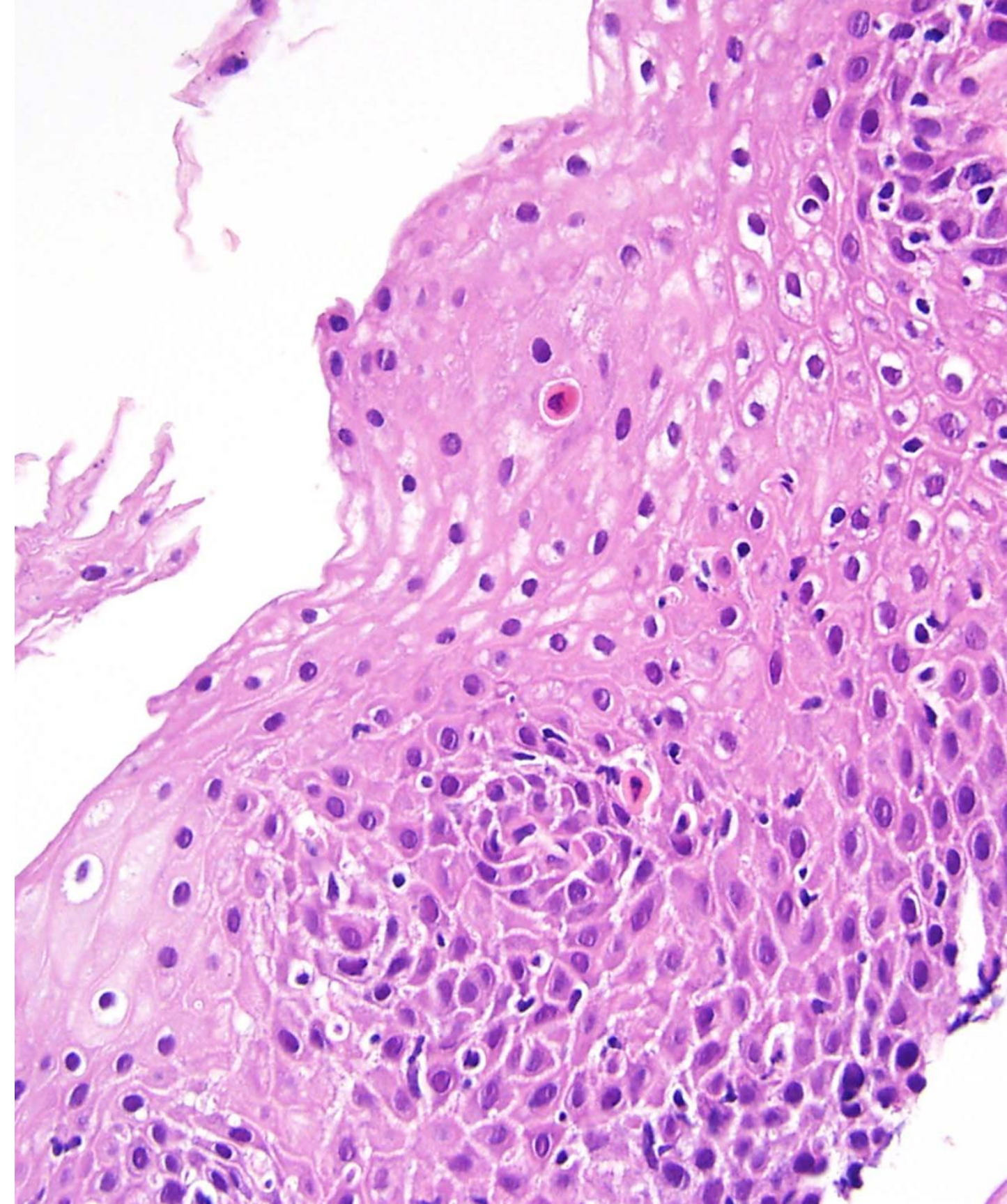


The International Academy of Pathology, Hong Kong Division

Update on Inflammatory Conditions of the Esophagus

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Nashville, TN
October 28, 2023



Topics

- **Eosinophils (gastroesophageal reflux disease (GERD), eosinophilic esophagitis)**
- **Lymphocytes (lichen planus, lymphocytic esophagitis)**
- **Corrosive/contact injury (pill esophagitis, sloughing esophagitis, “black esophagus”)**
- **Deformities and structural anomalies (webs, rings, diverticula)**

Objectives

- **Diagnose subtle examples of reflux esophagitis**
- **Apply histologic criteria and clinical features to differentiate between eosinophilic esophagitis pattern of injury and reflux esophagitis**
- **Categorize patterns of lymphocytic infiltration in the esophagus and differentiate between lichen planus and lymphocytic esophagitis patterns of injury**
- **Diagnose esophagitis dissecans superficialis (sloughing esophagitis)**
- **Diagnose and report medication-related esophageal injury**

Eosinophils in the esophagus

- **Reflux esophagitis**
- Eosinophilic esophagitis
- (PPI-responsive esophageal eosinophilia)

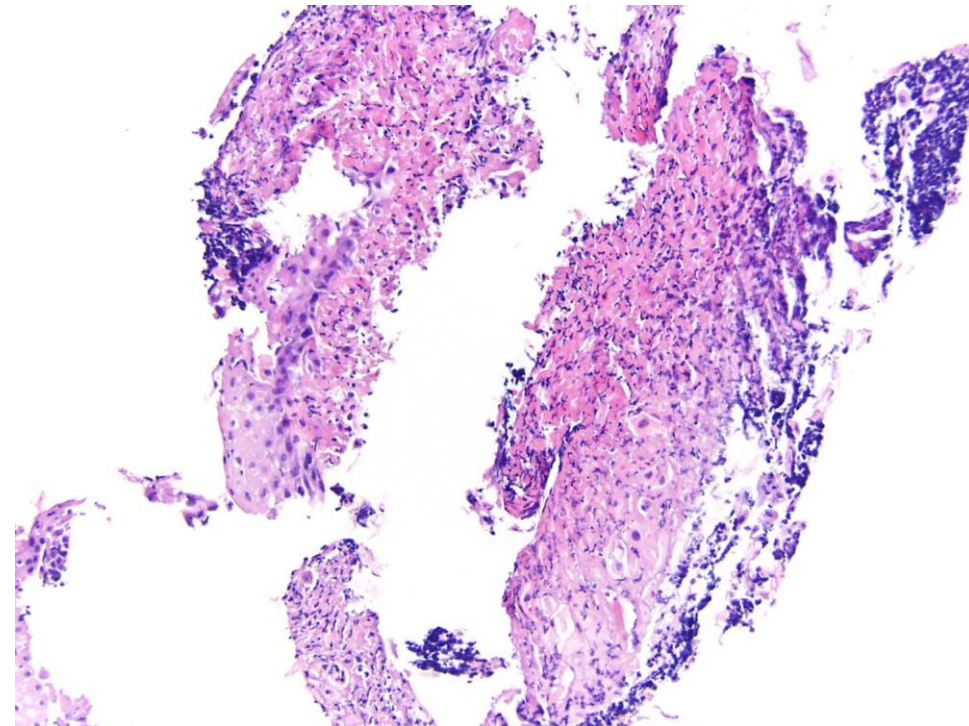
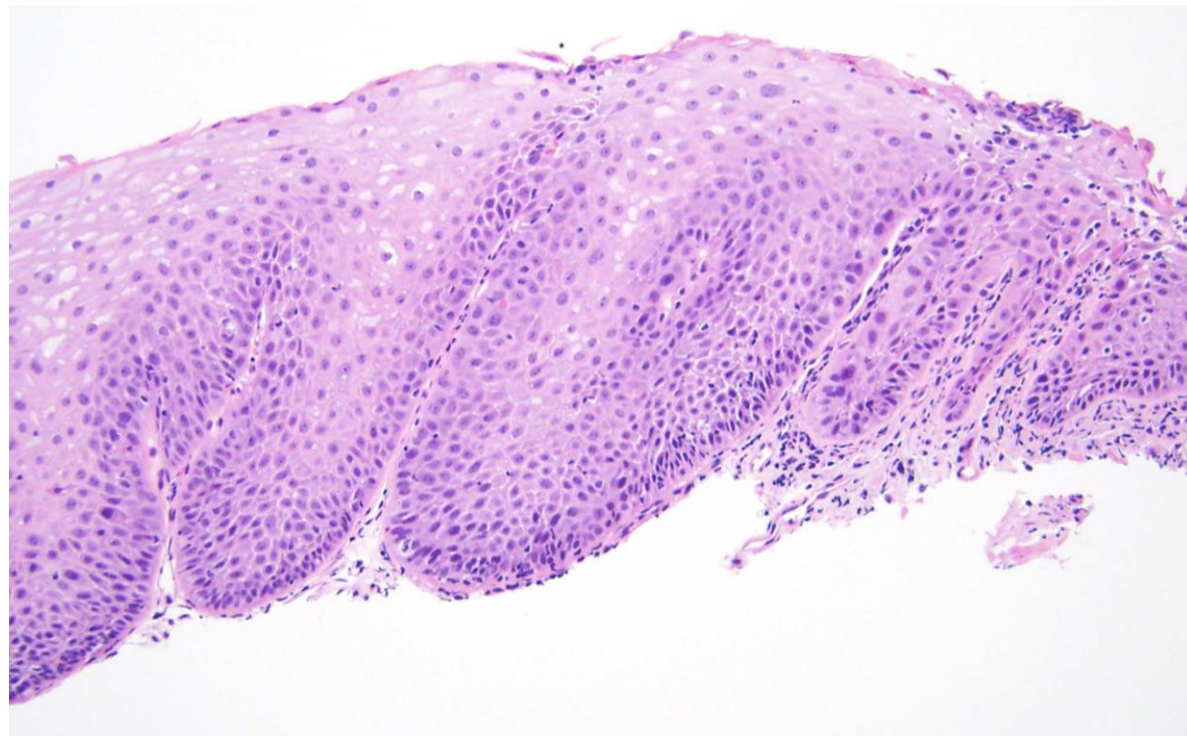
Gastroesophageal Reflux Disease (GERD)

- GERD affects ~4% of population
- Threshold distinction between physiologic reflux and reflux disease is ultimately arbitrary
- Montreal consensus: “When the reflux of stomach contents causes troublesome symptoms and/or complications”
- Categorized as symptom-based or defined by tissue injury
- Sensitivity of symptoms is only ~55% (but what is gold standard?)



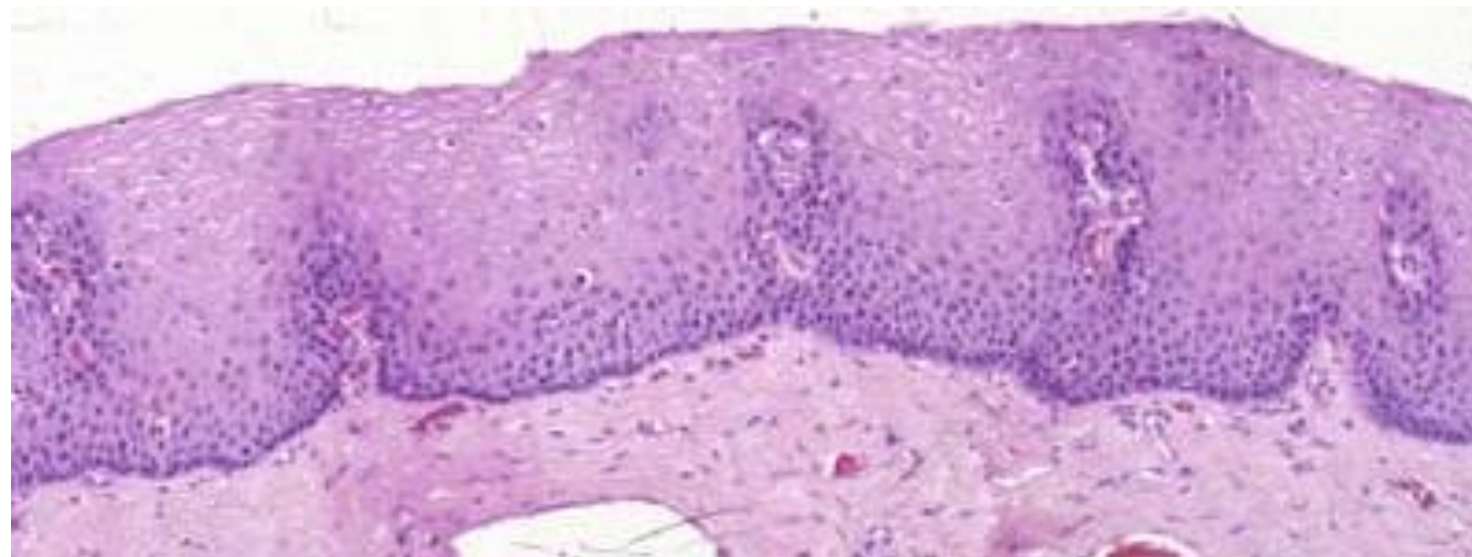
Reflux Esophagitis: Histology

- Basal layer hyperplasia
- Elongation of lamina propria papillae
- Erosive esophagitis: neutrophils, parakeratosis (associated with *Candida*), fibrinopurulent inflammatory debris, ulcer, granulation tissue



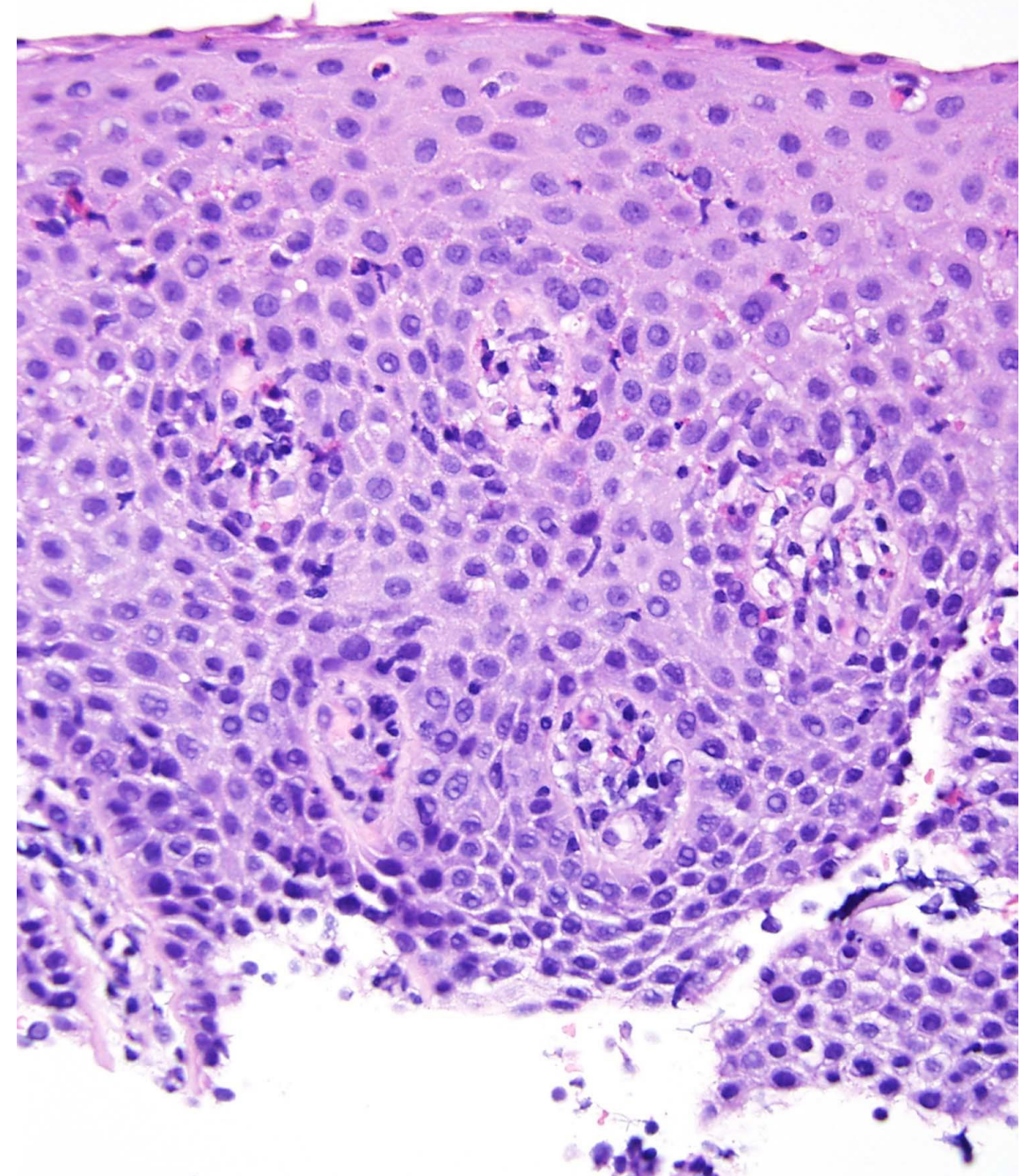
Criteria for Normal

Feature	Criteria
Basal layer thickness	<20% at Z-line; <15% at more proximal sites
Papillary length	<66% at Z-line; <50% at more proximal sites
IELs	<10 per hpf
Dilated intercellular spaces	Absent
Eosinophils	None to scant
Neutrophils	None



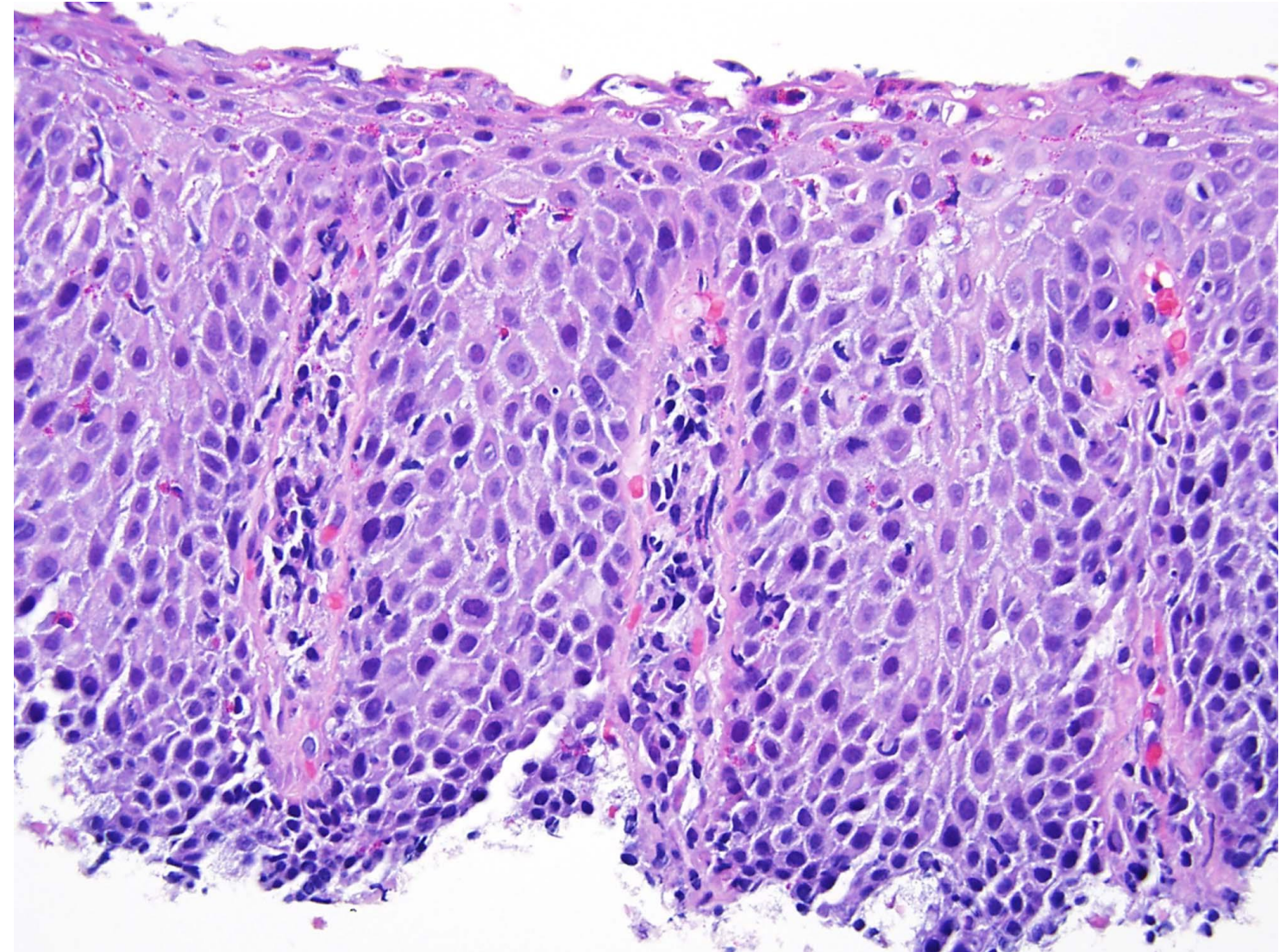
Basal Layer Hyperplasia

- Epithelial regenerative response
- Normally less than $\sim 1/6$ of mucosal thickness (15%); 2-3 cells thick
- Uppermost limit is the point where nuclei are separated by a distance of less than one nuclear diameter
- Biopsy orientation
- Specificity is only $\sim 45\%$
- Can be graded as mild or marked ($>30\%$); typically more severe in EoE



Papillary Elongation

- Papillae extend more than 2/3 of distance to luminal surface
- Increased turnover of overlying squamous layers
- More specific (80%) but not very sensitive (30%-60%)
- Can be graded as mild or marked (>75%)

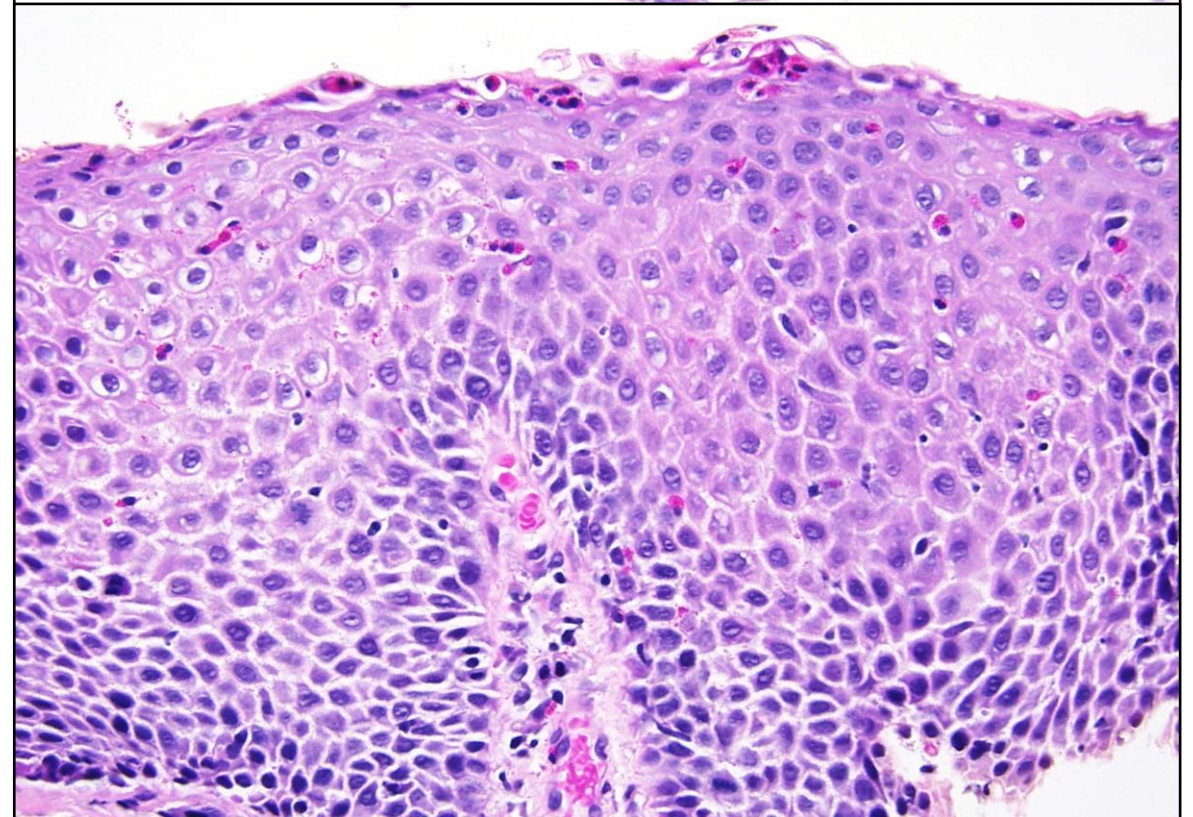
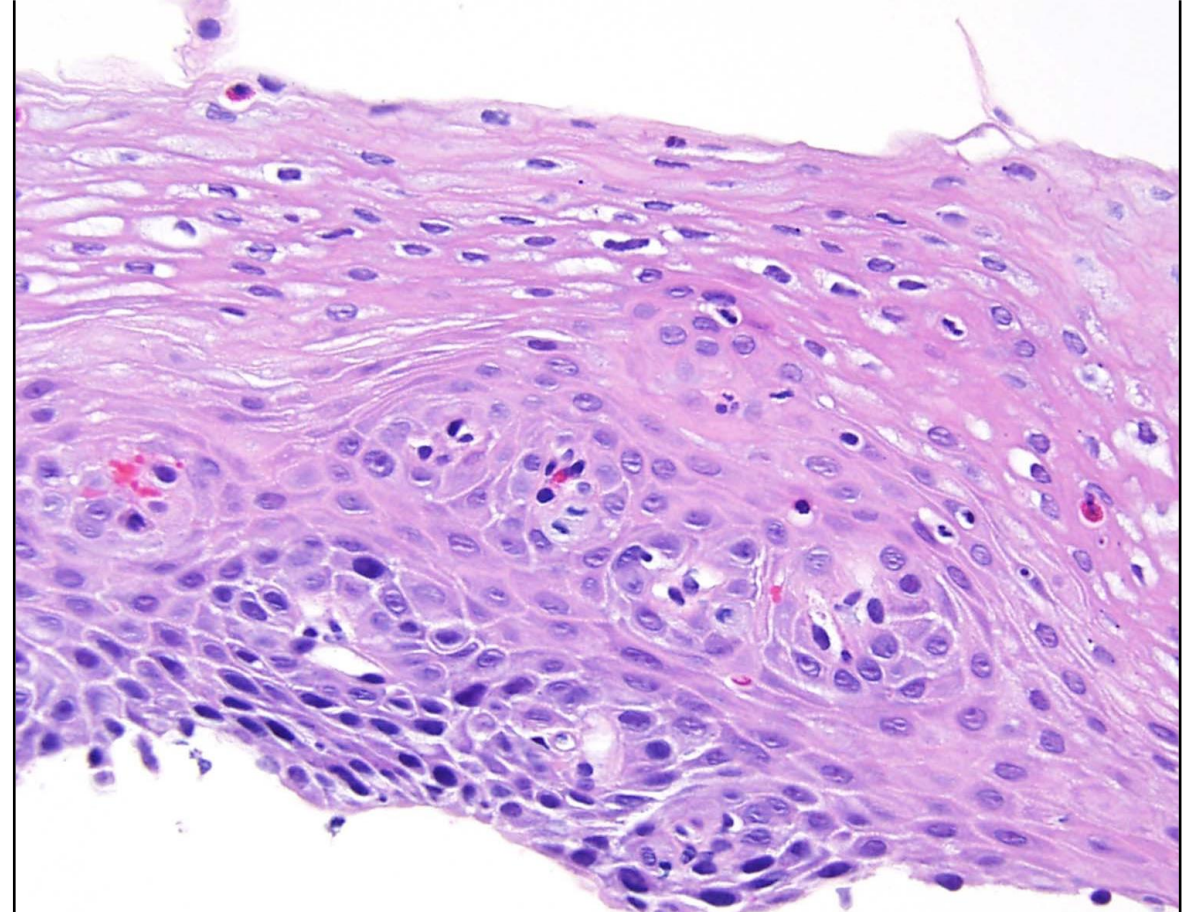


