants







Differential Diagnosis

- Reflux esophagitis
- Infectious esophagitis (fungal, viral, parasitic)
- Graft vs. host
- Crohn's disease
- Hypereosinophilia syndrome
- PPI responsive esophageal eosinophilia

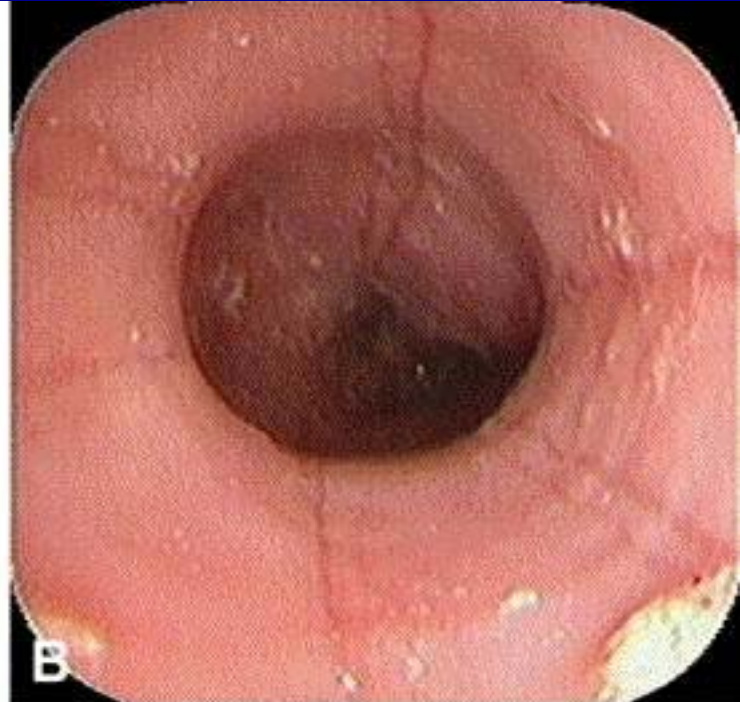
GERD and PPI responsive EE

- Substantial overlap in symptoms and histology
- One third of patients with EE respond to PPI (distinct clinical entity vs. subtype of GERD, or a phenotype of EoE?)
- Most authorities agree that if a trial of 20-40mg twice daily of PPI leads to symptom control and resolution of esophageal eosinophils, then PPI-REE is the dx; if persistent symptoms or eosinophils , then EoE is the dx.

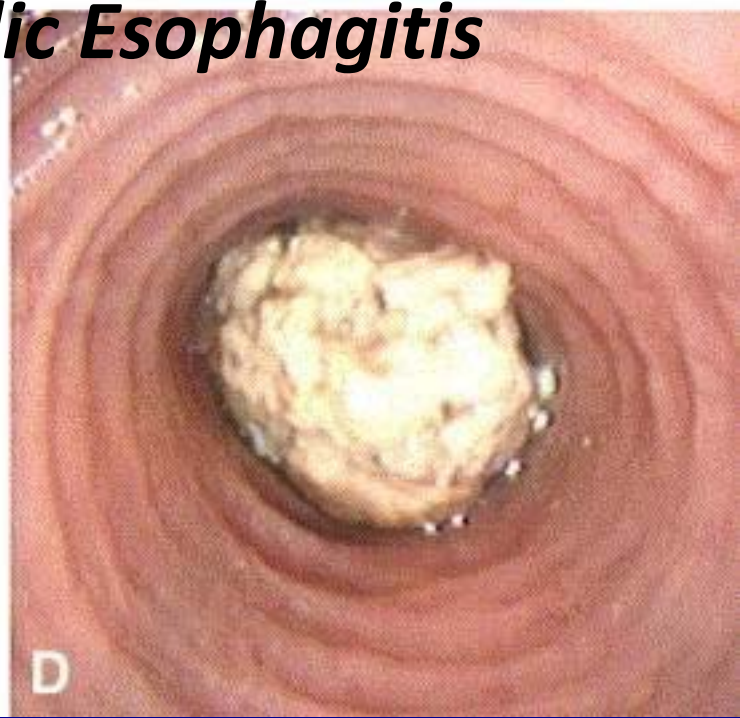
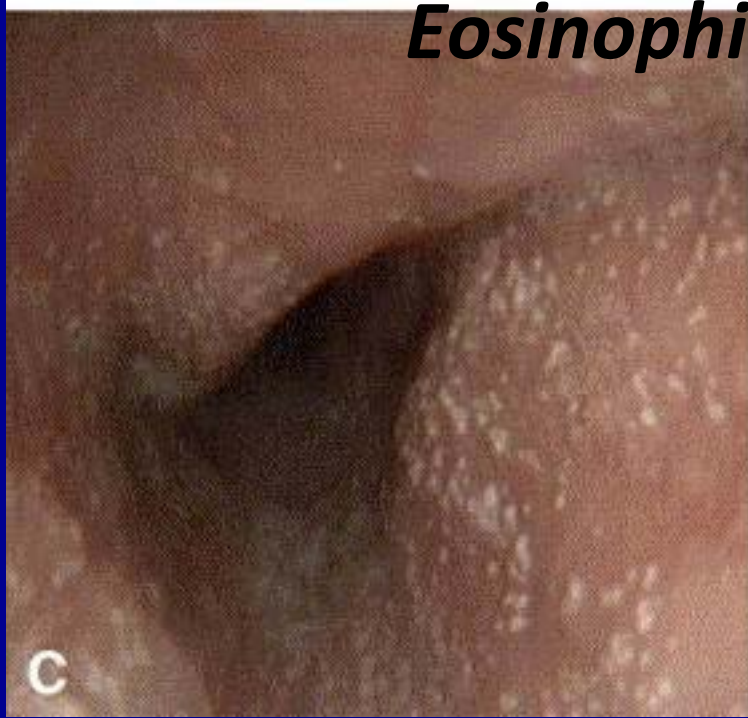
What is this?