Inflammation

- **Lymphocytes > eosinophils > neutrophils**
- **Specificity > sensitivity**
- **A few lymphocytes (cytotoxic T-cells) are normal (<10 per hpf)**
- **Lymphocytes correlate with severity of GERD; found in ~50% of cases in one study**
- **After stopping PPI therapy, lymphocytes rapidly return**
- **Contact with gastric contents may stimulate epithelial cells in the esophagus to secrete cytokines that attract immune cells, rather than a direct cytotoxic injury**

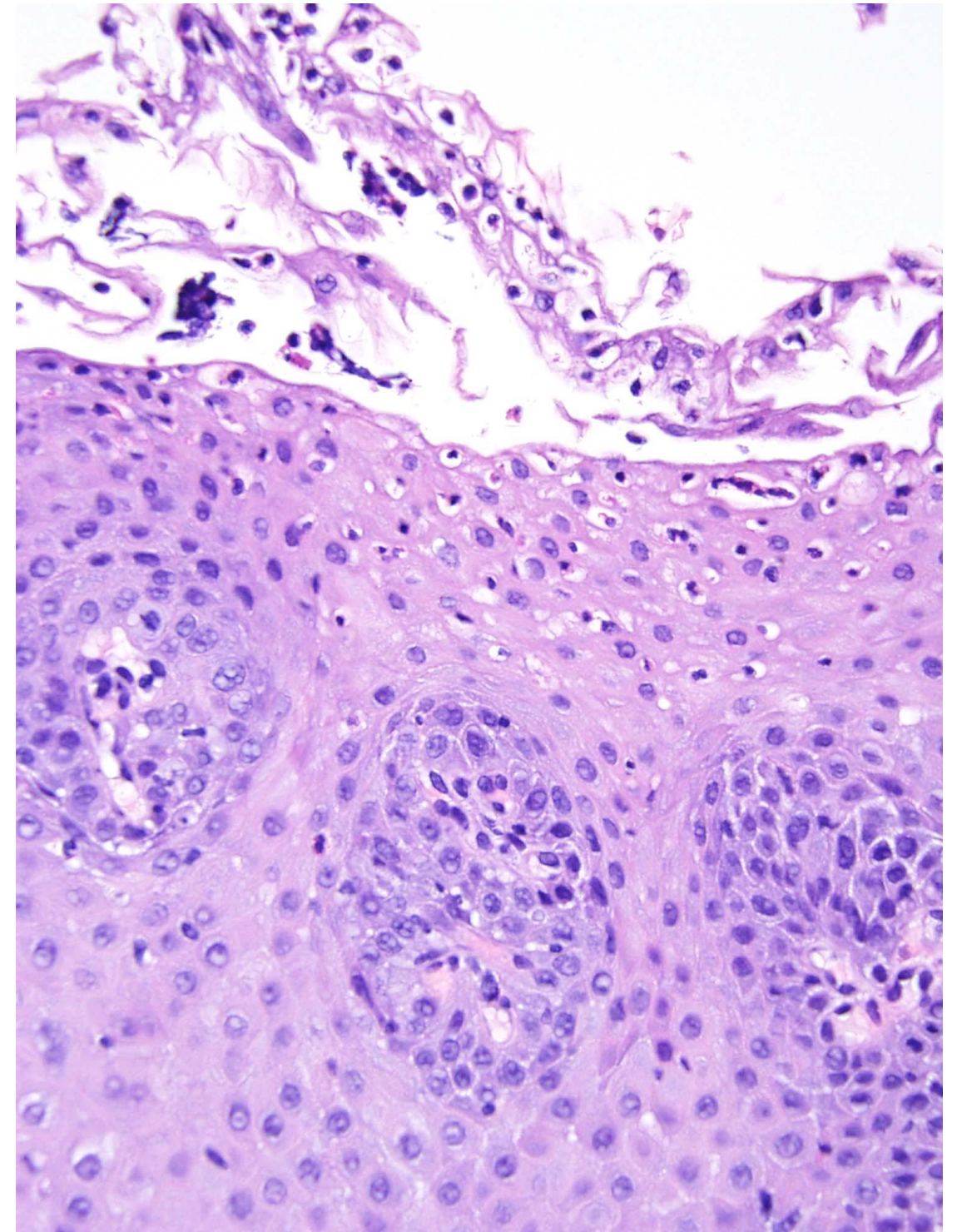
Eosinophils

- Normal not defined – none versus a few
- Insensitive – only 20%-40% will have eosinophils
- Specific (90%)
- Rarely, may exceed the threshold for EoE; should **not** have microabscesses or surface layering
- May also be seen in eosinophilic esophagitis, pill injury, infections



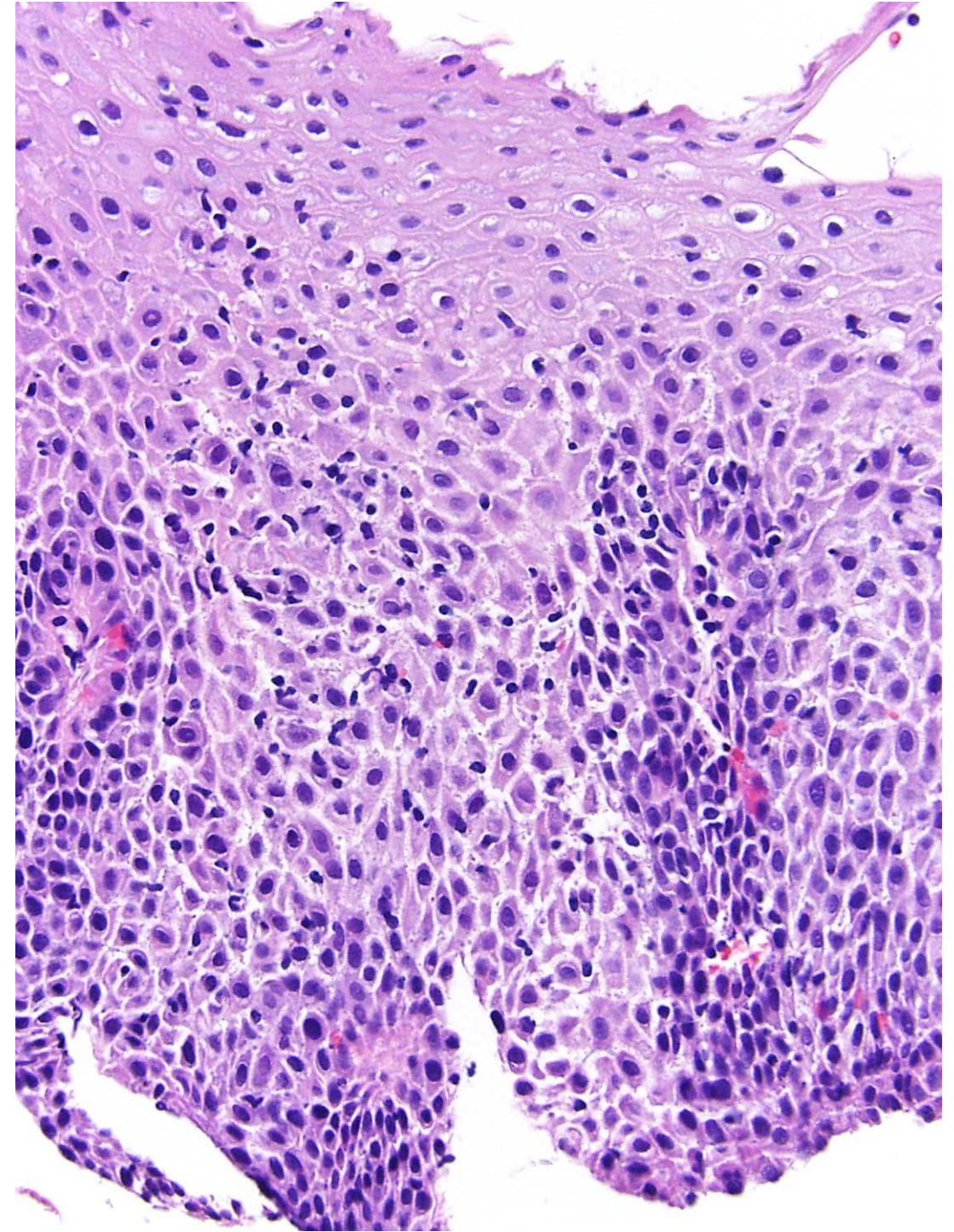
Neutrophils

- **Specific but not sensitive – seen in 10%-40% of cases**
- **Associated with erosions and ulcers (severe GERD)**
- **Differential diagnosis is other ulcerating conditions (pill injury), *Candida***



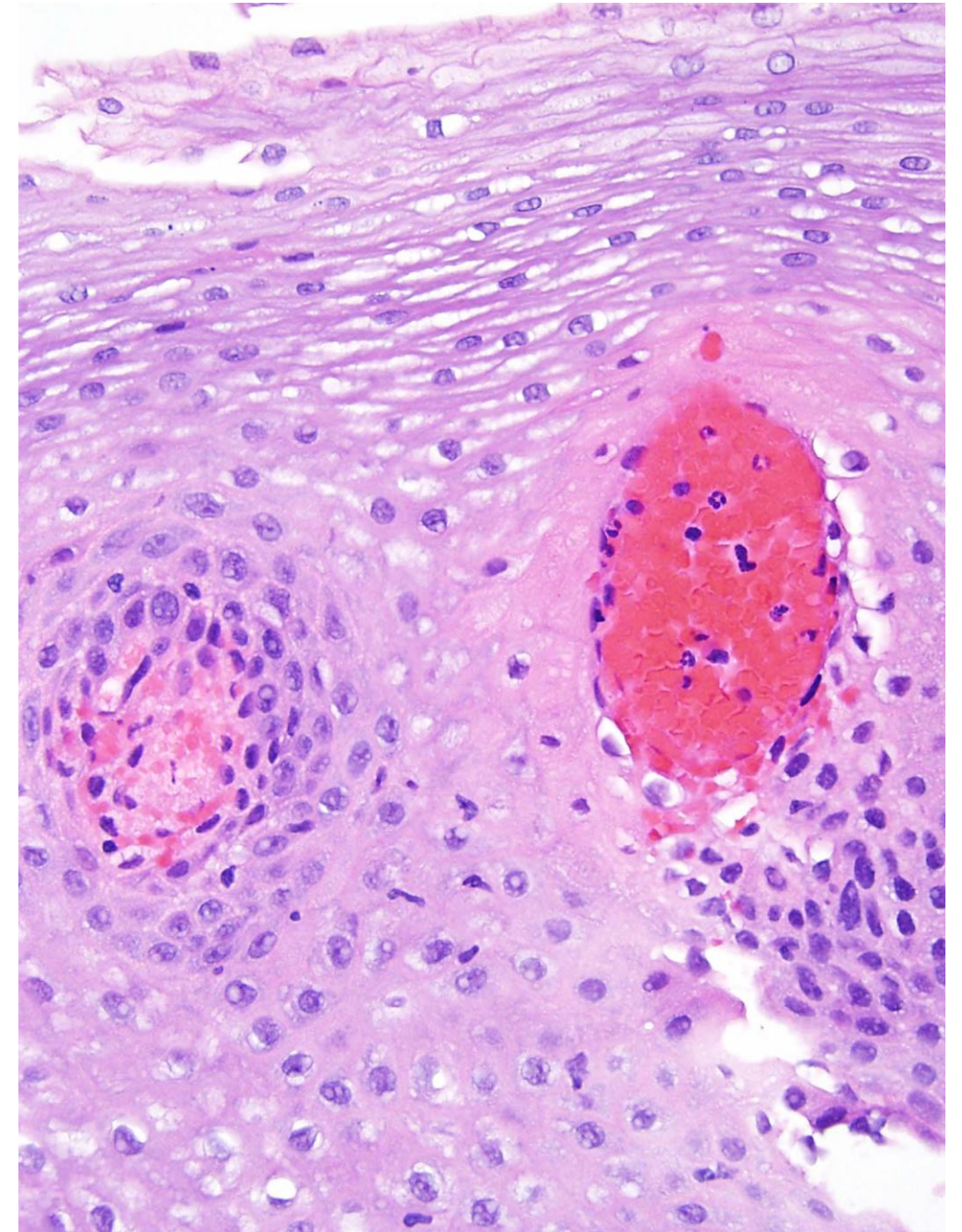
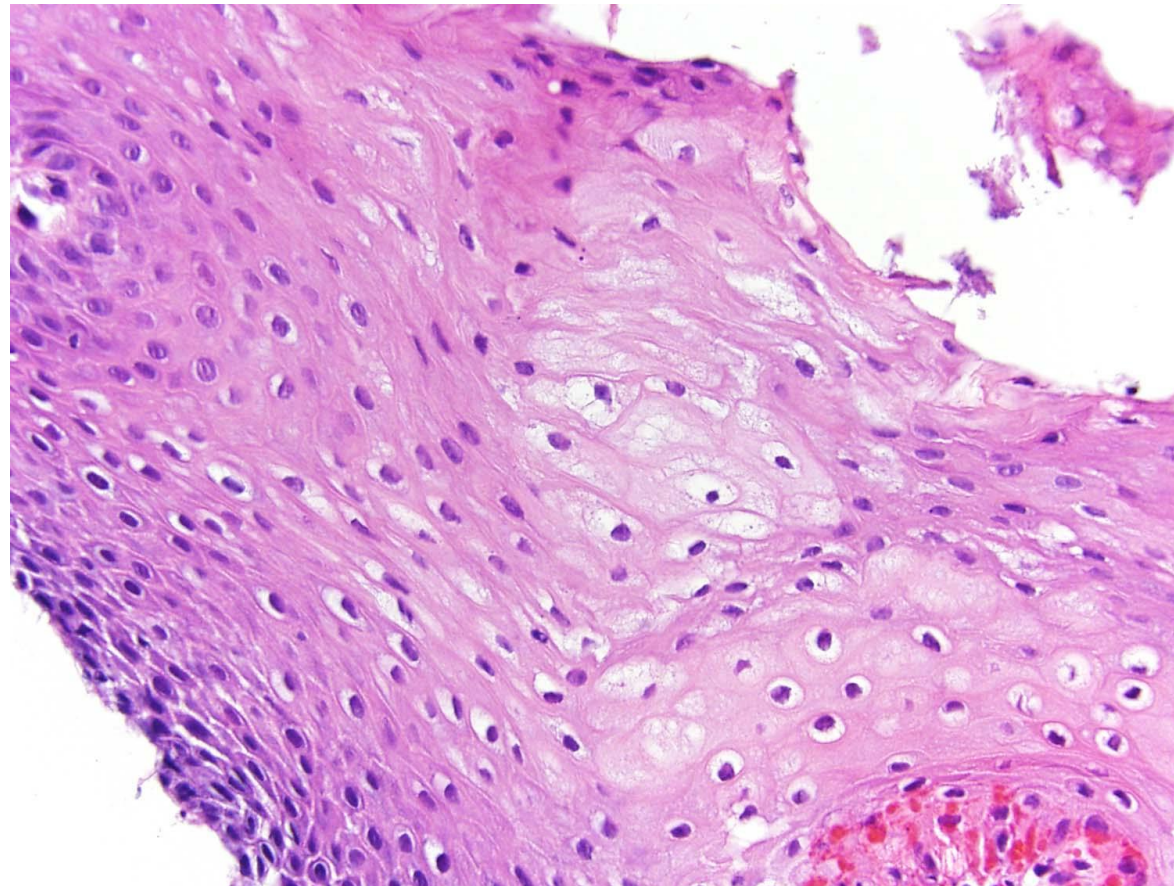
Dilated Intracellular Spaces

- **Spongiosis**
- **Related to loss of tight junctions, resulting in increased permeability**
- **Found in up to 95% of cases**
- **Also found in EoE; may explain pain in nonerosive GERD (more exposure to acidic fluids)**



Other Features

- **Ballooned squamous cells**
- **Vascular lakes – dilated and engorged small vessels within papillae (? biopsy artifact)**



Histologic Feature	Sensitivity	Specificity
Basal layer hyperplasia	93%	45%
Dilated intercellular spaces	86%	70%
Papillary elongation	62%	80%
Eosinophils	49%	90%
Neutrophils	7%	100%
Erosion or necrosis	8%	100%

- **119 participants with GERD symptoms; 20 normal controls with no symptoms and normal pH studies**
- **Biopsies taken at Z-line, 2 cm above, and 4 cm above**
 - 4-cm biopsies were noncontributory
 - Z-line biopsies improved sensitivity but decreased specificity

Mastracci L, Spaggiari P, Grillo F, et al. Microscopic esophagitis in gastro-esophageal reflux disease: individual lesions, biopsy sampling, and clinical correlations. *Virchows Archiv.* 2009;454(1):31-39.
doi:10.1007/s00428-008-0704-8

Composite Score

Feature	Score	Criteria
Basal layer hyperplasia	0, 1, 2	>15% at 2 and 4 cm and >20% at the Z-line
Papillary elongation	0, 1, 2	>50% at 2 and 4 cm and >66% at the Z-line
Dilated intercellular spaces	0, 1, 2	Score based on size
Eosinophils	0, 1, 2	1 = 1 eosinophil, 2 = >1 eosinophil
Neutrophils	0, 2	Absent/present
Erosion	0, 2	Absent/present
Total score >2 considered to represent histologic features of GERD	0-12	(The most severe areas were scored; did not score lymphocytes)

Zentilin P, Savarino V, Mastracci L, et al. Reassessment of the diagnostic value of histology in patients with GERD, using multiple biopsy sites and an appropriate control group. *Am J Gastroenterol*. 2005;100(10):2299-2306. doi:10.1111/j.1572-0241.2005.50209.x

Minimal Criteria?

- **No consensus**
- **Mild changes common at squamocolumnar junction in “normal” individuals but some studies show greater changes at Z-line in GERD patients**
- **Variation in findings from distal to proximal, and around circumference**
- **Unclear how reproducible pathologists are in assessing changes**

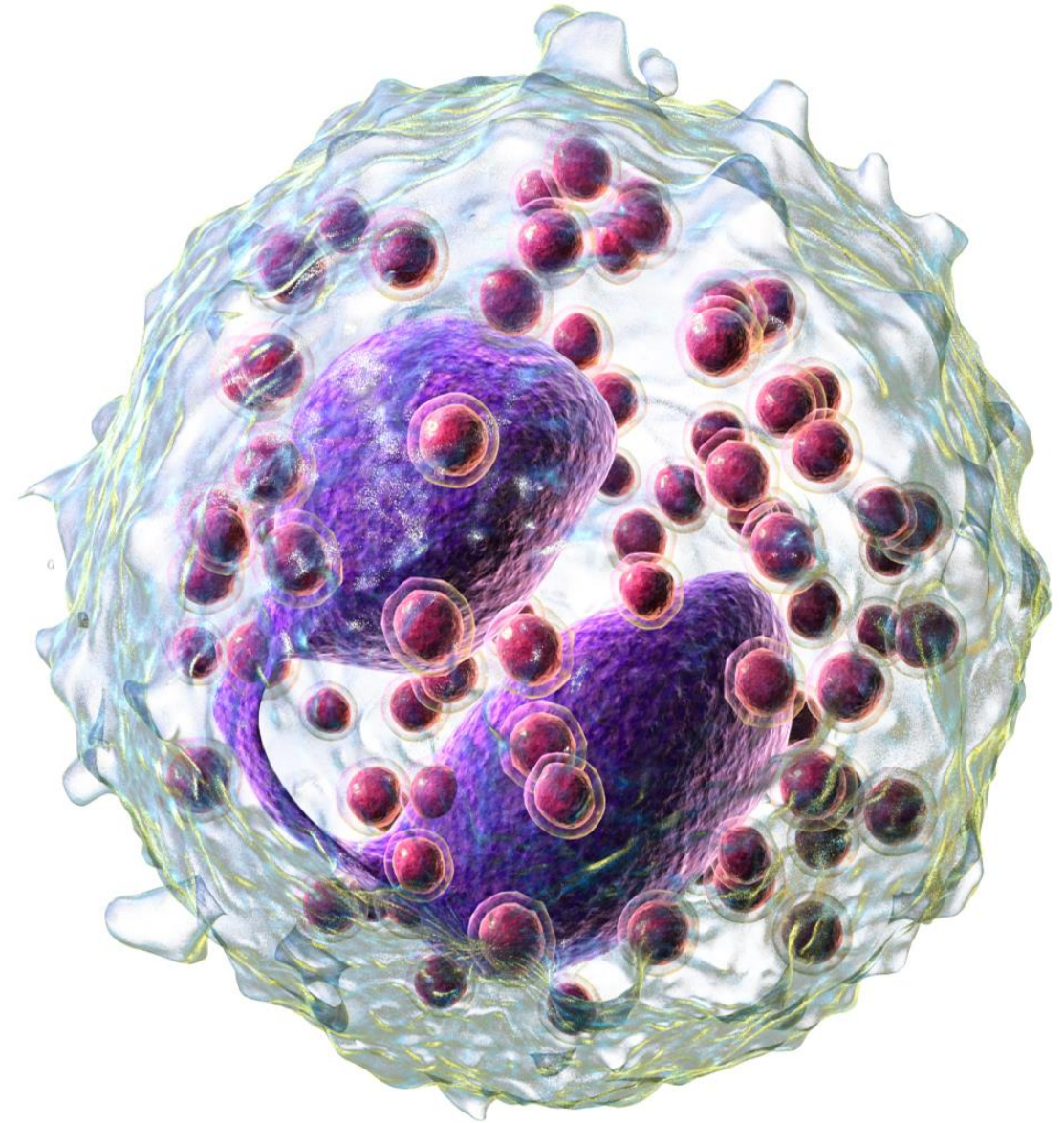
Bottom line: Basal layer hyperplasia, papillary elongation, increased lymphocytes, spongiosis +/- a few eosinophils is most commonly due to GERD