Candida Esophagitis



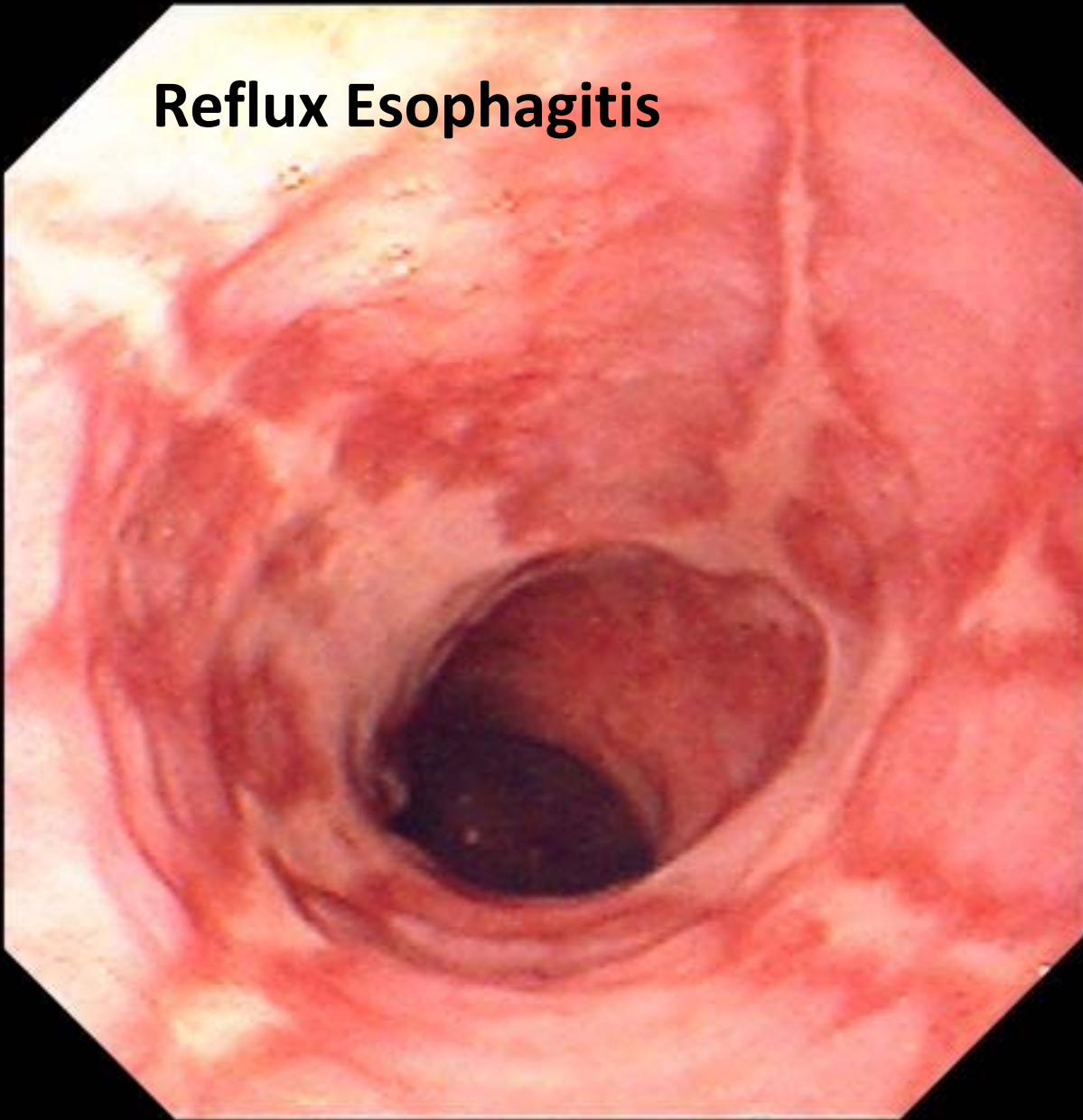
Eosinophilic Esophagitis



EoE



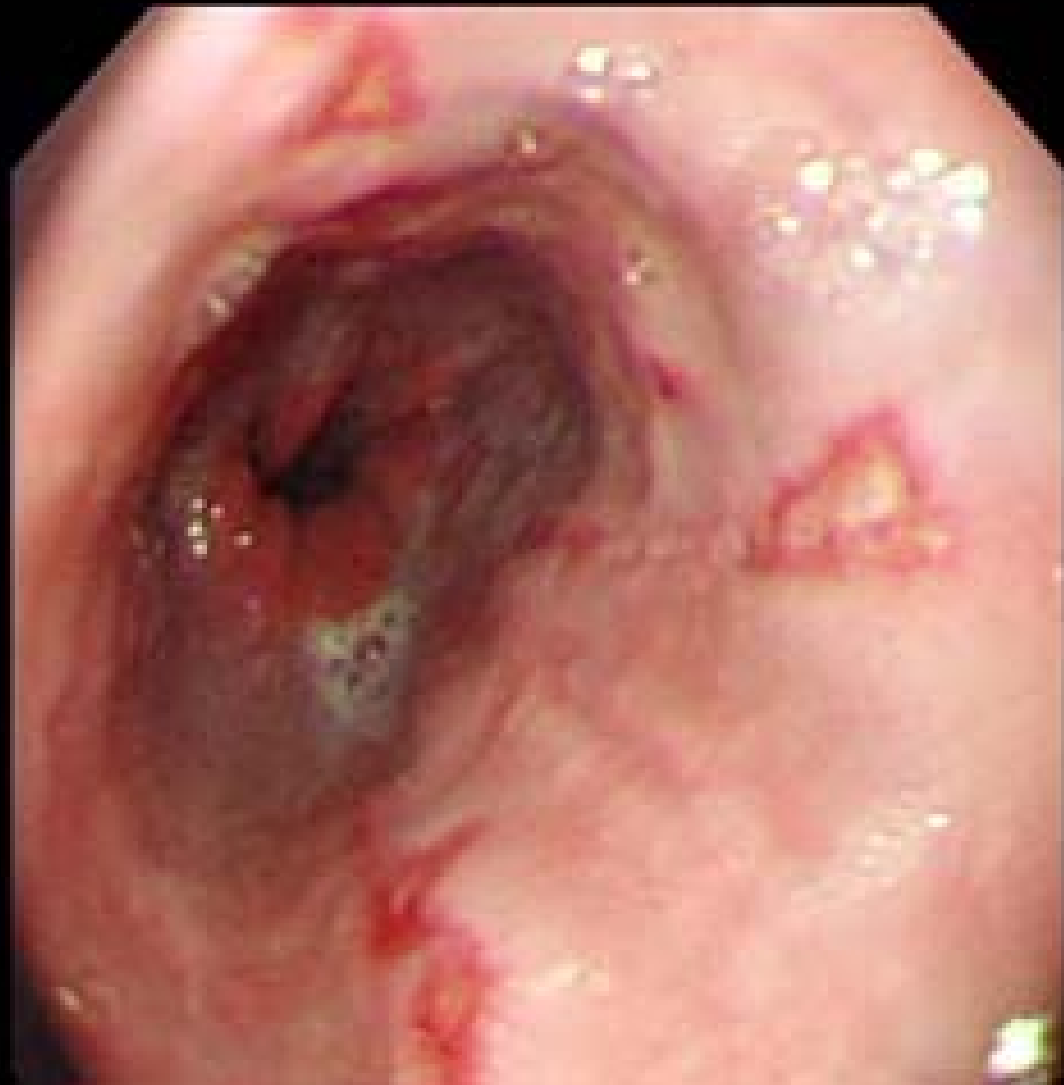
Reflux Esophagitis



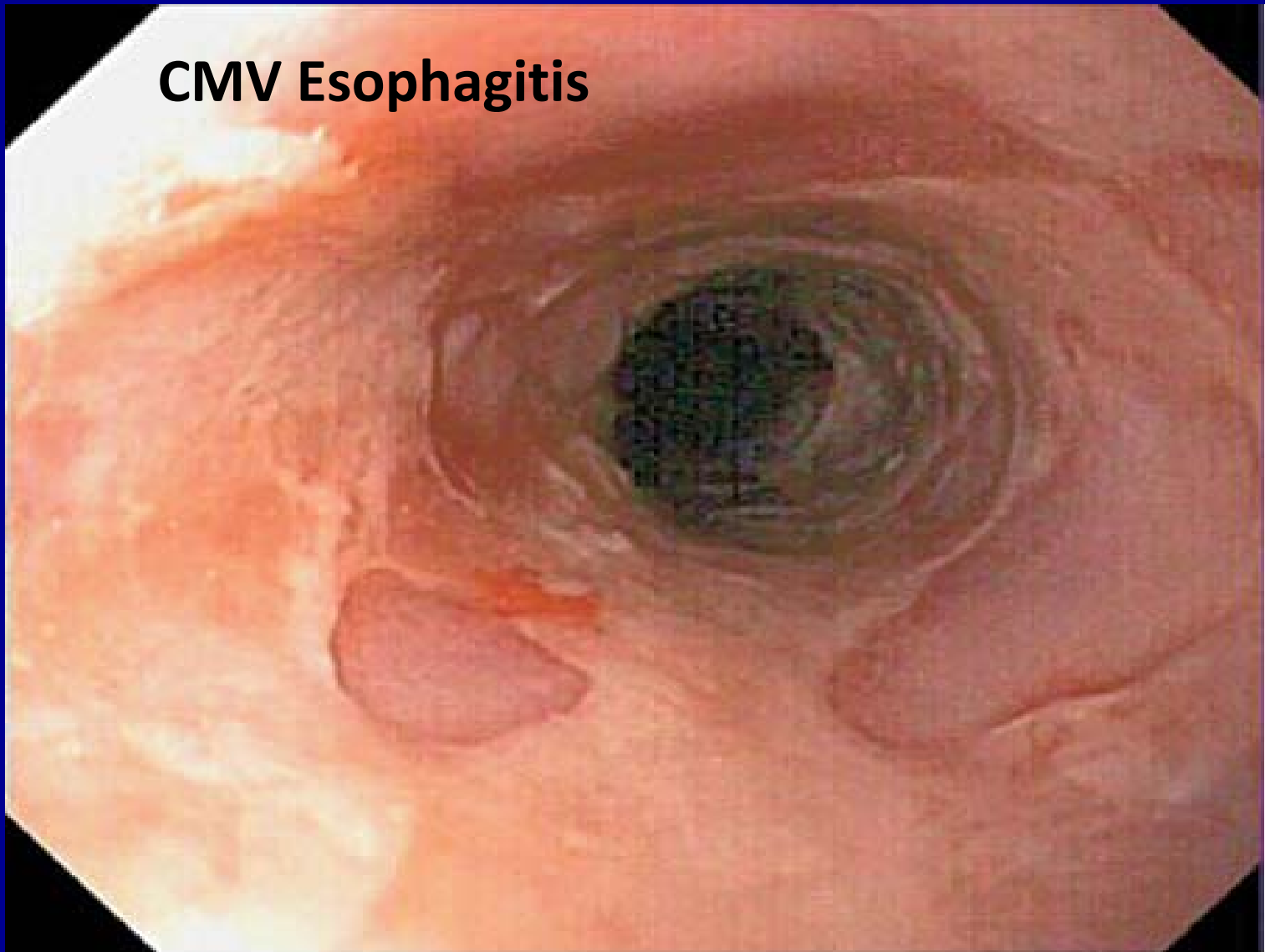
Reflux Esophagitis

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CMV Esophagitis

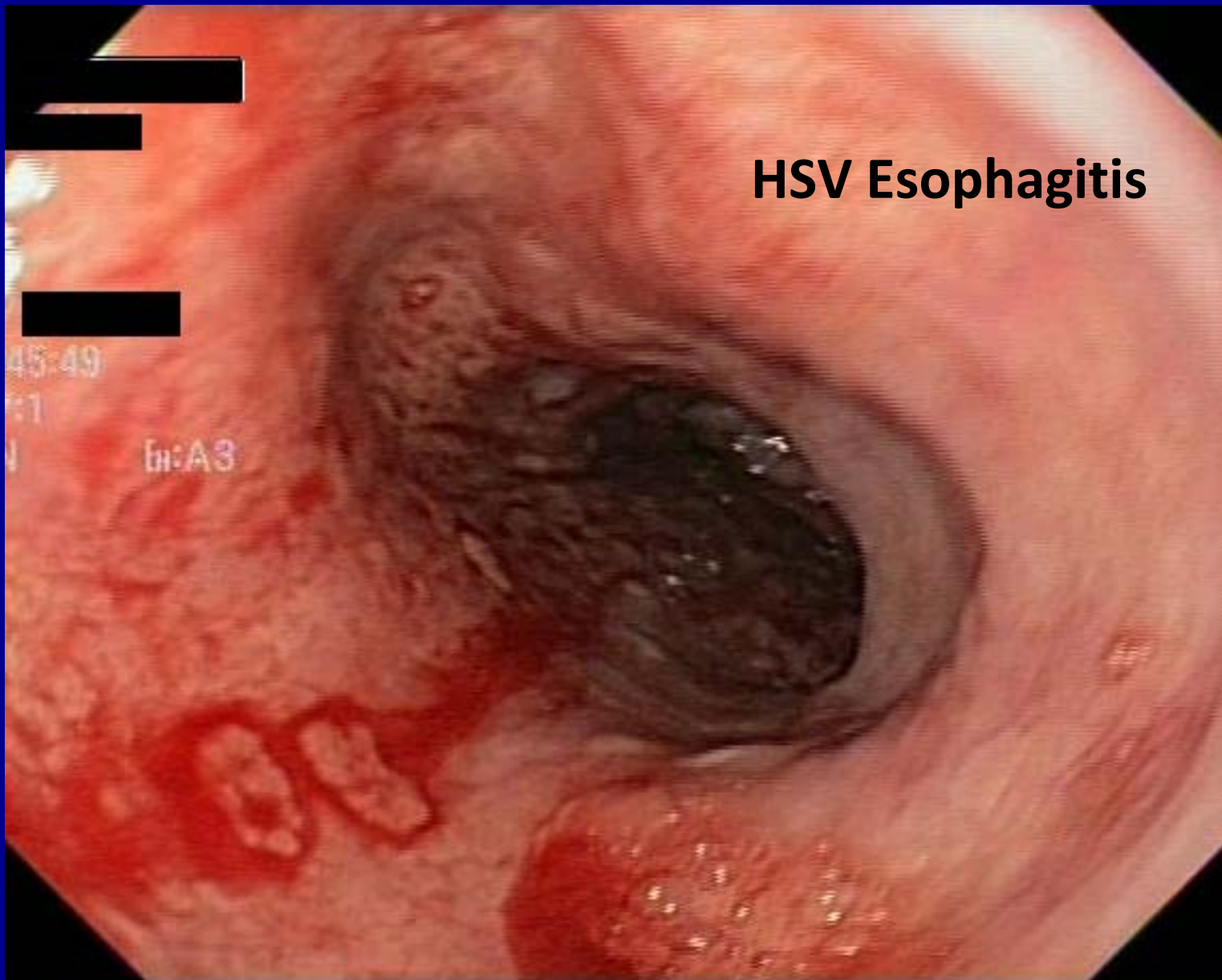


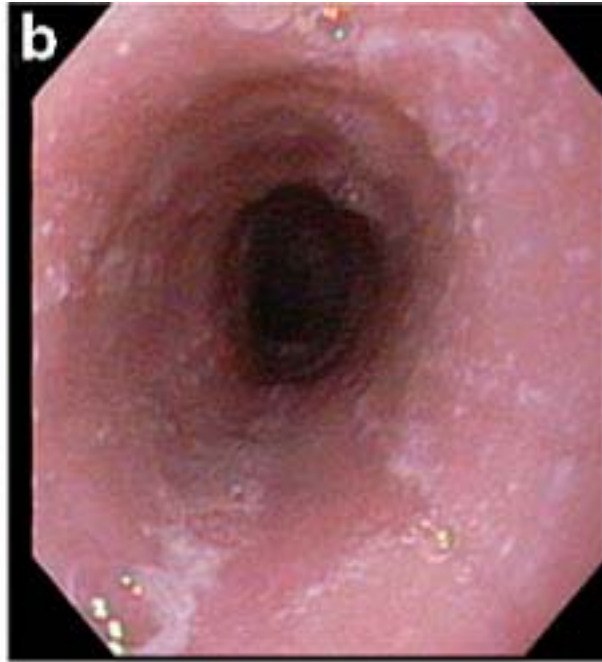
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Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: <http://www.accessmedicine.com>

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HSV Esophagitis





EoE

Treatment Options-Pharmacologic

- No-FDA approved treatments (off label)
- BID PPI ? How long, with or without other agents
- Fluticasone, beclomethasone compared to prednisone (some randomized controlled trials) showed equivalence, so topical treatments are favored
- Budesonide 2-6mg daily usually given as a slurry mixed with sucralose, or fluticasone 880 to 1760 microgram/d show marked histologic response compared to no response with placebo

Biologic Agents

- Mepolizumad and reslizumab (monoclonal anti-interleukin-5 antibodies), studies in 3 RCTs (1 adult, 2 children) showed mild to moderate improvement in eosinophil counts, but symptoms did not improve
- Infliximab –no response
- Omalizumab (monoclonal ab against IgE, studies in 30 adults with EoE, -no response

Other Agents for EoE

- Montelukast 20-40mg-effective in some cases, ineffective in others. High side effects (nausea and vomiting)
- Cromolyn sodium (mast cell stabilizer) not effective
- Ketotifen (antihistamine with anti-mast cell properties) potential but no data
- Immunomodulators (immuran and 6-mp) limited data, not recommended
- Antiinterleukin 13 and anti-eotaxin-3 antibodies as well as prostaglandin D2 receptor antagonists are being investigated as treatment options

Non-Pharmacologic Treatments

- Elimination Diet
- Elemental diet (children and infants)
- Esophageal dilation (reduces symptoms but does not reduce inflammation)

Dietary Treatment Outcomes

- In 51 children with EoE elemental diet, **96%** had near complete resolution of esophageal eosinophilia and symptoms within 2 weeks
- Downside: expensive, unpalatable, may require delivery through gastrostomy

6 Food Elimination Diet for Adults

- Stop the most highly allergenic foods: dairy, egg, wheat, soy, nuts (tree nuts and peanuts), seafood (fish and shellfish)
- **$\frac{3}{4}$ had resolution of esophageal eosinophilia and almost all had improved symptoms**
- *Can add back food items every two weeks until symptoms recur in order to define specific triggers

Food Allergy Testing

- Avoid foods that were demonstrated on reactive skin or serum testing, response rate less favorable compared to elimination diet.
- Overall response rate in children 50-75%, lower in adults, depending on center and method of testing