Eosinophils in the esophagus

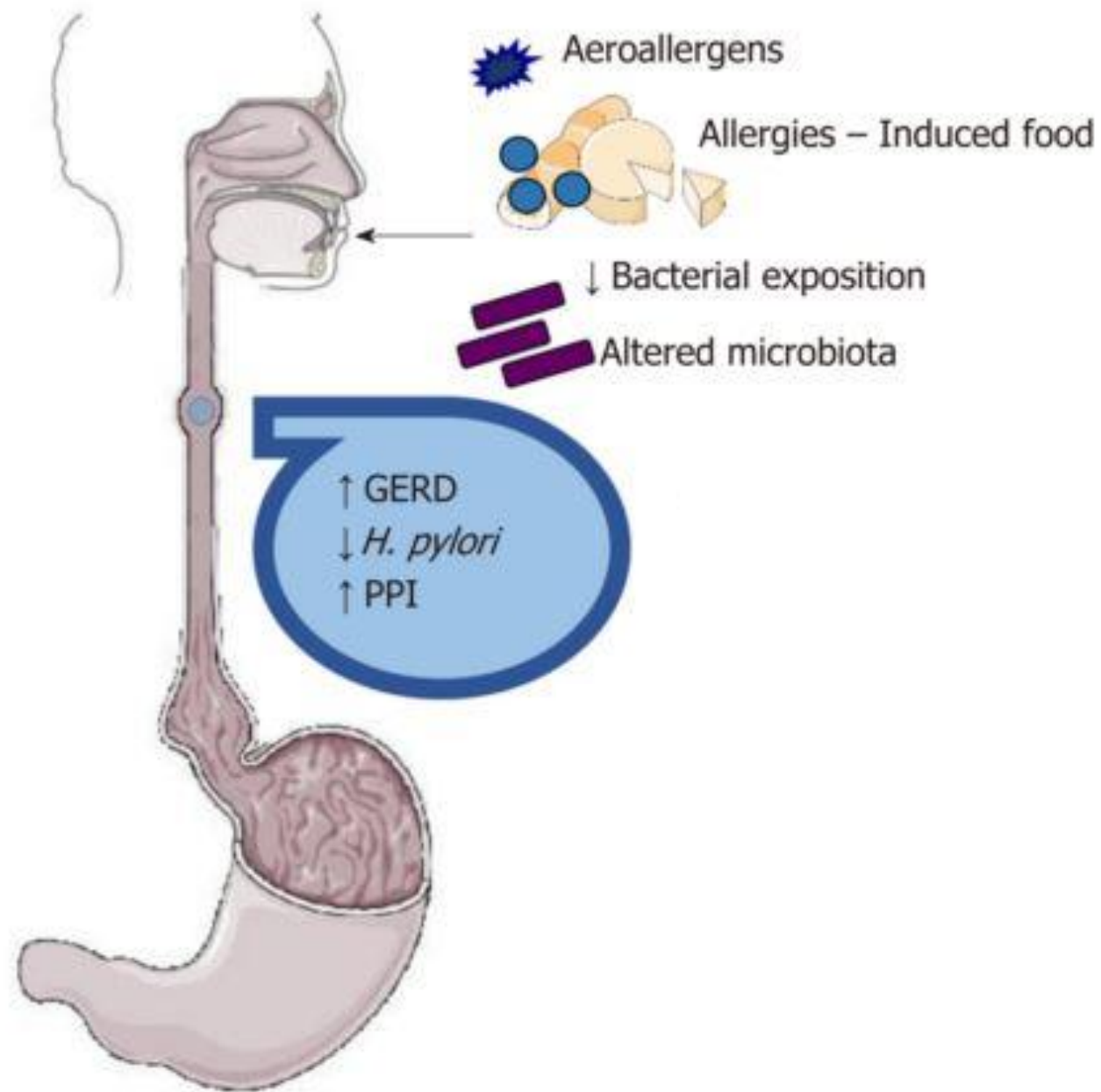
- **Reflux esophagitis**
- **Eosinophilic esophagitis**
- **(PPI-responsive esophageal eosinophilia)**

Eosinophilic Esophagitis

- **Chronic immune-mediated disease**
- **First report was in 1977**
- **2nd most prevalent form of esophagitis, after GERD; prevalence increasing**
- **Prevalence is low in Asian, higher in Western countries, rural areas**
- **Mostly white males (3:1 male predominant)**



Blausen Medical. Eosinophil granulocyte. WikiJournal of Medicine. 2014;1(2):20. Licensed under [CC BY-SA 4.0](https://creativecommons.org/licenses/by-sa/4.0/)



Multifactorial disorder

- **Genetic predisposition**
- **Deficient esophageal mucosal barrier**
- **Abnormal immune reaction to environmental allergens (foods, others)**
- **Mediated by Th2 interleukins**

EoE: Clinical Features

- Abdominal pain 54%
- Dysphagia 50%
- Nausea/vomiting 40%
- Food impaction 38% (most common cause in ED)
- Heartburn 37%
- Diarrhea 32%
- Chest pain 21%
- GERD 54%
- Food allergy 67%
- Allergic rhinitis 69%
- Atopic dermatitis 46%
- Asthma 45%

Higher in children

Age-related increase

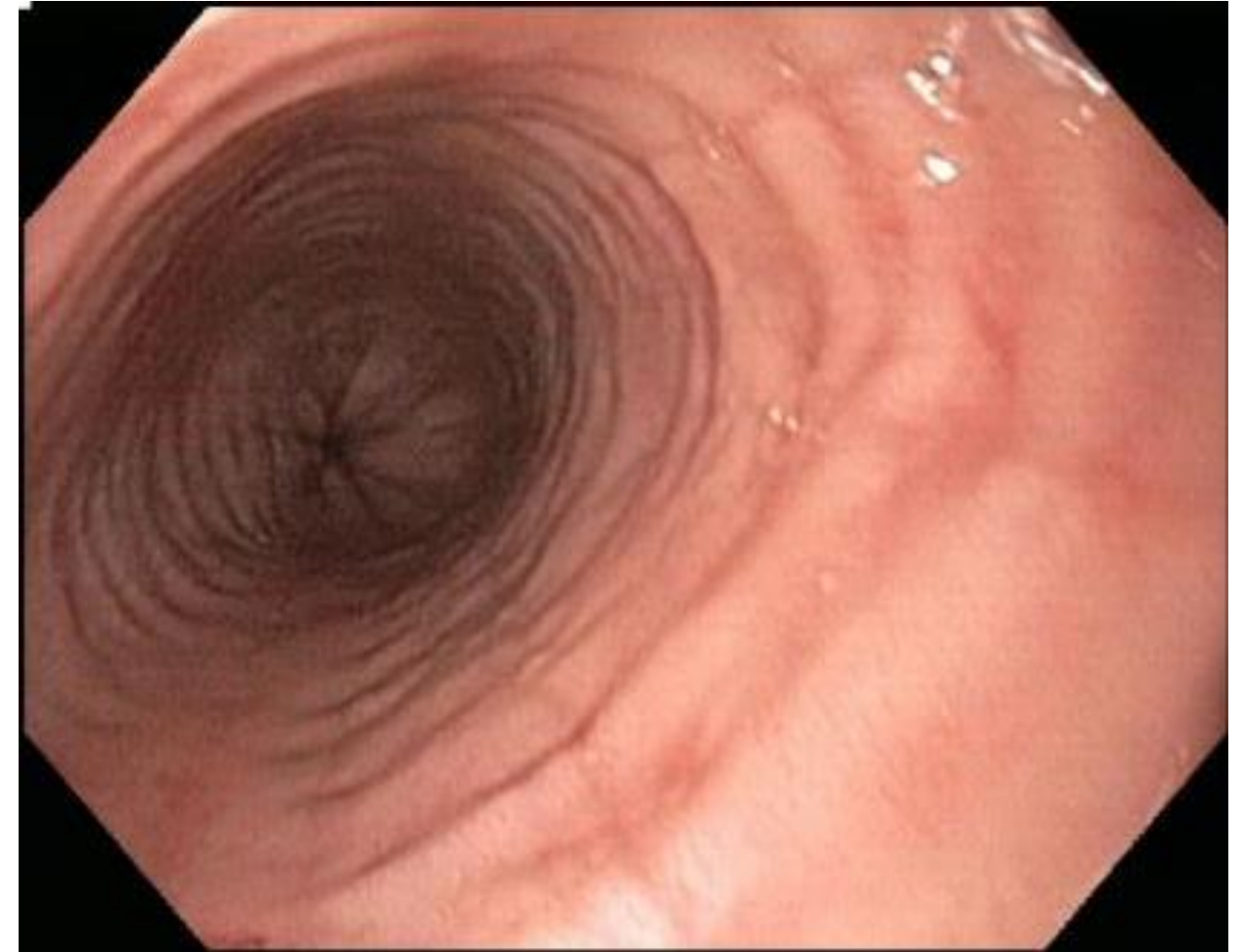
Chegade M, Jones SM, Pesek RD, et al. Phenotypic Characterization of Eosinophilic Esophagitis in a Large Multicenter Patient Population from the Consortium for Food Allergy Research. *J Allergy Clin Immunol Pract.* 2018;6(5):1534-1544.e1535. doi:10.1016/j.jaip.2018.05.038

EoE: Overlap With GERD?

- **EoE and GERD are not mutually exclusive**
 - EoE can cause secondary reflux
 - Acid exposure from GERD could increase mucosal permeability
- **EoE versus proton pump inhibitor-responsive esophageal eosinophilia**
 - Similar histology, endoscopy, gene expression profiling, clinical symptoms
 - PPIs may block Th2-cytokine mediated secretion of eotaxin-3, the cytokine that recruits eosinophils to the mucosa; they may improve epithelial barrier function
 - Eotaxin-3, tryptase, major basic protein cannot distinguish between the two
- **Extraesophageal eosinophilia may be seen in EoE (5% gastric, 1.7% colon, small bowel less common)**

EoE: Endoscopic Findings

- **Linear grooves**
- **Concentric rings (“feline esophagus”)**
- **Punctate white exudates (can resemble candidal infection)**
- **Schatzki rings**
- **Small lumen**
- **Superficial tears**



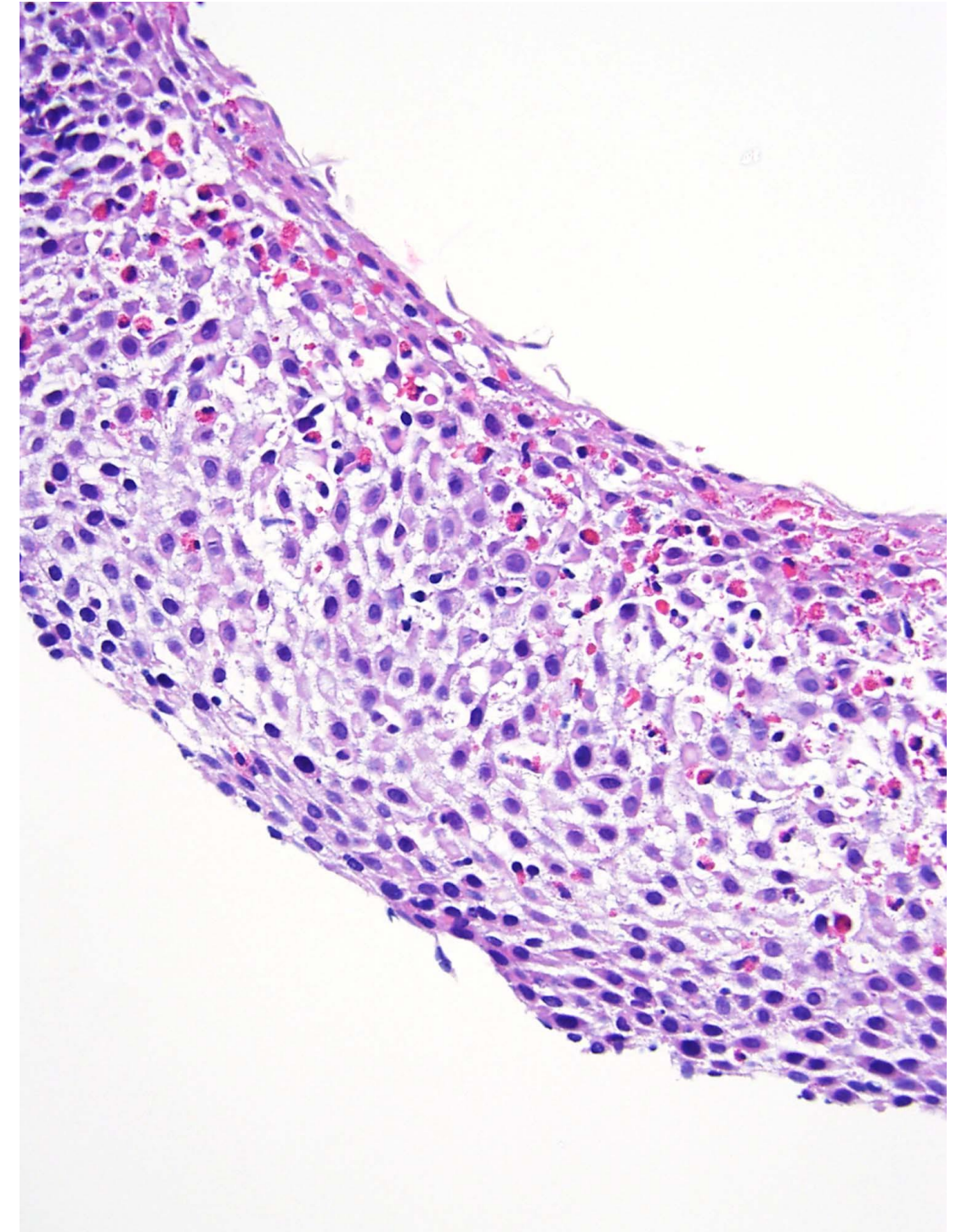
EoE: Consensus Criteria for Diagnosis (AGREE)

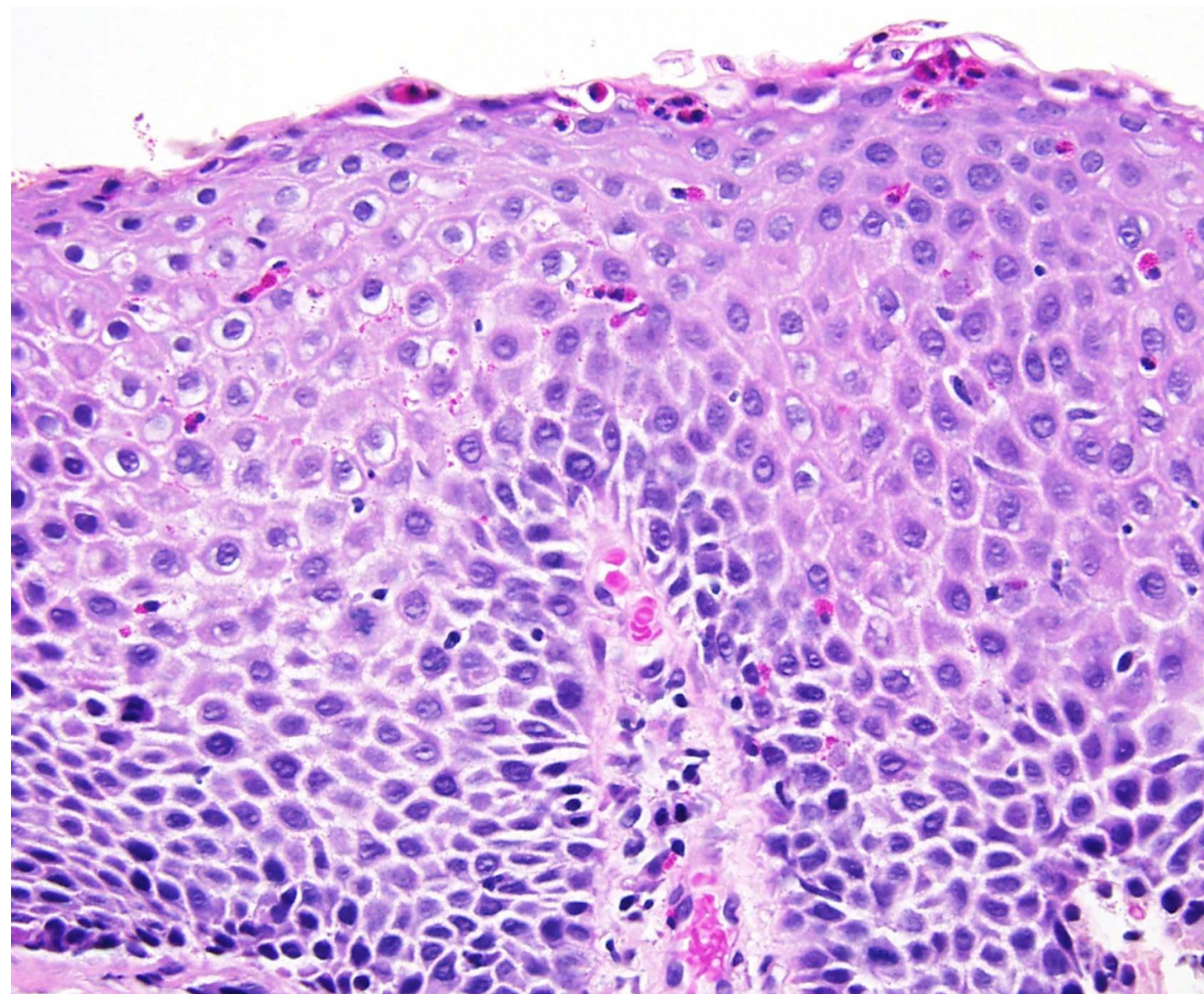
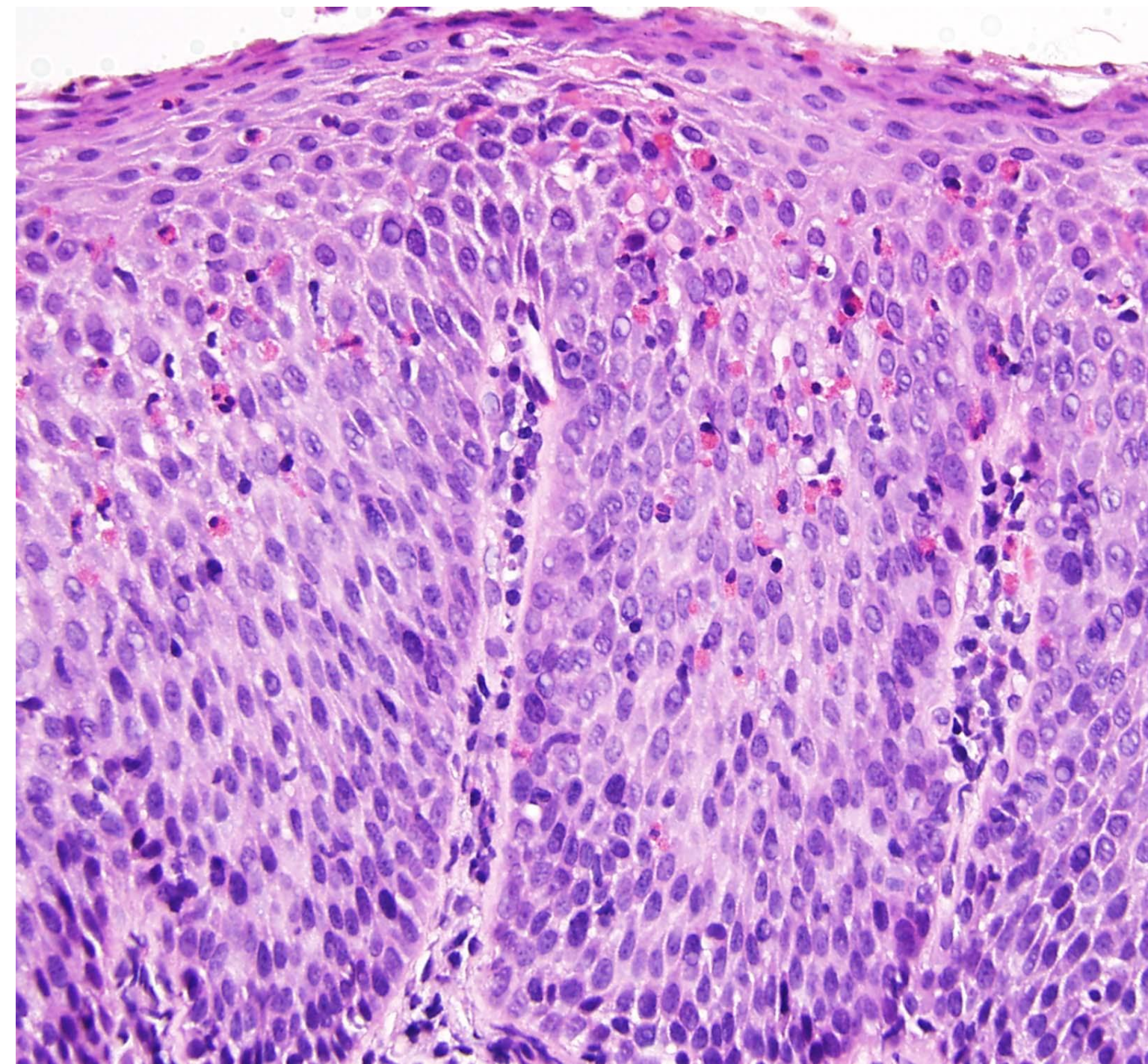
- Esophagus-related symptoms
- Esophageal bx with at least 15 eosinophils in at least one hpf,
(nonresponse to PPI treatment has been dropped)
 - Histologic cutoff somewhat arbitrary
 - Separation from PPI-REE may not be warranted (essentially identical disease)
- Exclusion of other causes of eosinophilia
 - Reflux esophagitis
 - Celiac disease
 - Crohn's disease
 - Infection
 - Achalasia
 - Drug hypersensitivity
 - Vasculitis and eosinophilic granulomatosis polyangiitis (Churg-Strauss syndrome)

Dellon ES, Liacouras CA, Molina-Infante J, et al. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. *Gastroenterology*. 2018;155(4):1022-1033.e1010. doi:10.1053/j.gastro.2018.07.009

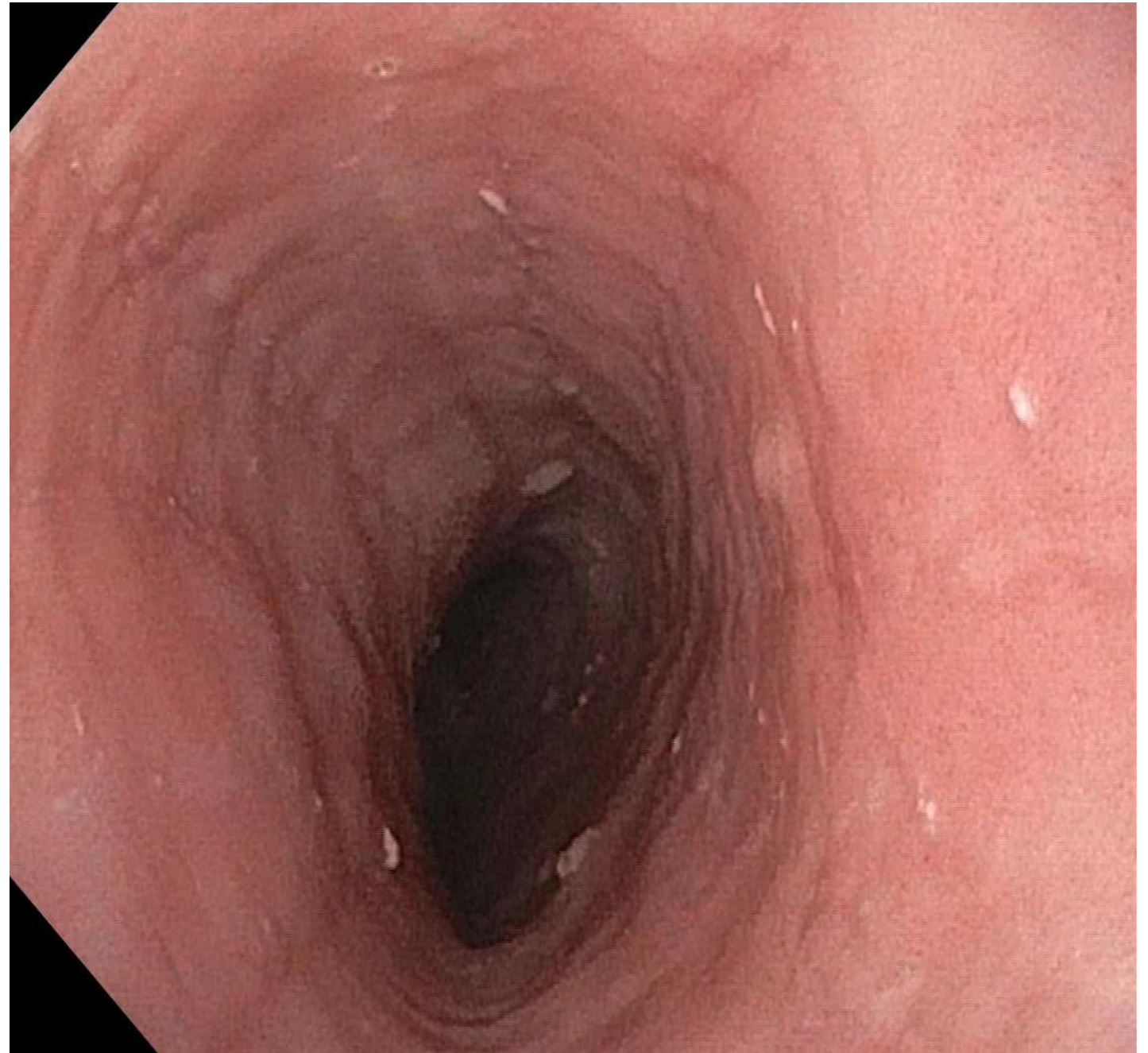
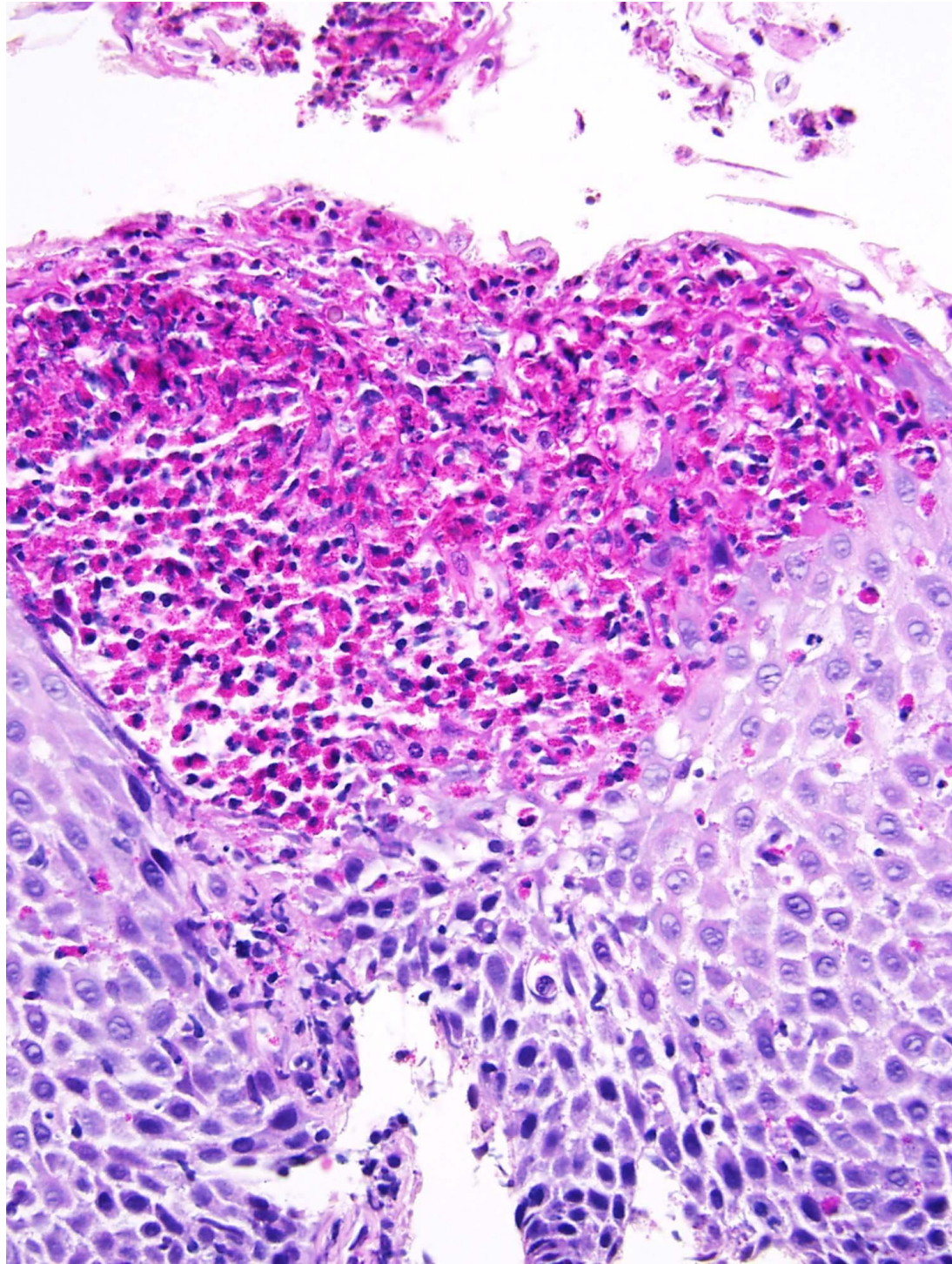
EoE: Histology

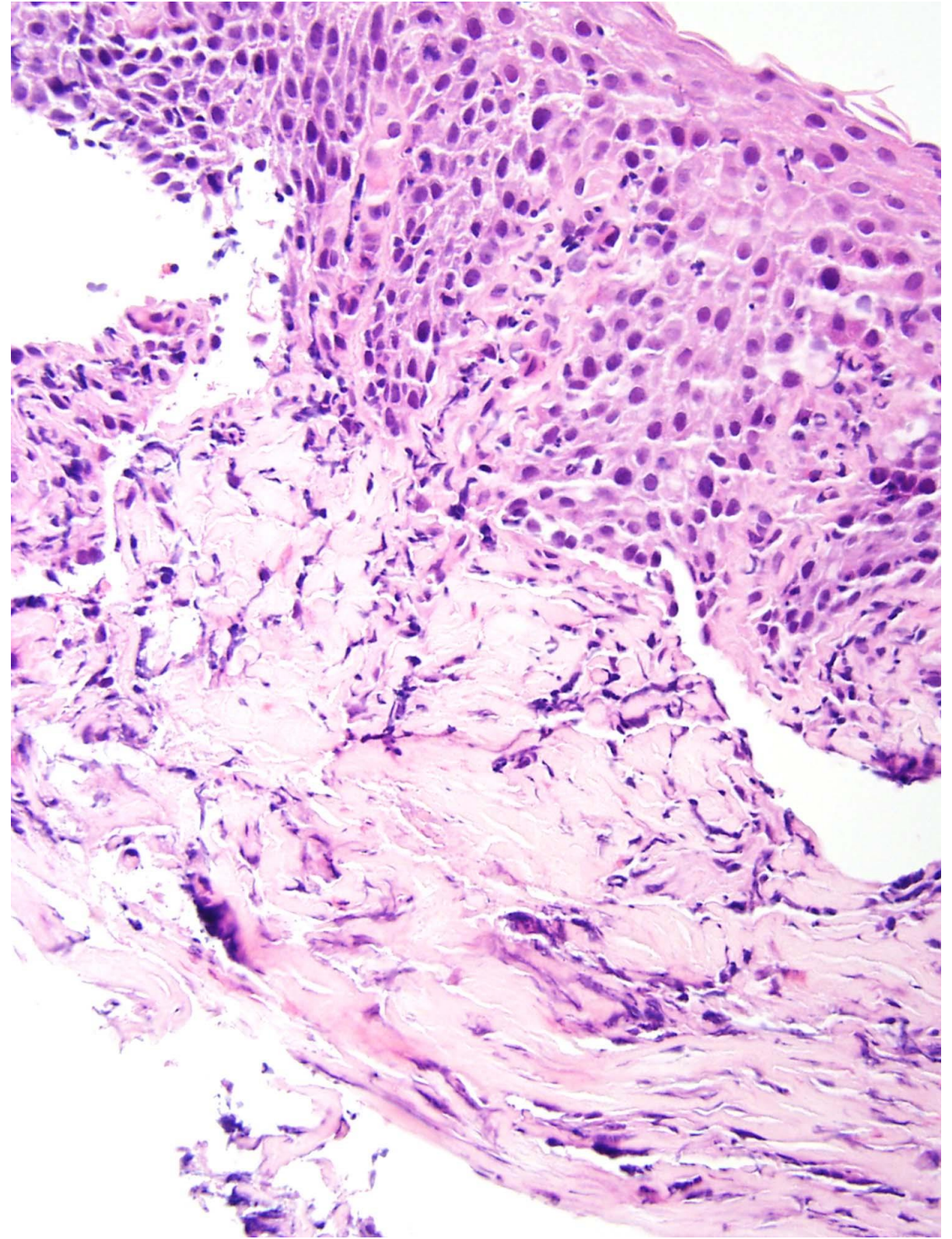
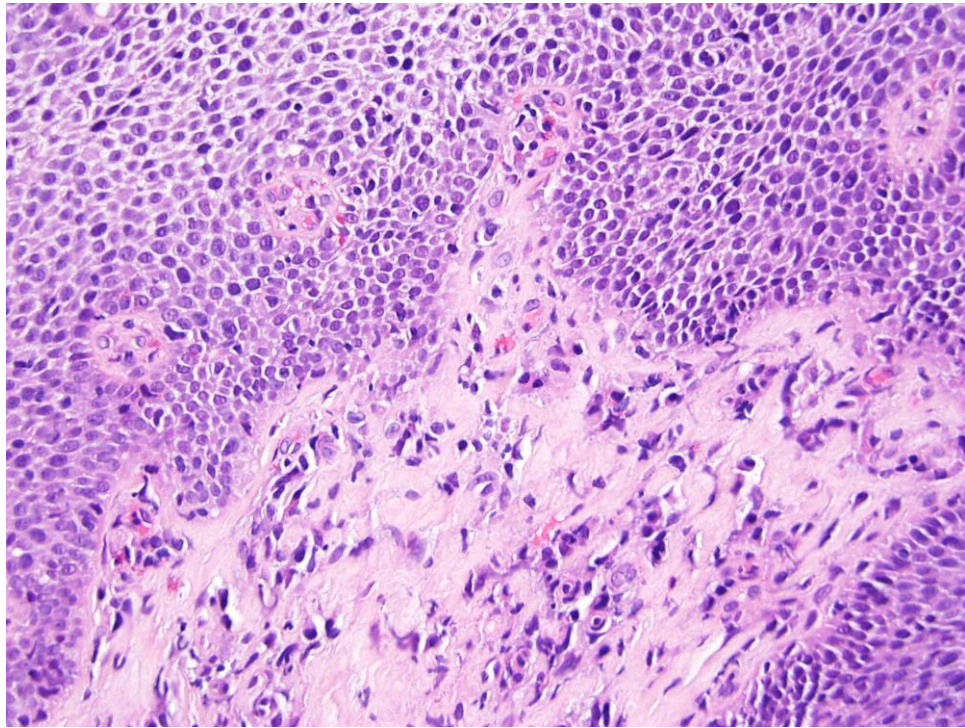
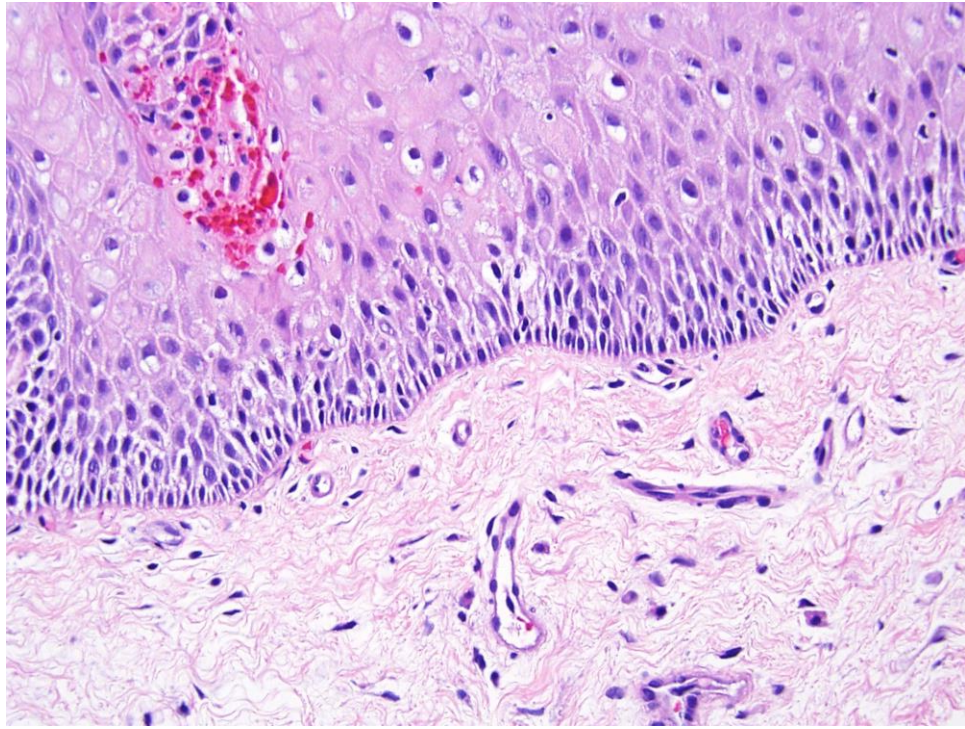
- **At least 15 eosinophils per hpf, but may be patchy; often degranulated**
- **Eosinophilic microabscesses and layering at surface**
- **Prominent basal layer hyperplasia and spongiosis**
- **Increased T-cells (CD3+, CD4+, CD8+) and mast cells**
- **Lamina propria and submucosal fibrosis**





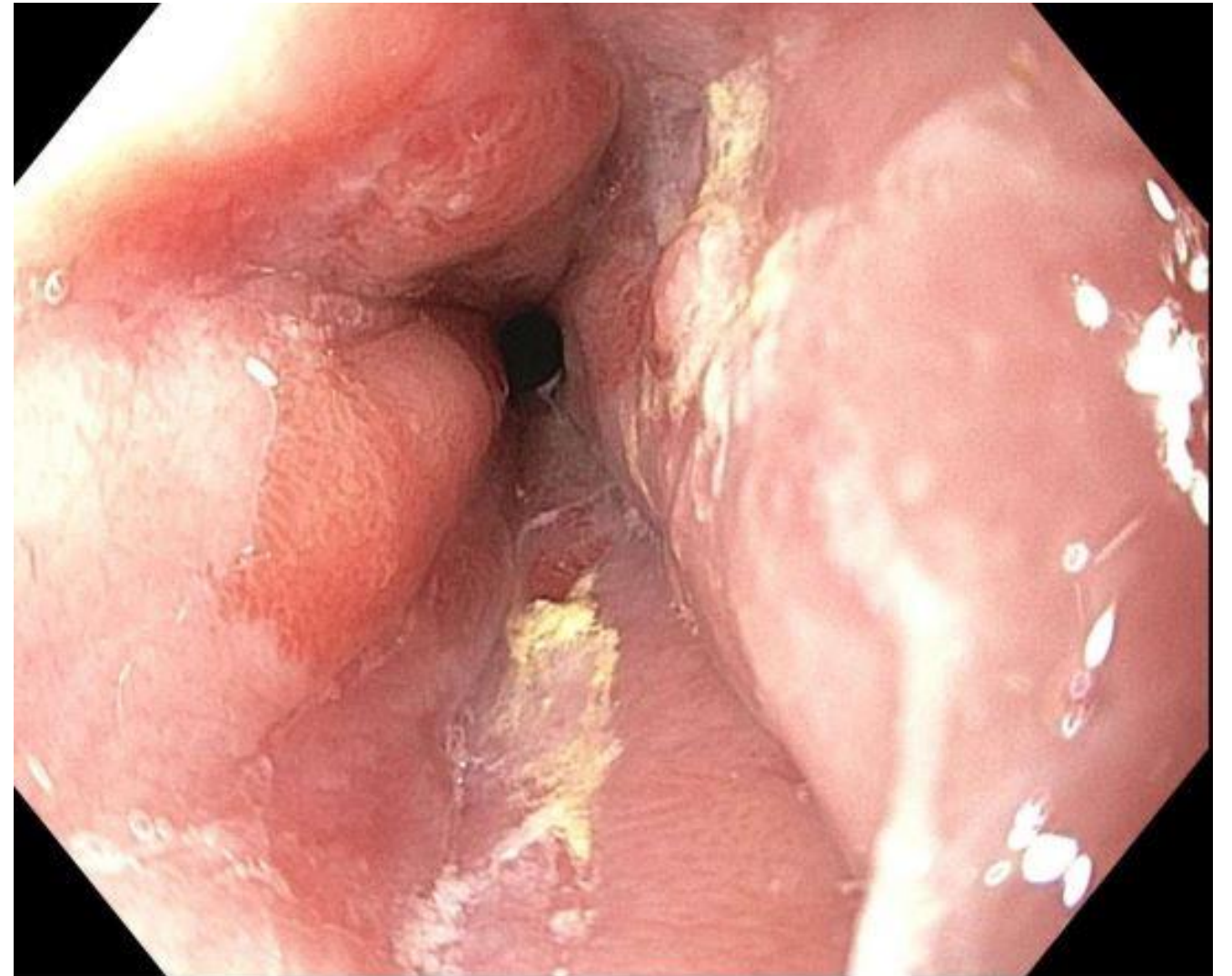
Eosinophilic Microabscesses





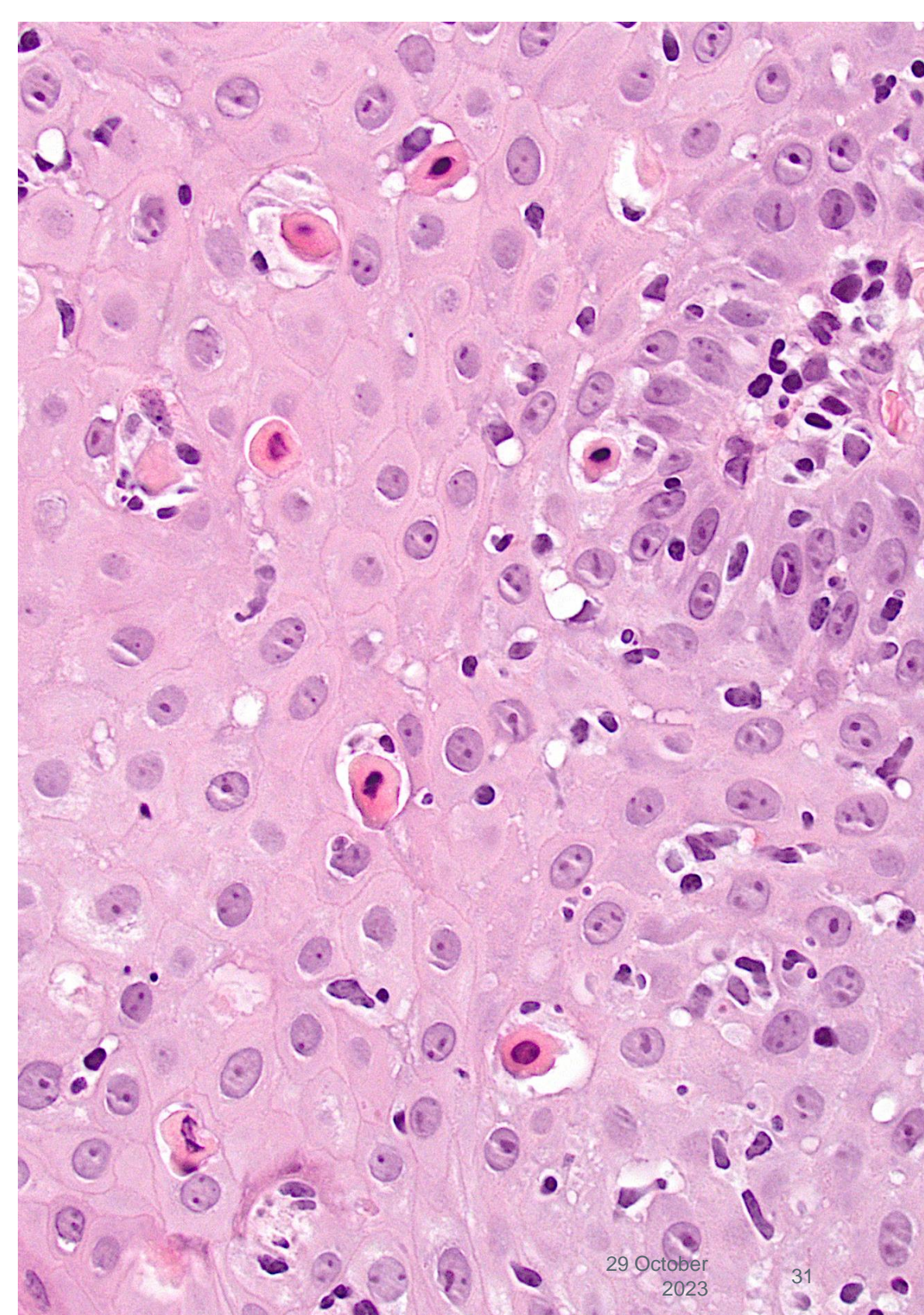
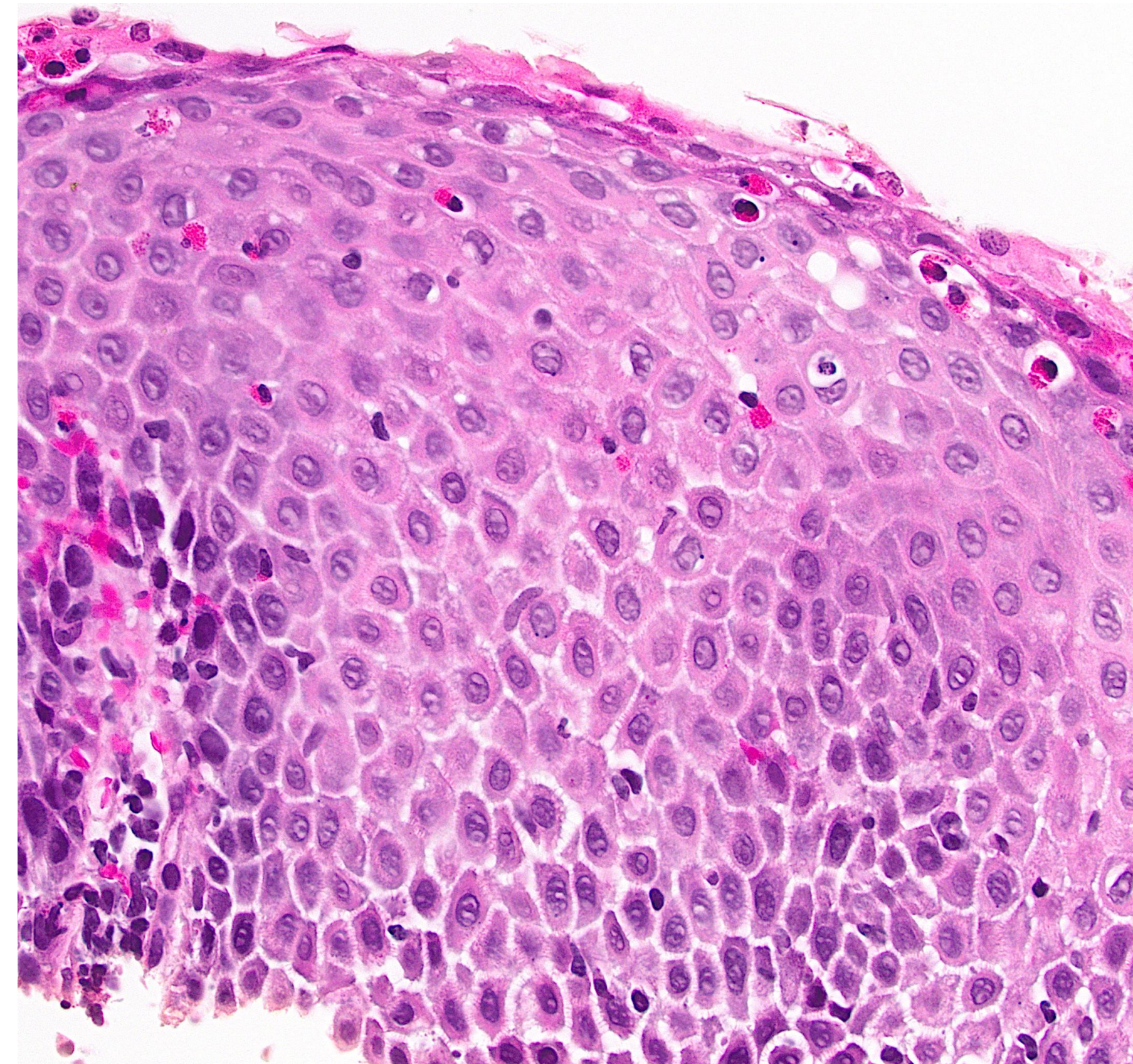
EoE Treatment: The “3 Ds”

- **Drugs:** PPIs, topical corticosteroids, immunosuppressants
- **Diet:** Up to 95% of children and 70% of adults respond to elemental diet
 - Milk, wheat, soy, eggs, peanuts, tree nuts, fish, shellfish
- **Dilation:** Treatment of fibrotic stenoses
- Dupilumab recently approved (monoclonal antibody against IL-4 α receptor subunit)