Endoscopic Dilation

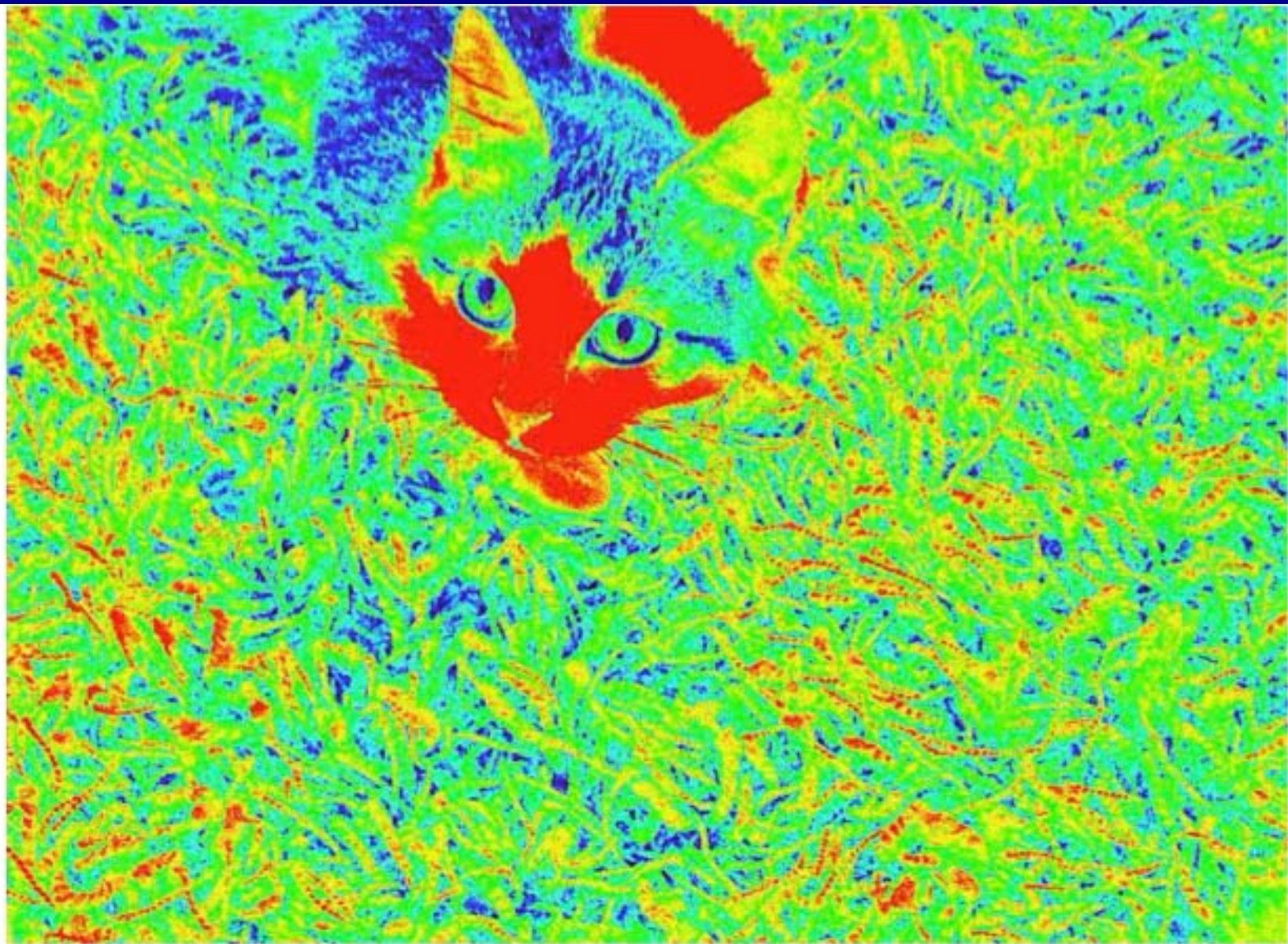
- Initially felt to have higher perforation rate but now similar to other reasons for dilation without EoE (0.3%)
- No consensus on superior benefit of balloon or bougie; use judgment

Back to the Patient over the last ten years:

- He has intermittently required dilation
- He has taken budesonide and fluticasone,
- Has had negative food allergy testing but has not tried elimination diet
- Has multiple aeroallergens, but continues to work outdoors
- He is compliant with histamine 1 and 2 blockers (Zantac and Zyrtec), which he believes help the most

Summary EoE

- Chronic immuno-allergic condition manifest by esophageal dysmotility and tissue eosinophilia
- Most patients will have resolution of symptoms and histologic improvement with elimination diet, or topical corticosteroids
- PPI-REE in 20-40%; need trial of BID PPI to distinguish these individuals
- Many patients will end up in the care of an allergist along with gastroenterologist





References

- Dellon, ES. Eosinophilic Esophagitis, Gastroenterol Clin N Am 42 (2013) 133-153
- Lieberman, JA., Chehade M. Eosinophilic Esophagitis: Diagnosis and Management Immunol Allergy Clin N Am 32 (2012) 67-81