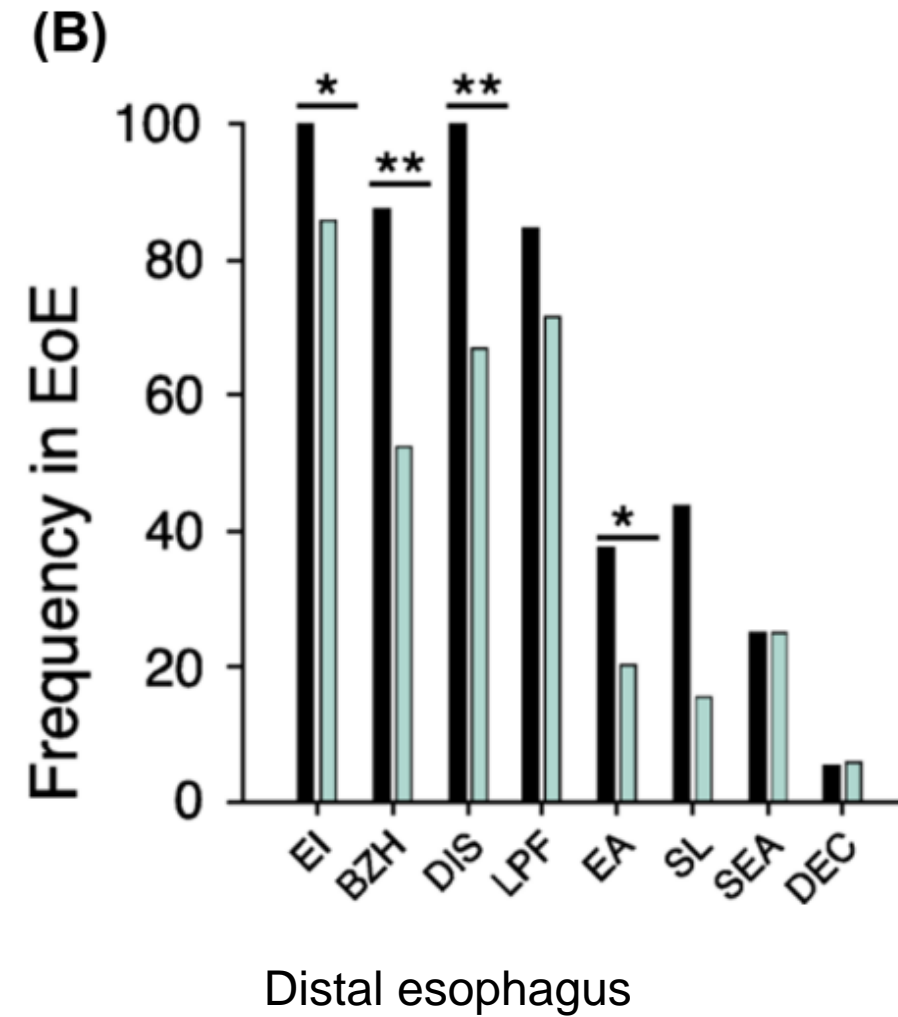
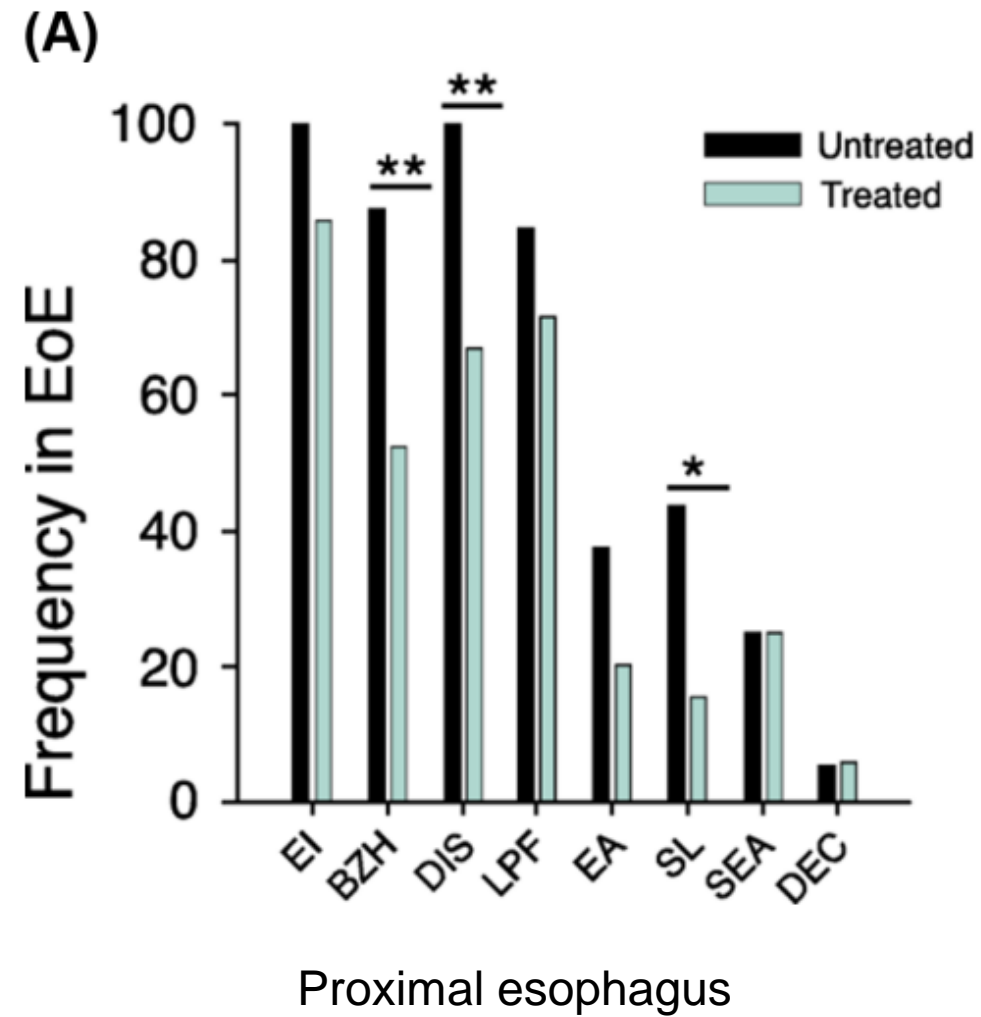


EoE Histology Scoring System (EoEHSS)

Feature	Score	Description
Eosinophilic inflammation	0-3	1=PEC <15/hpf; 2=15-59/hpf; 3=>60/hpf
Basal zone hyperplasia	0-3	1=>15% but less than 33% of total epithelial thickness, 2=33-66%, 3=>66%
Eosinophil abscesses	0-3	1=4 to 9 eos aggregate, 2=10-20; 3=>20
Eosinophil surface layering	0-3	Linear alignment of eosinophils in surface
Dilated intercellular spaces	0-3	1=visible at 400x, 2=200x, 3=100x
Surface epithelial alteration	0-3	1=SEA w/o eos; 2=with any eos; 3=admixed with eos exudate
Dyskeratotic epithelial cells	0-3	1=1/hpf; 2=2-5/hpf; 3>5/hpf
Lamina propria fibrosis	0-3	Based on fiber diameter
Stage score (per feature)	0-3	Based on amount of biopsy involved; varies with feature
EoEHSS (grade and stage, given separately)	Total score of 0-24, divided by maximum possible score	



Frequency of EoEHSS Features in EoE



Collins MH, et al. Diseases of the Esophagus 2017;30:1-8

A Clinical Severity Index for Eosinophilic Esophagitis: Development, Consensus, and Future Directions

Inflammatory features		
Endoscopy (edema, furrows, and/or exudates)	Localized	Diffuse
Histology ^c	15–60 eos/hpf	>60 eos/hpf
Fibrostenotic features		
Endoscopy (rings, strictures)	Present, but endoscope passes easily	Present, but requires dilation or a snug fit when passing a standard endoscope ^d
Histology	–	BZH or LPF (or DEC/SEA if no LP)

EoE: Reporting Recommendations

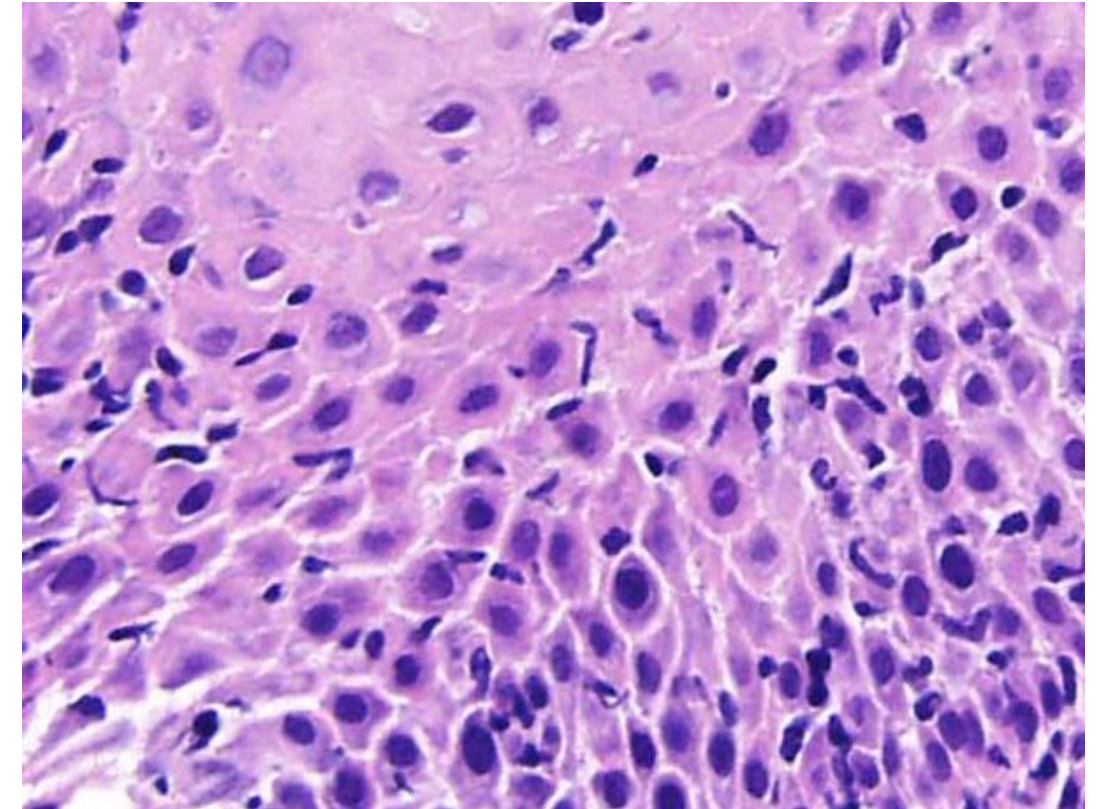
- Report the highest number of eosinophils present per hpf, up to 60 per hpf
- If eosinophils are numerous, it's ok to give an estimate such as >60 per hpf or >100 per hpf
- Include basal layer hyperplasia, spongiosis, lamina propria fibrosis, eosinophilic microabscesses in comment or microscopic description
- Include a statement on extent of abnormalities- focal, patchy, diffuse
- If prior biopsies are available, provide statement regarding improvement or lack thereof
- Use of EoEHSS is not indicated for clinical practice

Lymphocytes in the Esophagus

- **Lichen planus**
- **Lymphocytic esophagitis**
- **Reflux esophagitis**

Lymphocytes in the Esophagus

- Normally a few (5-6 per hpf) but often more near GEJ (Up to 62 per hpf)
- CD3+CD8+ T-cells, suppressor cytotoxic phenotype – “squiggle cells”
- Most lymphocytes in the esophageal lamina propria are CD4+
- Increased in epithelium in 30% of *Candida* esophagitis cases (but most will have PMNs); these are CD4+
- Common post-ablation in Barrett’s esophagus



Lichen Planus

- Skin, hair, nails, oral, genital mucosa, esophagus



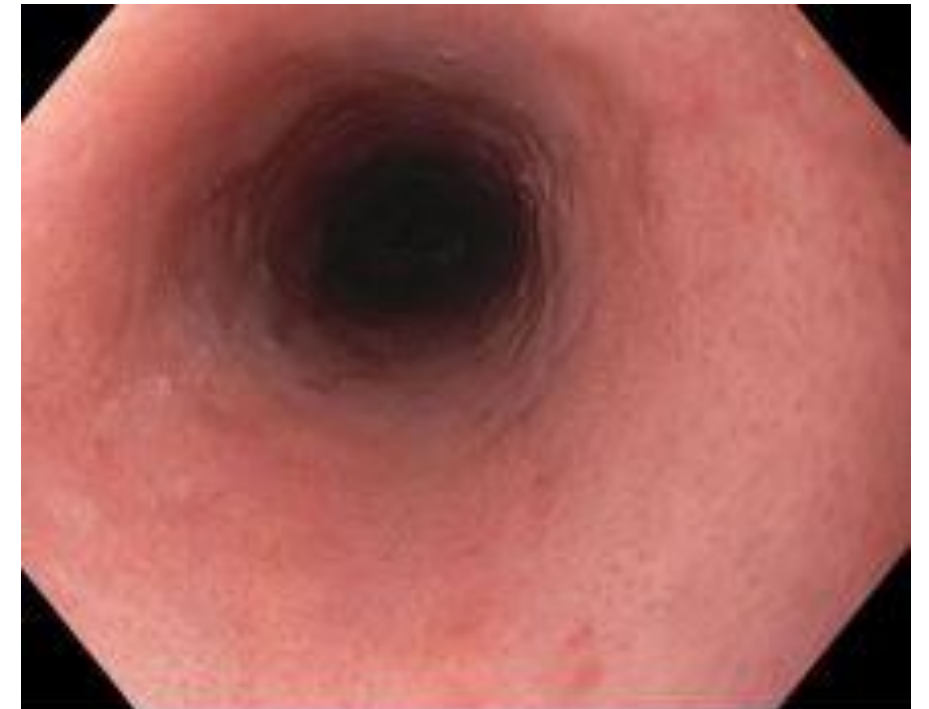
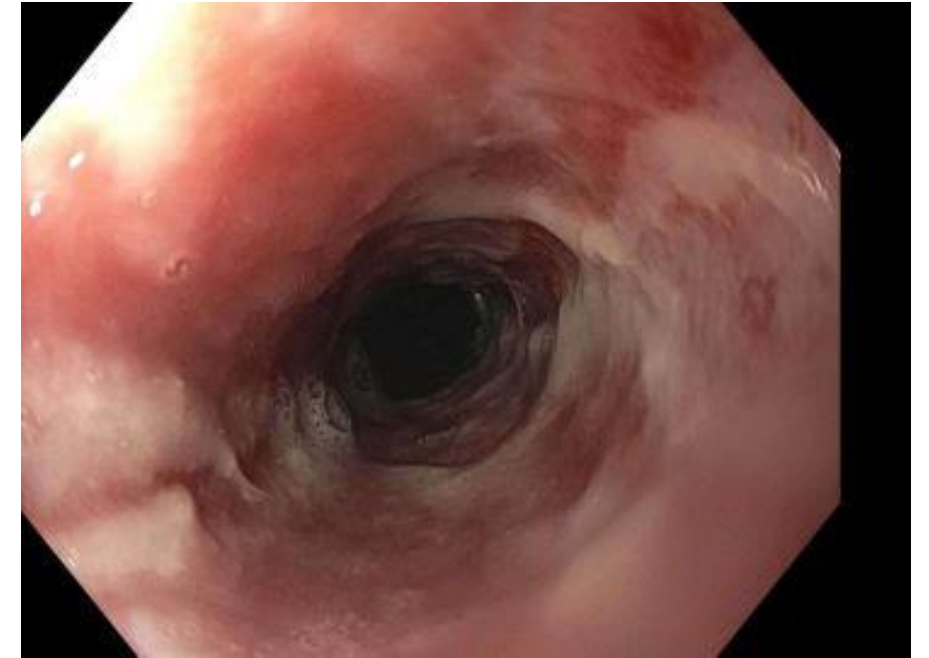
Lichen Planus: Clinical Features

- **0.2%-1.0% of population; first reported in 1982**
- **T-cell-mediated immune response to an induced antigenic change in the mucosa**
- **62% in one consecutive series had esophageal involvement**
 - Patients have lichen planus in other locations; most have oral involvement
- **Dysphagia (PPV 93%) but can be asymptomatic**
- **Mostly women (69%), mean age 55 (range, 27-74)**

Kern JS, Technau-Hafsi K, Schwacha H, et al. Esophageal involvement is frequent in lichen planus: study in 32 patients with suggestion of clinicopathologic diagnostic criteria and therapeutic implications. *Eur J Gastroenterol Hepatol.* 2016;28(12):1374-1382. doi:10.1097/MEG.0000000000000732

Lichen Planus: Endoscopy

- White, rough mucosal surface, sometimes lacy
- Denudation/sloughing
- Mucosal tears
- Stenosis or stricture
- No predilection for site



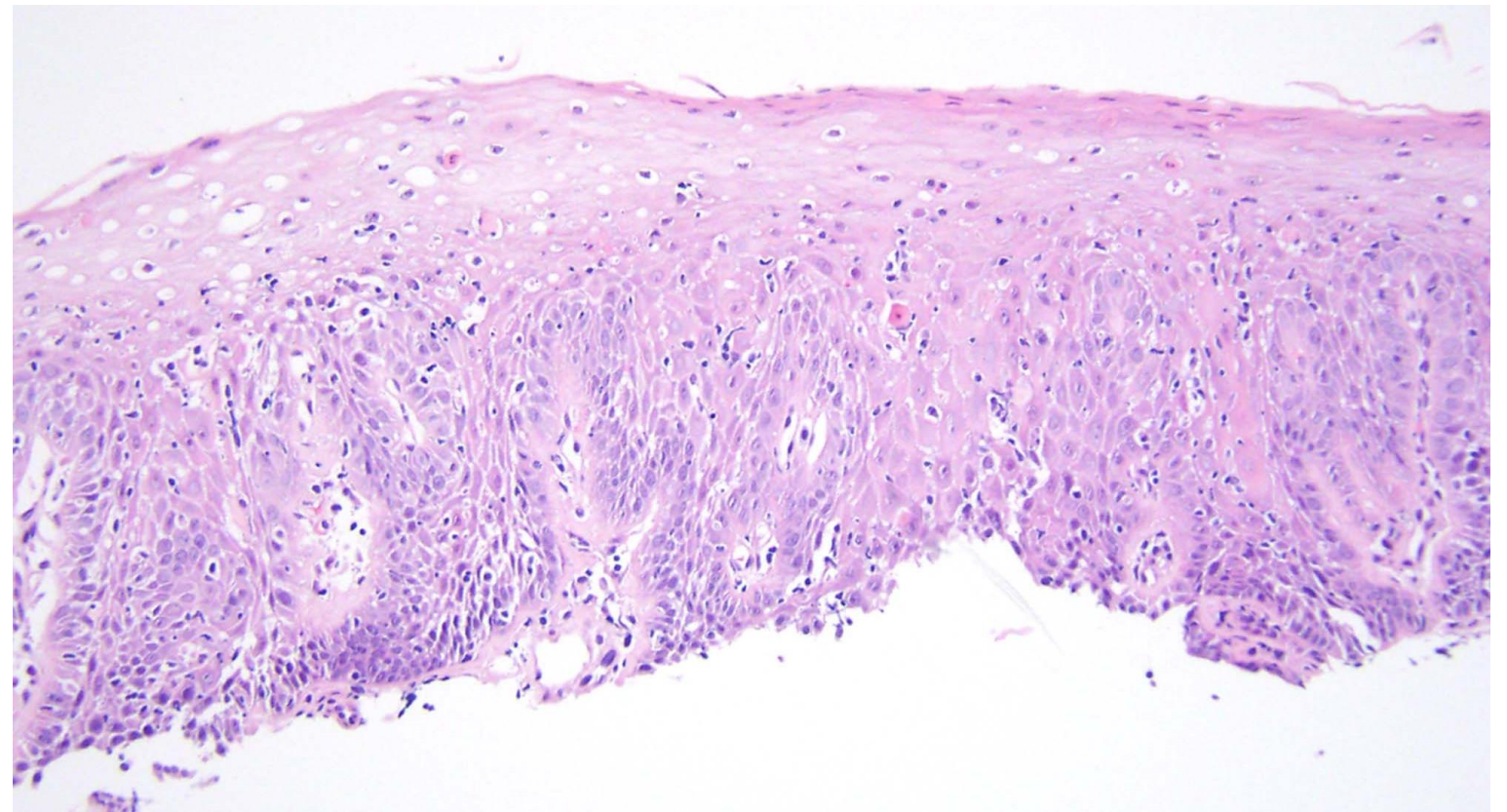
Lichen Planus of the Esophagus: When to Suspect

- Middle-aged to older woman with dysphagia or odynophagia
- Other erosive mucosal lesions
- Band-like lymphocytic infiltrate with Civatte bodies
- Esophageal stricture, especially in mid- or proximal esophagus
- Usually have oral lichen planus but may present with esophageal involvement

Consider using “lichenoid esophagitis pattern of injury” in patients not known to have lichen planus.

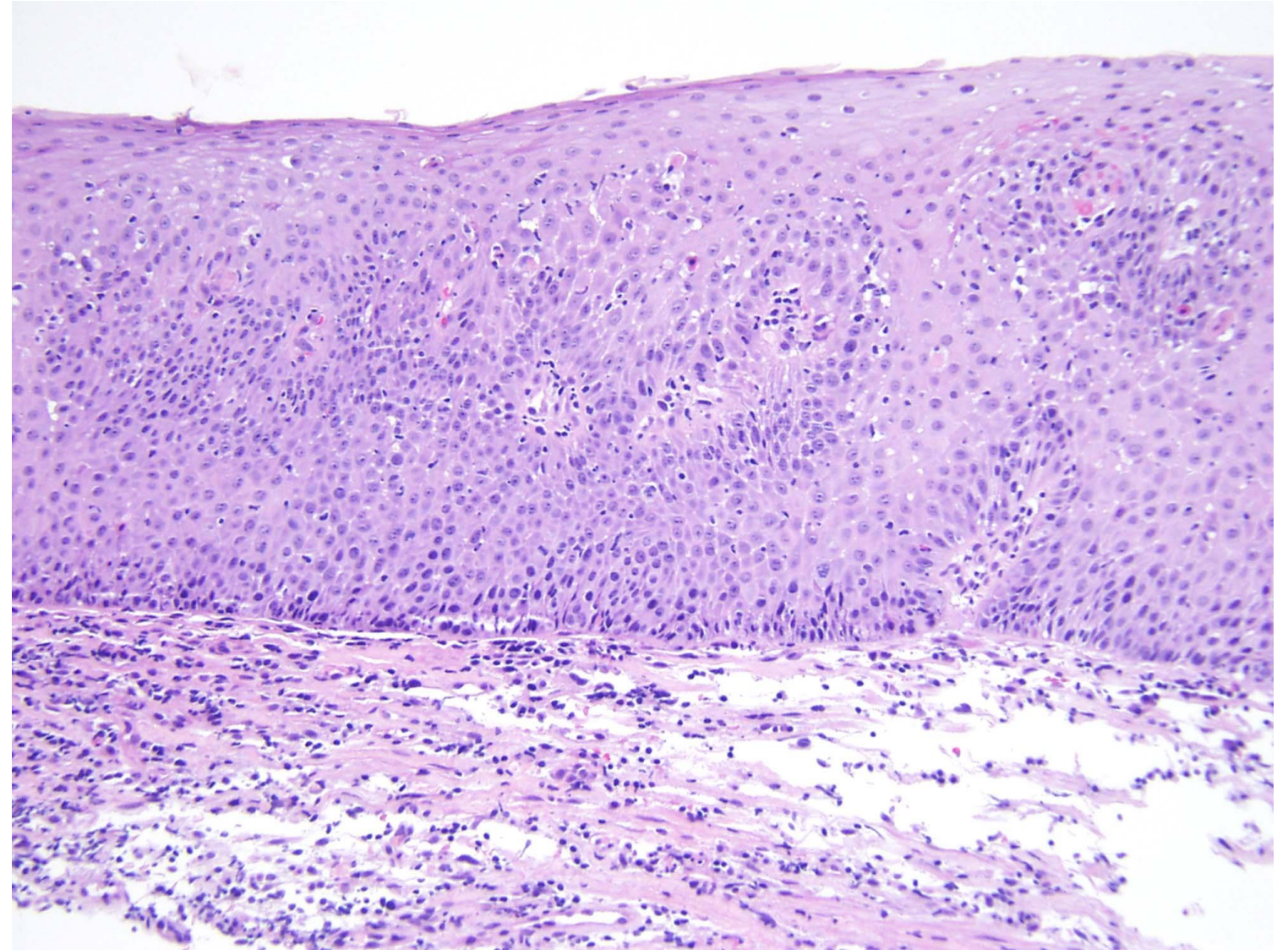
Lichen Planus: Histology

- Epithelial detachment (most important)
- Lymphocytic infiltrate – band-like, mostly CD3+ T-cells, some macrophages
- IgM deposition along the dermo-epidermal junction (direct immunofluorescence)
- Apoptotic/dykeratotic cells (Civatte bodies)
- Fibrosis of lamina propria
- Spongiosis

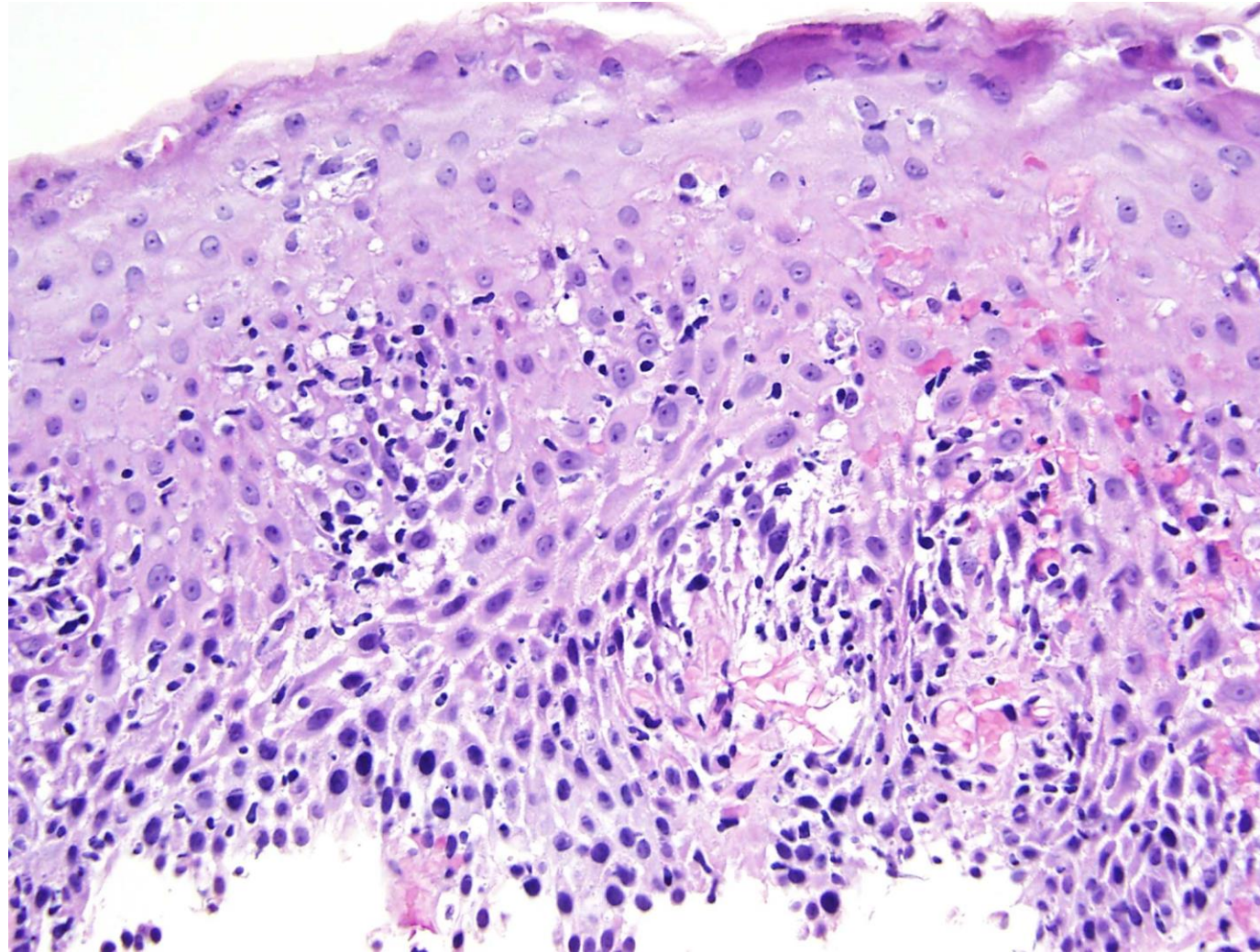


Lichen Planus: Histology, cont'd

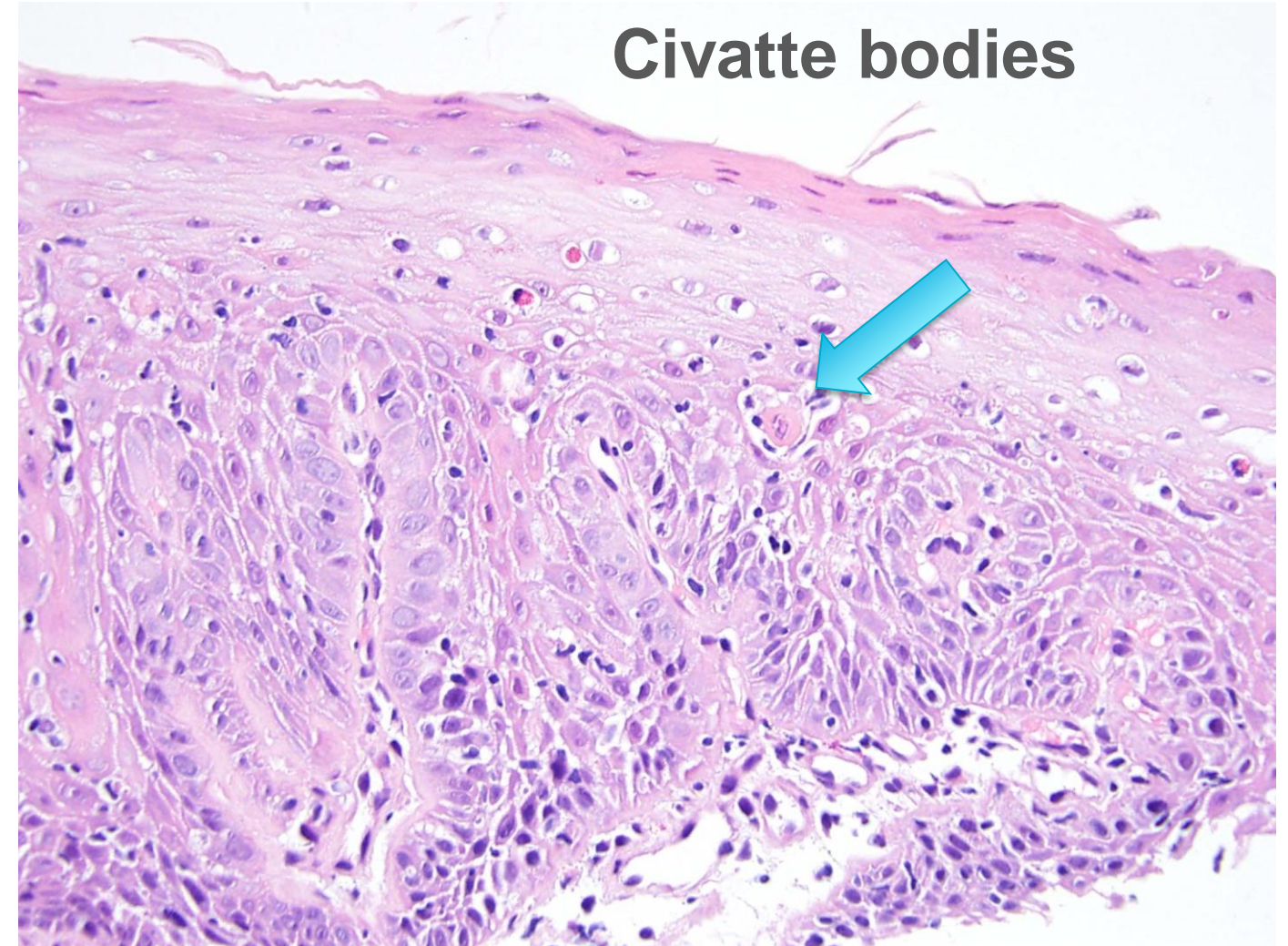
- Epithelial detachment
- Band-like lymphocytic infiltrate at junctional zone



Lichen Planus: Histology, cont'd

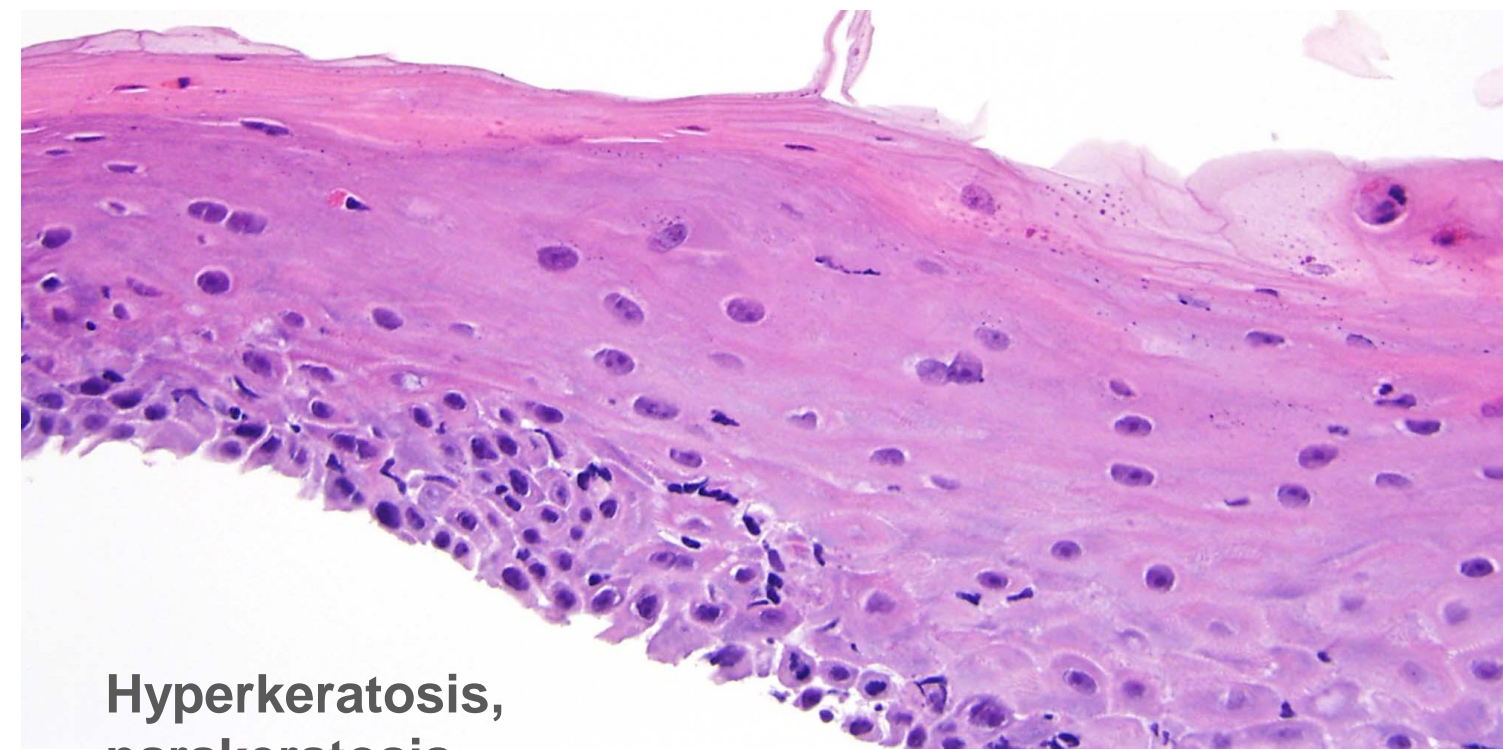


Spongiosis

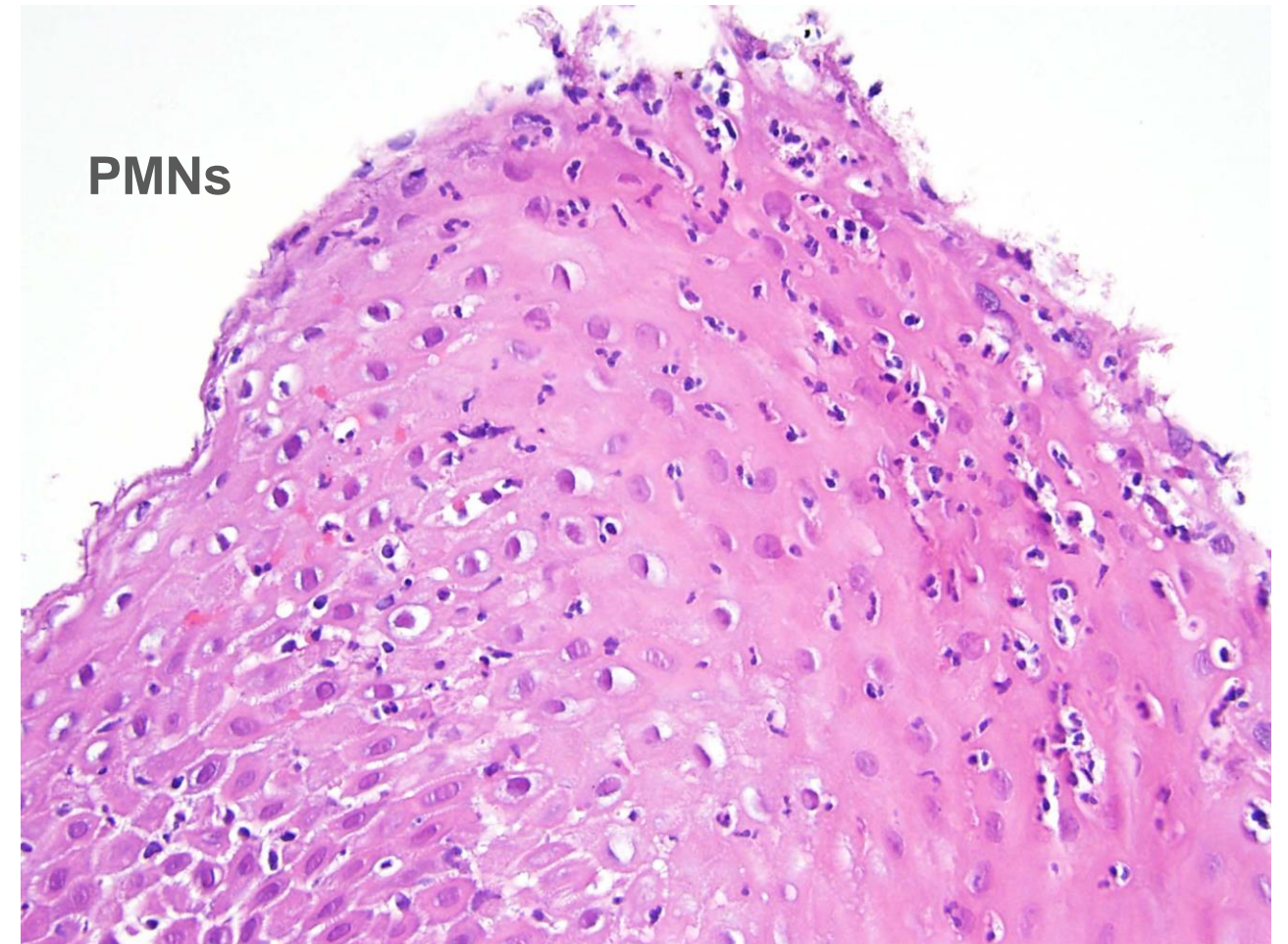


Civatte bodies

Lichen Planus: Histology, cont'd



Hyperkeratosis,
parakeratosis

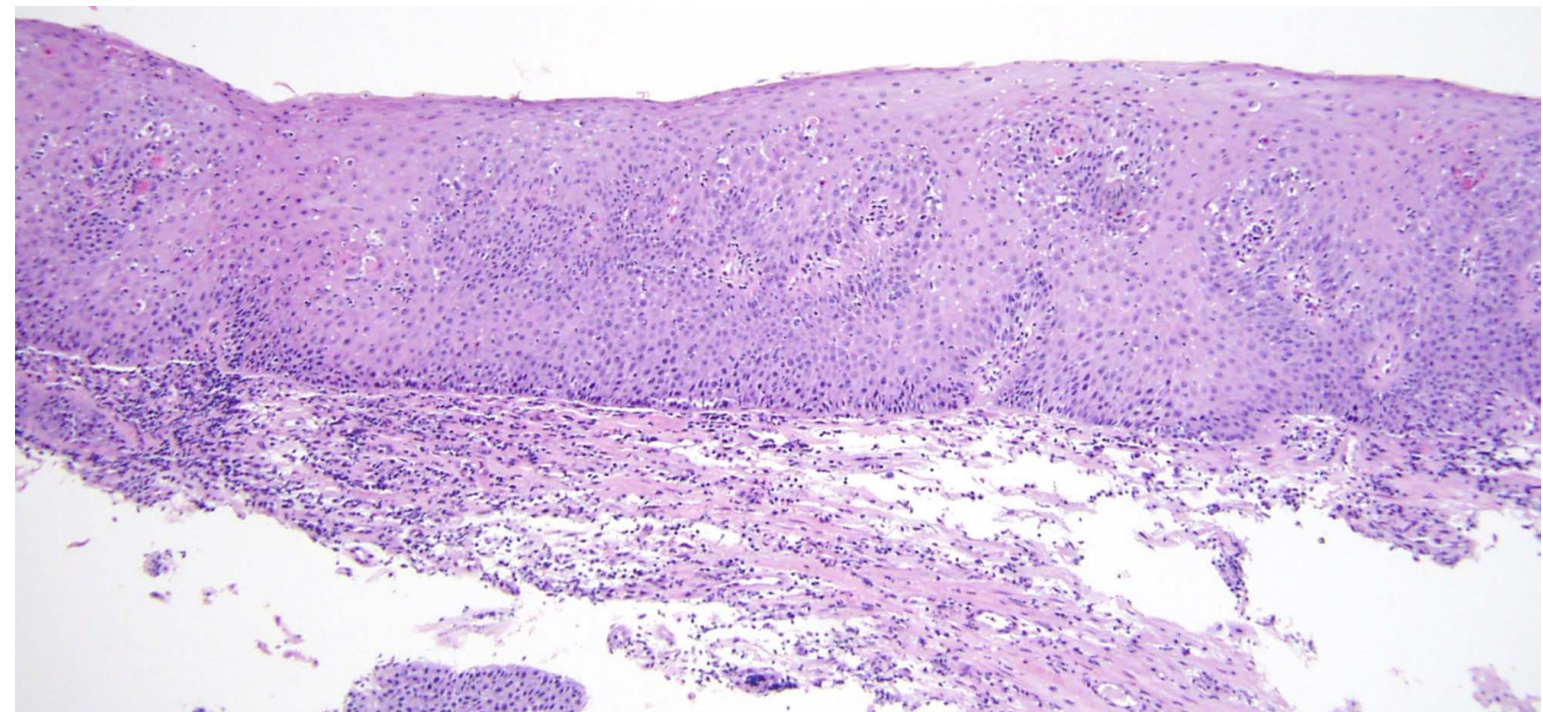
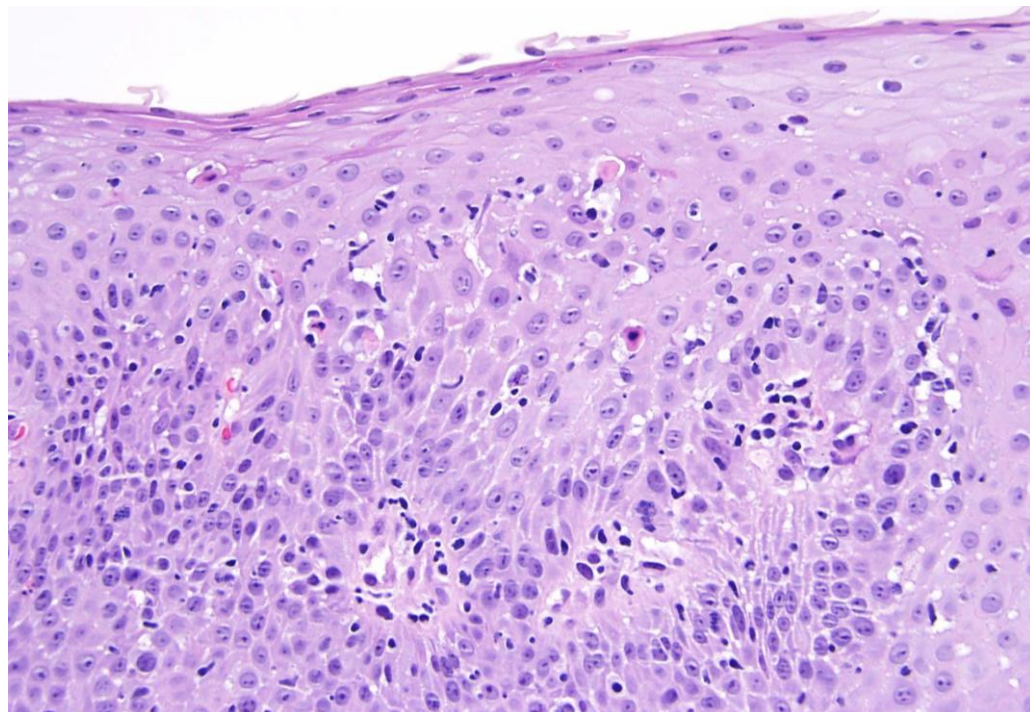


PMNs

Lichen Planus: Proposed Criteria

	Endoscopy	Histology	Direct IF
Proven	+	+	Not necessary
Proven	+	Suggestive	+
Probable	-	+	+
Probable	Suggestive	Suggestive	+

Kern JS, Technau-Hafsi K, Schwacha H, et al. Esophageal involvement is frequent in lichen planus: study in 32 patients with suggestion of clinicopathologic diagnostic criteria and therapeutic implications. *Eur J Gastroenterol Hepatol.* 2016;28(12):1374-1382. doi:10.1097/MEG.0000000000000732

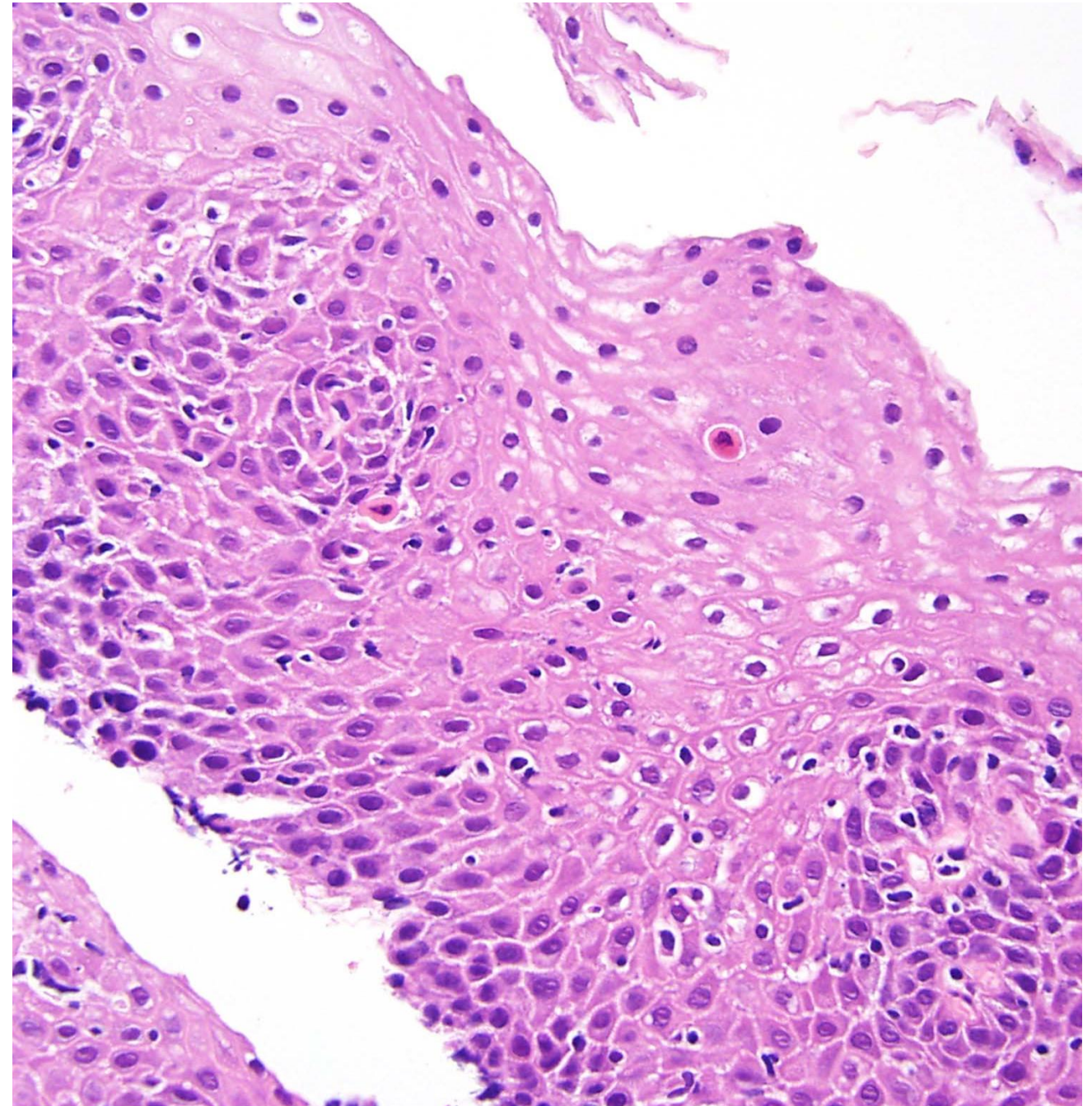


Lichen Planus: Differential Diagnosis

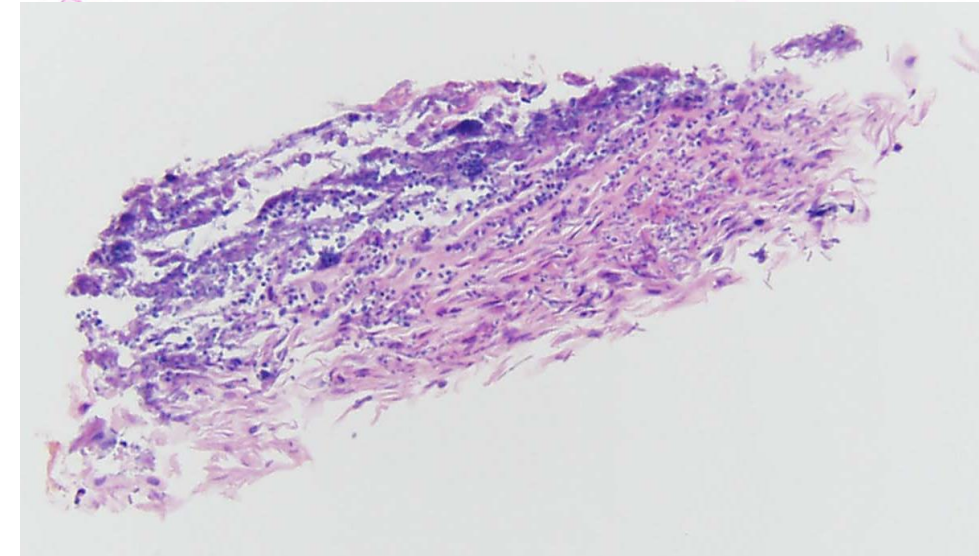
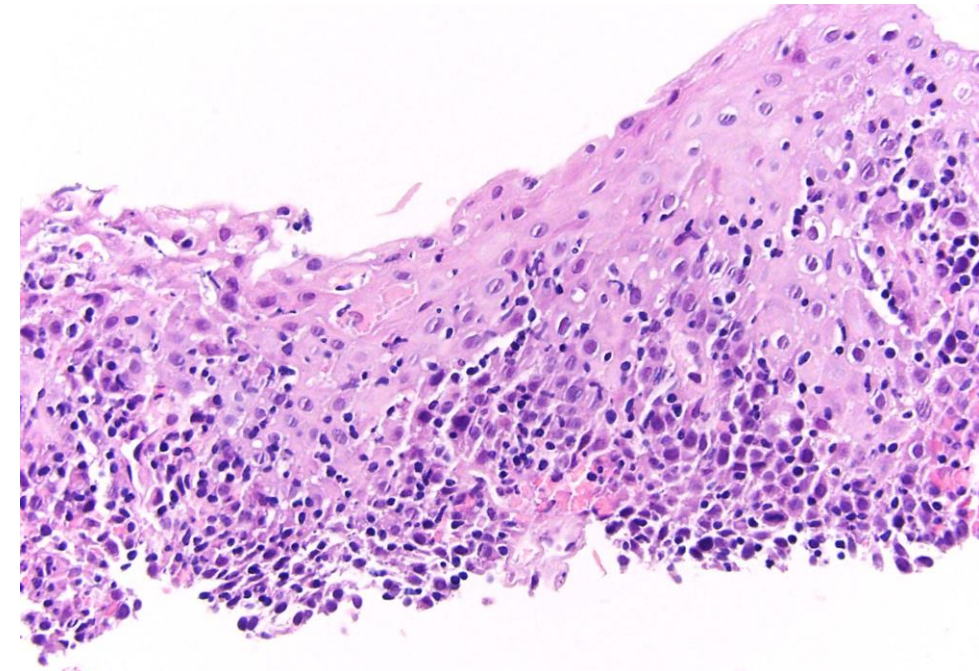
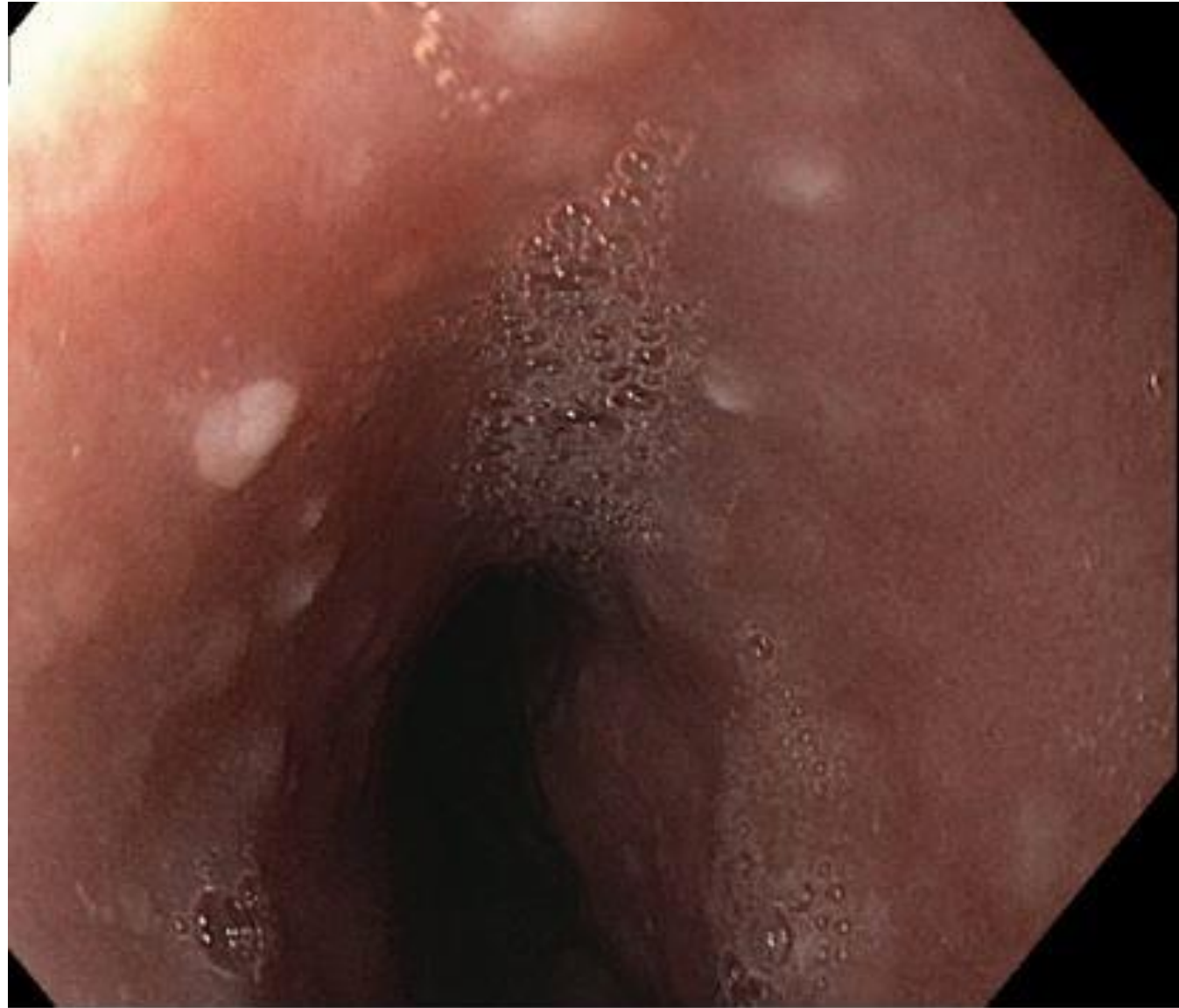
- **Lymphocytic esophagitis: no Civatte bodies**
- **Sloughing esophagitis (esophagitis dissecans superficialis): minimal inflammation**
- **Mucous membrane pemphigoid**
 - Skin lesions have different appearance
 - Inflammation is usually PMNs, eosinophils
 - IgA, IgG, or complement is deposited along the basement membrane
- **Pemphigus vulgaris**
 - Intraepithelial blisters
 - Test for circulating autoantibodies against desmosomal antigens

Lichenoid Esophagitis Pattern of Injury

- Patients without a diagnosis of lichen planus
- Histologically indistinguishable
- Polypharmacy
- Rheumatological diseases
- Viral infections
- Strictures more likely in patients with established lichen planus



Differential Diagnosis: *Candida*



Lichen Planus: Natural History and Treatment

- Goal is to avoid esophageal stenosis
- Topical steroids (swallowed fluticasone, budesonide) or prednisone
- Treatment for skin lesions – azathioprine, acitretin
- Strictures may need to be dilated
- ? Increased risk of squamous cell carcinoma; 8/132 patients in one series, mostly incident cancers

Ravi K, Codipilly DC, Sunjaya D, Fang H, Arora A, Katz D. Esophageal Lichen Planus Is Associated With a Significant Increase in Risk of Squamous Cell Carcinoma. *Clin Gastroenterol Hepatol*. 2019;17(9):1902-1903.e1. doi:10.1016/j.cgh.2018.10.018

Lymphocytes in the Esophagus

- **Lichen planus**
- **Lymphocytic esophagitis**
- **Reflux esophagitis**

Lymphocytic Esophagitis

- First described in 2006
- Poorly characterized, with no consensus definition
- Reportedly more common in older women (but this doesn't hold up on systematic review)
- Children with Crohn's disease
- Endoscopic findings may mimic eosinophilic esophagitis (1/3)

Is it a unique entity or a form of GERD?

Overlapping features with lichenoid esophagitis

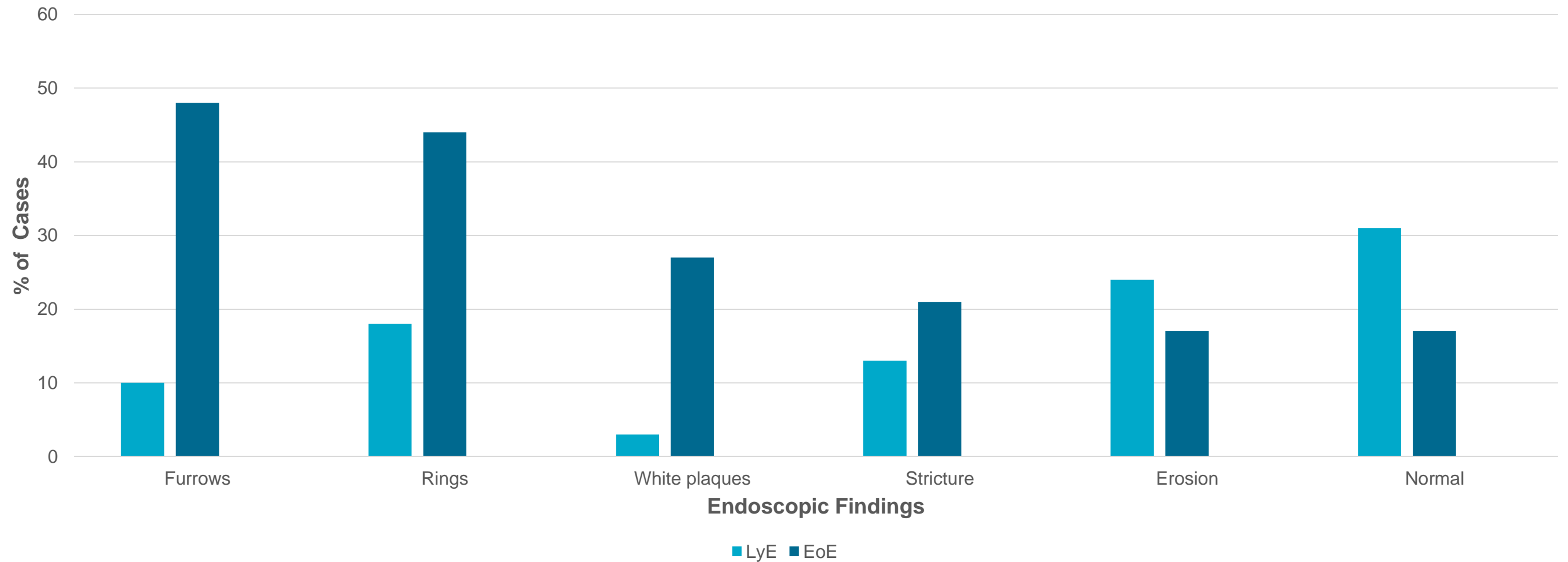
Lymphocytic Esophagitis, cont'd

- Prevalence estimated as 0.1% in adults, 5.7% in children
- 8.6% in adults with food bolus impaction
- Dysmotility – achalasia (67%), nutcracker esophagus (40%), diffuse esophageal spasm (20%)
 - Mucosal irritation secondary to luminal stasis?
 - CD4+ cells rather than CD8+
- GERD – lymphocyte-rich esophagitis at GEJ may be related to reflux
- Prudent not to diagnose LyE on distal esophageal biopsy alone

Lymphocytic Esophagitis: Endoscopy



Endoscopic Findings in Lymphocytic and Eosinophilic Esophagitis

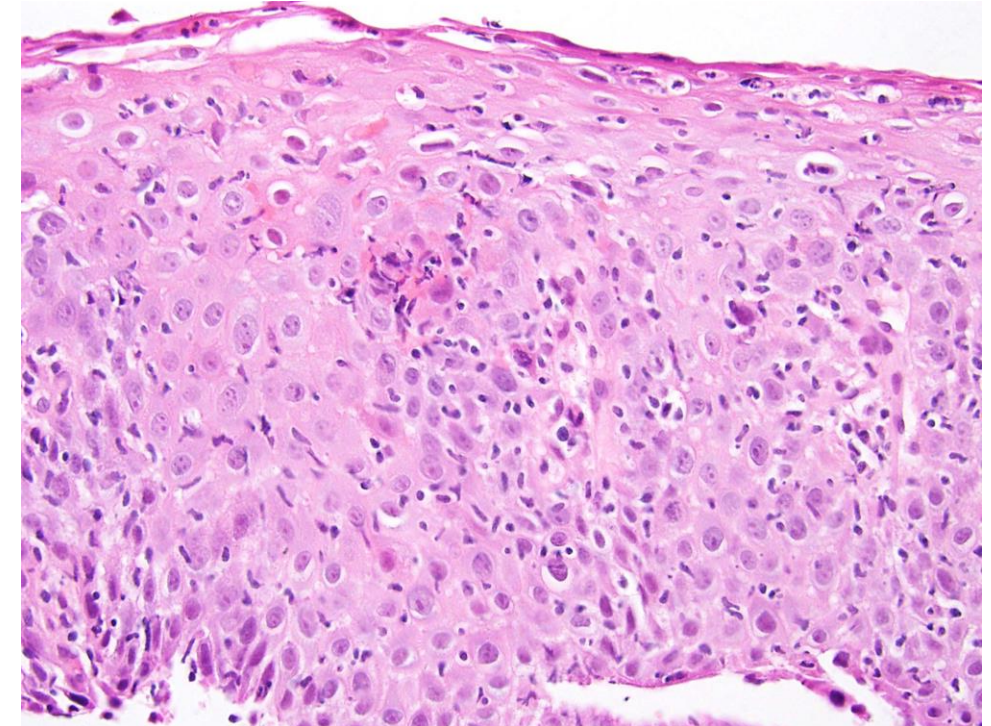
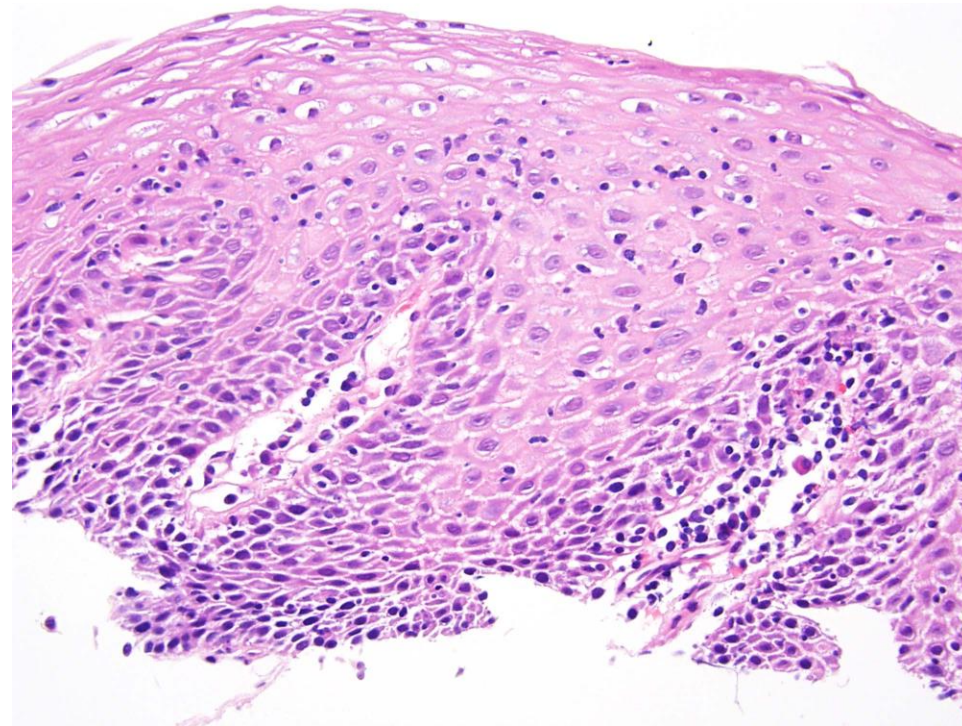
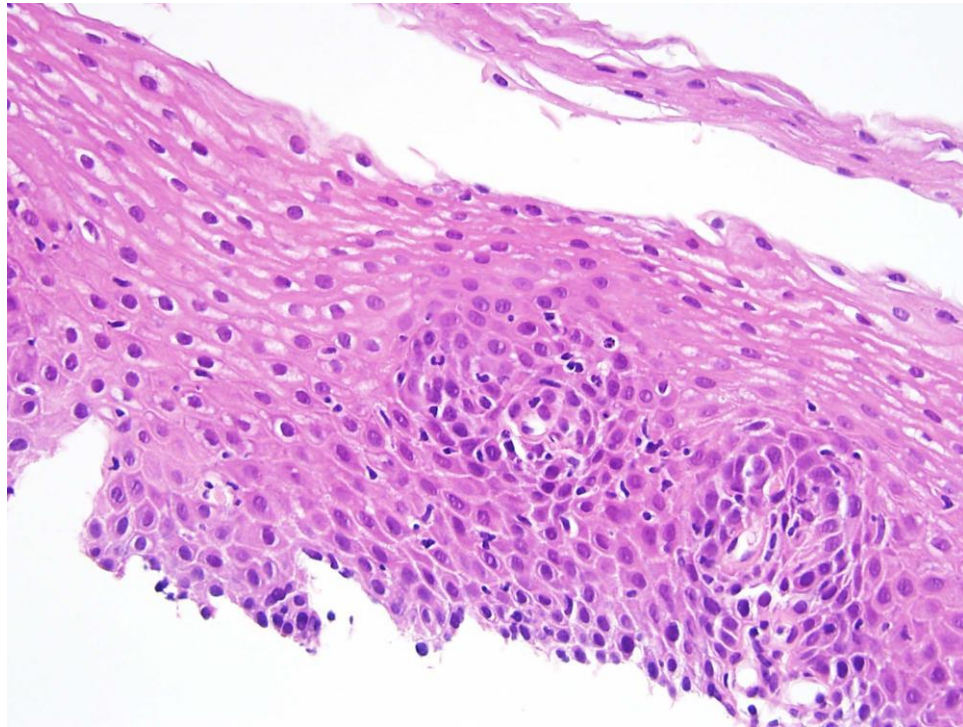


Lymphocytic Esophagitis: Histology

- Defined as increased intraepithelial lymphocytes (IELs)
- Threshold number varies among studies (≤ 10 to >100 per hpf); most commonly, >20 IELs per hpf
- No intraepithelial PMNs in some but not all studies
- No eosinophils
- IELs are predominantly peripapillary
- Spongiosis, usually severe

Caveat: Most studies rated as “poor” on systematic review – failed to control for age, sex, etc.

Lymphocytic Esophagitis: Histology



Natural History

- Understanding is hampered by low prevalence
- Mostly treated with proton pump inhibitors
- Lymphocytes and symptoms may persist or improve without therapy
- Anecdotal chronic but benign course

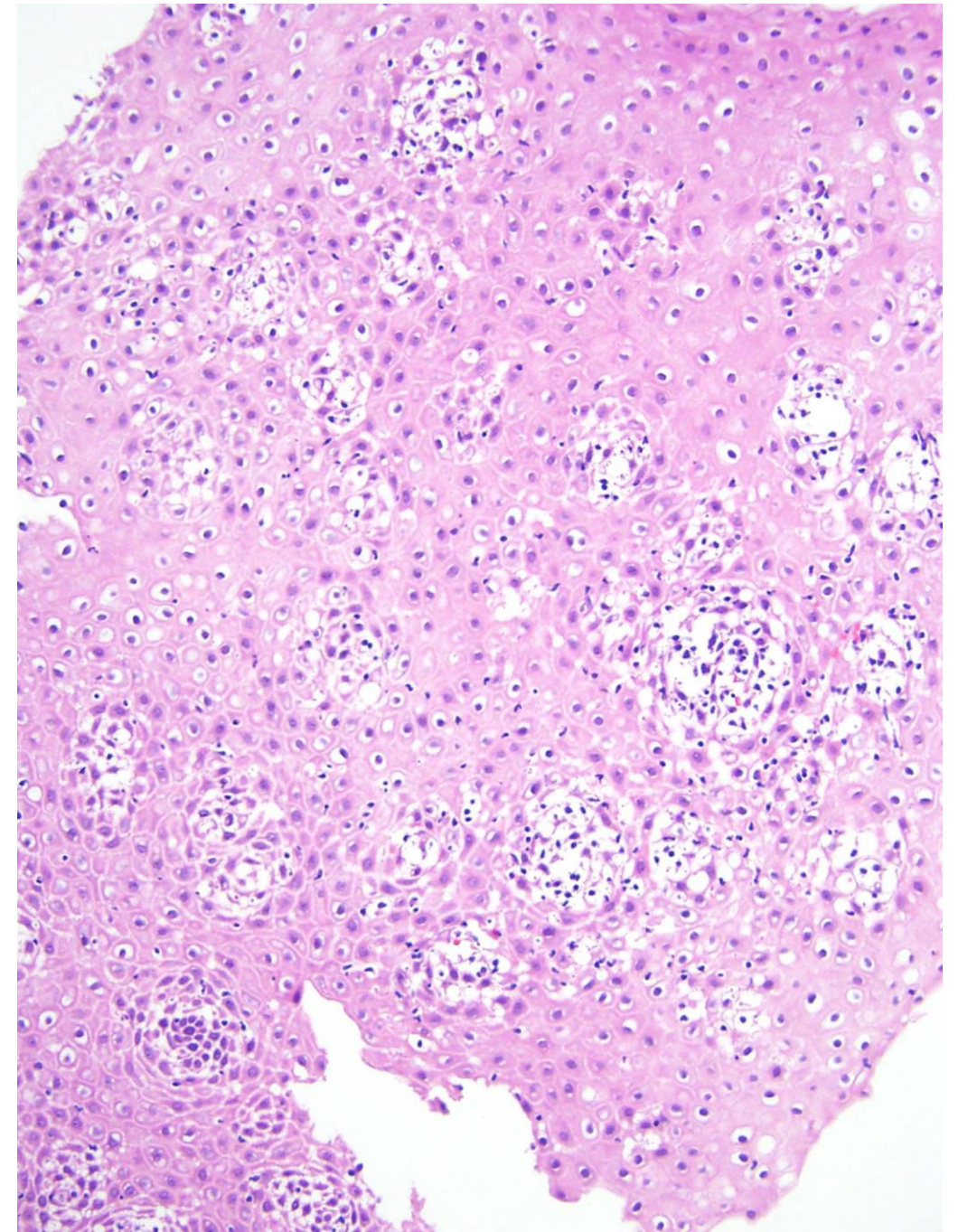
- Reporting: Some recommend using “lymphocytic esophagitis pattern of injury”; others “lymphocyte-predominant esophagitis”

Lymphocytic Esophagitis

- **Lack of consensus histologic definition is problematic**
- **Many studies don't specify biopsy location**
- **LyE has distinctive endoscopic abnormalities compared to GERD but not EoE, distinction from EoE is histologic**
- **Clinical significance is diluted by nonspecificity of findings (infection, Crohn's disease, dysmotility)**
- **Cannot be categorized as a specific disease: no well-defined etiology, characteristic endoscopy, or standard therapy**

Lymphocytic Esophagitis: Varied Approaches to Diagnosis

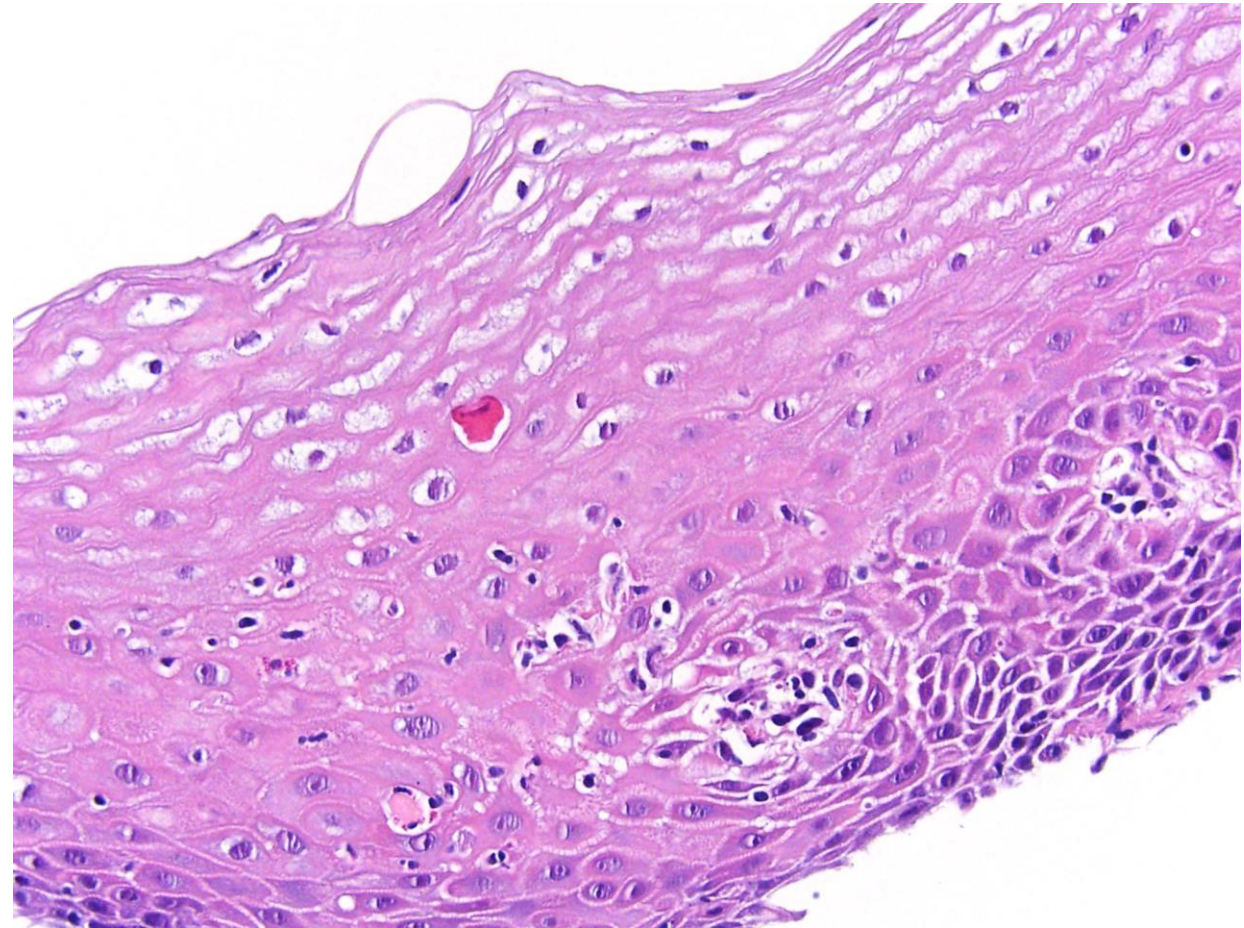
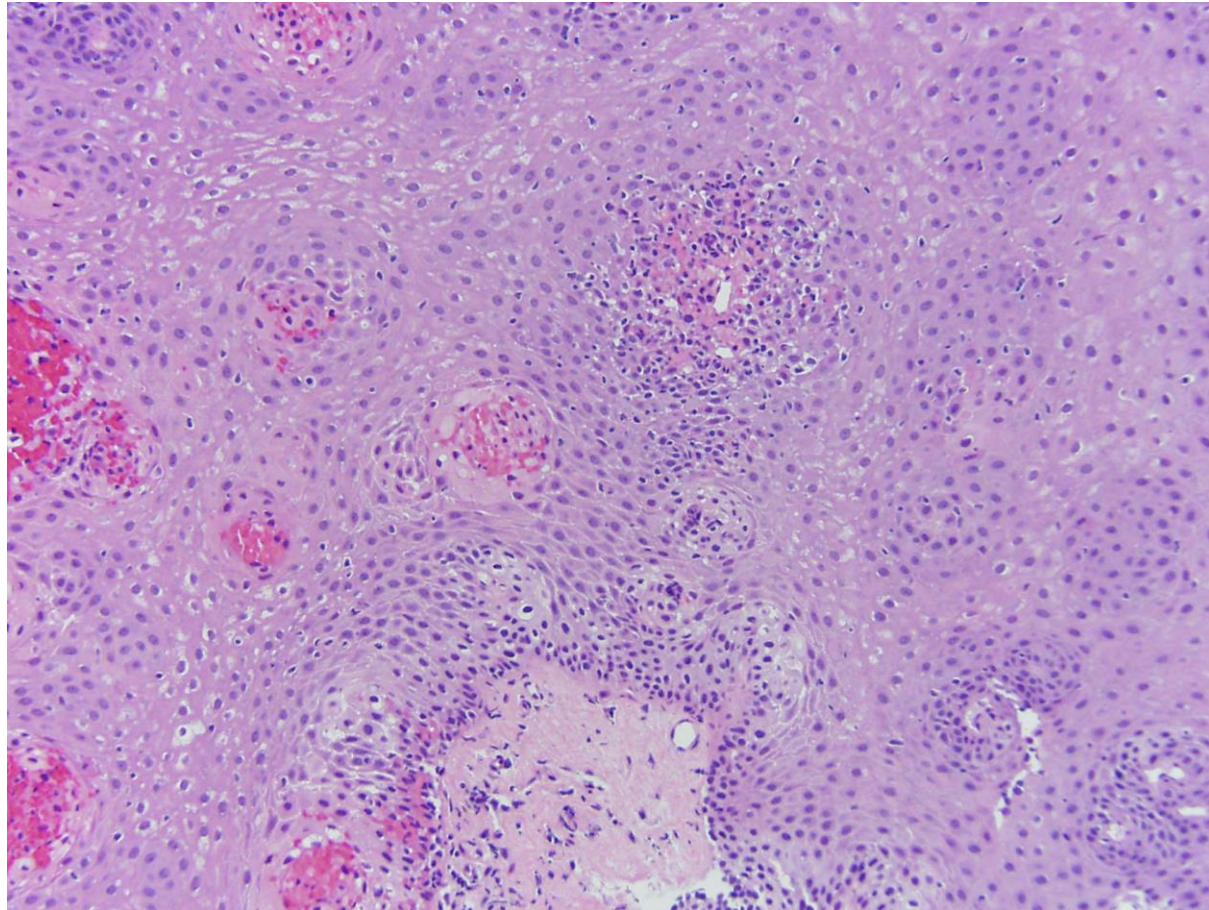
- Still “a condition in search of a disease”?
- Combination of dysphagia plus normal endoscopy plus lymphocytes with no eosinophils
- Density of infiltrate – some call even a single peripapillary lymphoid infiltrate LyE
- Some avoid setting a threshold, emphasizing peripapillary location and edema
- IELs in GERD are CD8+, those in dysmotility CD4+



Lymphocytic Esophagitis: A Practical Approach?

- No need to count lymphocytes – no consensus agreement and the clinical need is not established. Normal number probably variable.
- Some studies required increased IELs **and** evidence of mucosal injury not limited to GEJ.
- When defined in this way, most patients with LyE are women with immune-mediated disorders.

Other Considerations: Crohn's Disease



Corrosive and Contact Injuries

- **Pill esophagitis**
- **Esophagitis dissecans superficialis (sloughing esophagitis)**
- **“Black esophagus”**

Pill Esophagitis

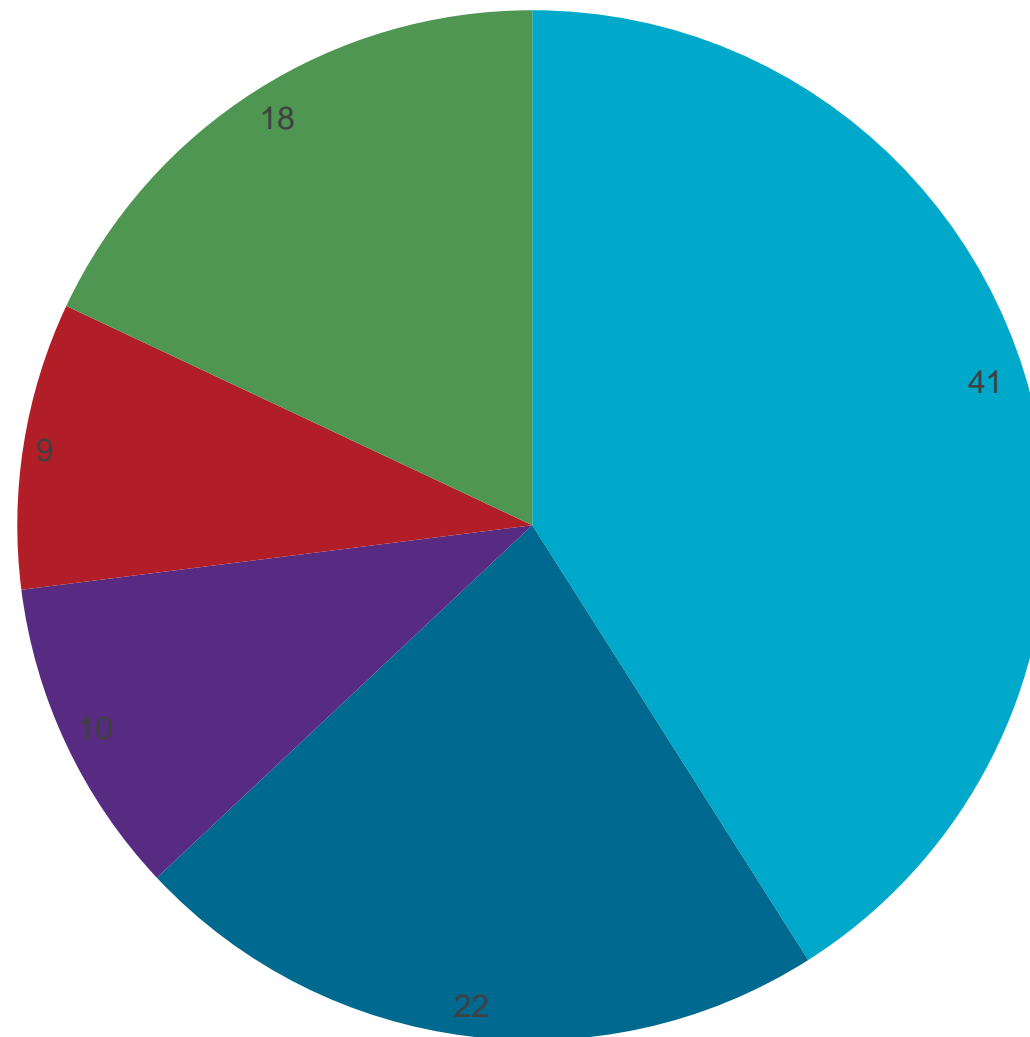
- **Symptoms:**
 - **Odynophagia**, dysphagia, vomiting
 - Hematemesis (rare, associated with NSAIDs)
- **Associations:**
 - Advanced age
 - Female > male
 - Diabetes, ischemic heart disease
- **Endoscopy:**
 - Erythema (83%)
 - Erosions (58%) and ulcers (26%)
 - Stricture (9%)

Pill Esophagitis: Mechanisms of Injury

- **Pill remains in esophagus – large pills, sticky gelcaps**
- **Release of contents**
- **Usually involves the middle portion of the esophagus because of compression by the aortic arch**
- **Sustained release pills may be more injurious than standard preparations**
- **Direct caustic injury: KCl, quinidine**
- **Acid burns: tetracycline, ferrous sulfate, ascorbic acid**



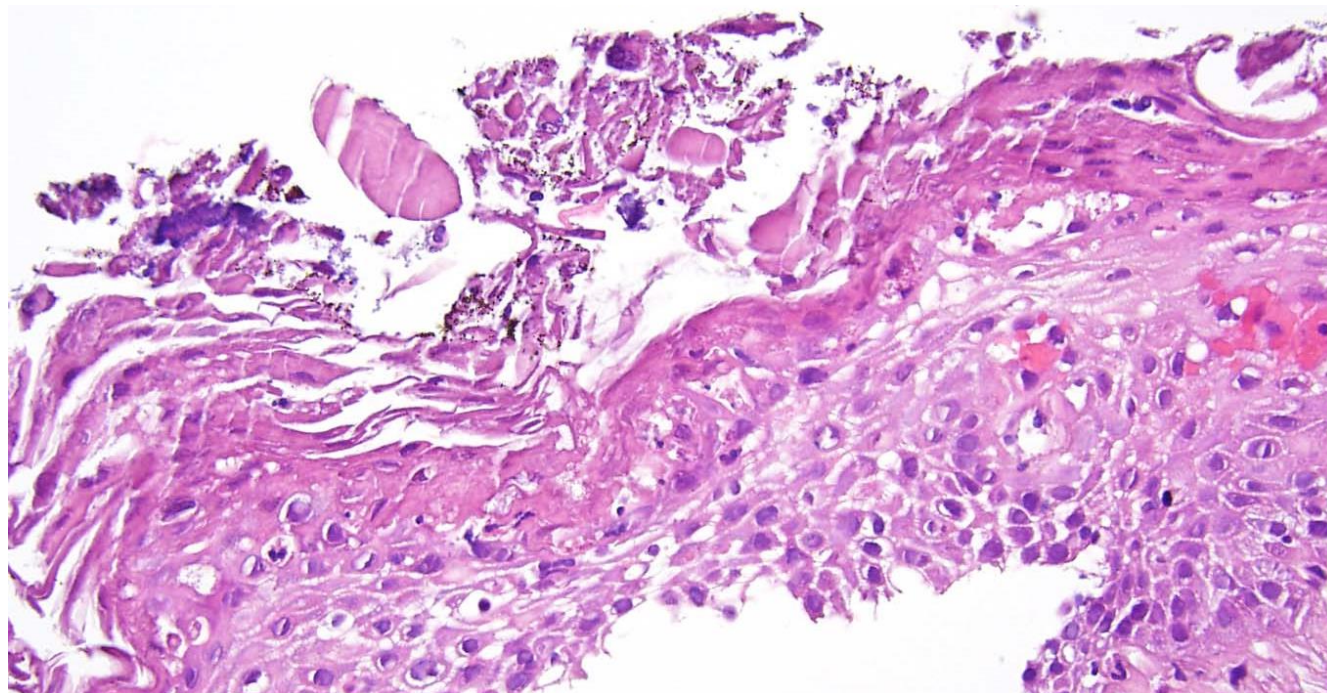
Culprit Medications: NSAIDs are Major Offenders



■ NSAIDs ■ Tetracyclines ■ KCl ■ Alendronate ■ Other

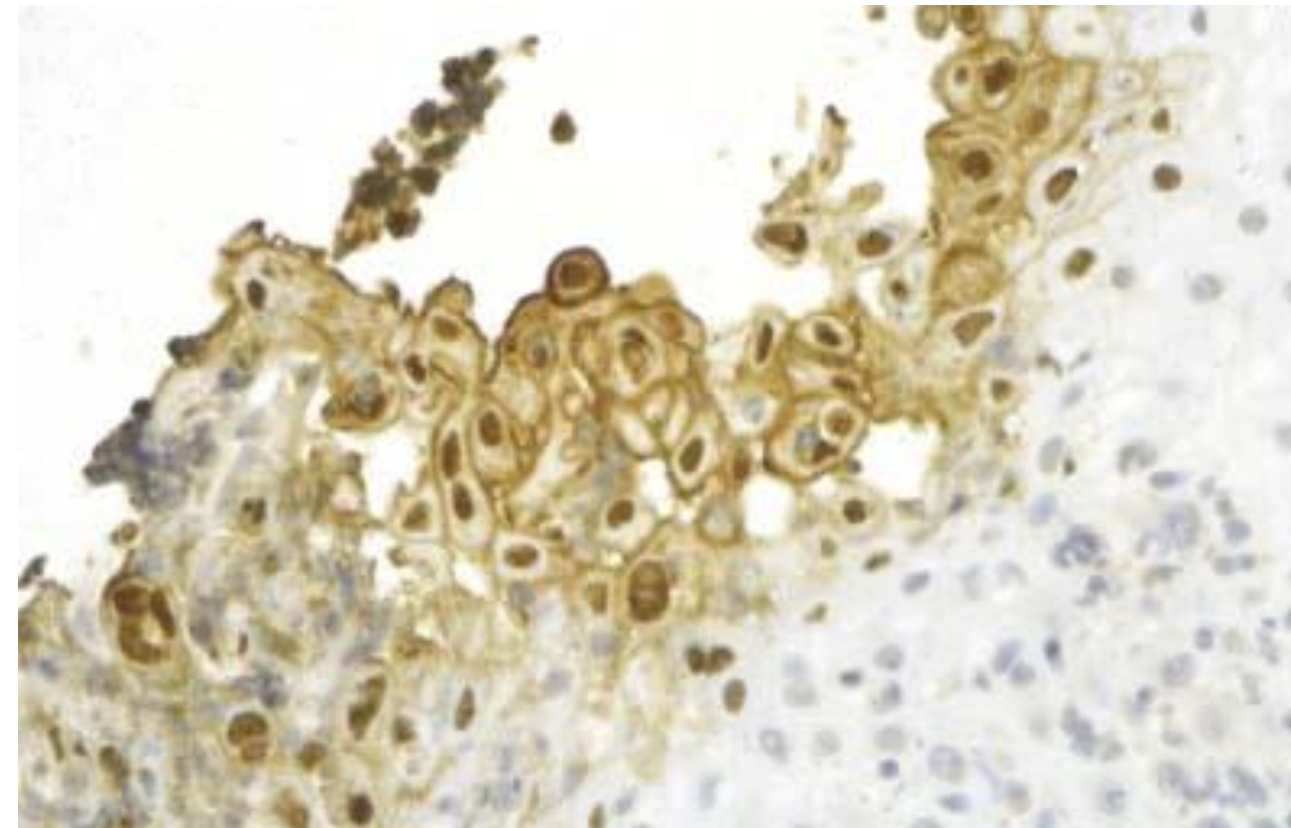
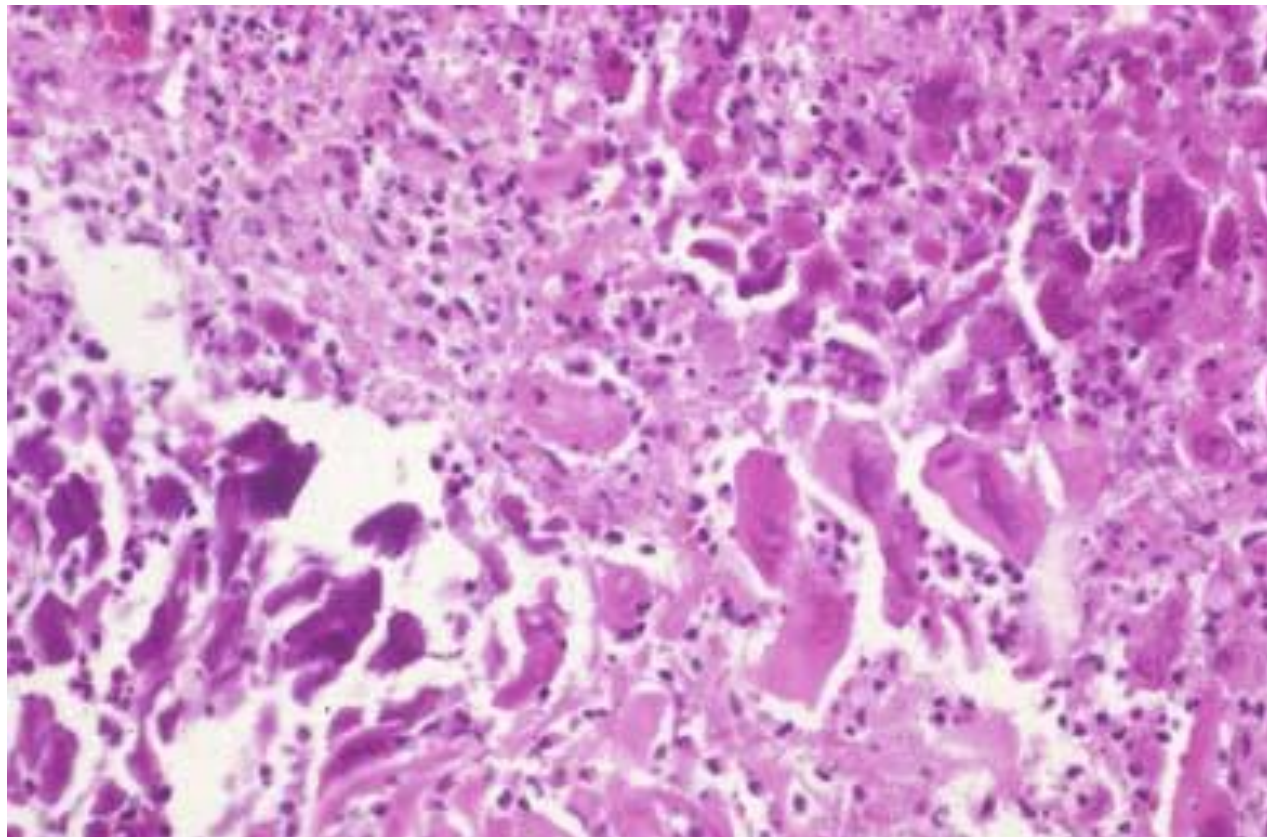
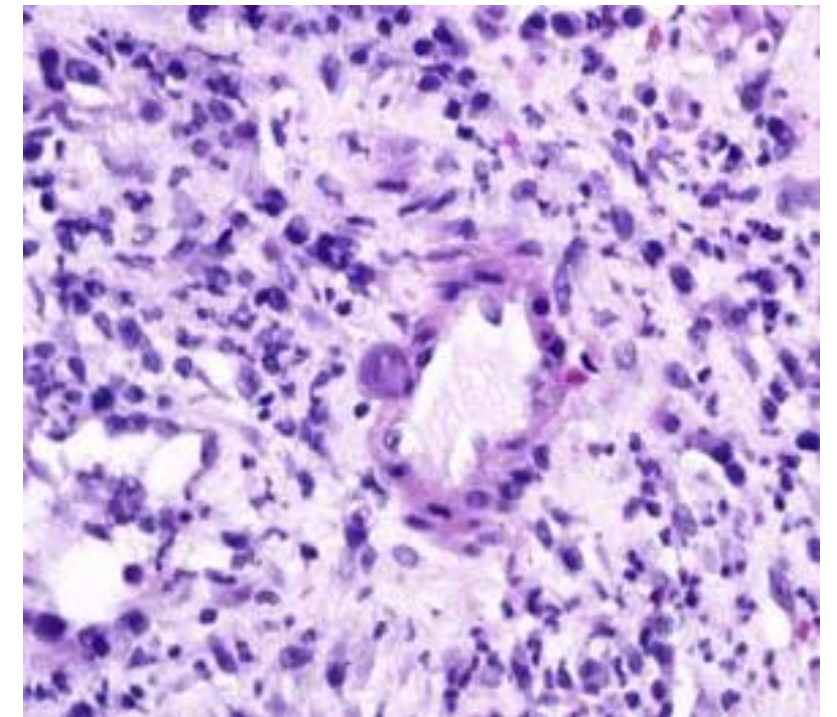
Abid S, Mumtaz K, Jafri W, et al. Pill-induced esophageal injury: endoscopic features and clinical outcomes. *Endoscopy*. 2005;37(8):740-744. doi:10.1055/s-2005-870129

Drug	Endoscopy	Histology
Alendronate	Ulcers, stricture, sloughing	Exudate; translucent polarizable crystals (60%); multinucleated giant cells; esophagitis dissecans superficialis
Ferrous sulfate	Erosion, sloughing	Brown crystals in sloughed epithelium
Tetracyclines	Ulcers, mid- or distal esophagus	Ulcer, granulation tissue, acute inflammation Secondary <i>Candida</i> esophagitis
NSAIDs	Ulcers, mid- or distal esophagus	Ulcer, granulation tissue, acute inflammation.



Erosions and Ulcers: Differential Diagnosis

- Reflux: typical changes in intact mucosa
- Viral esophagitis: CMV, HSV inclusions
- Pill: fragments of pills, location in mid-esophagus

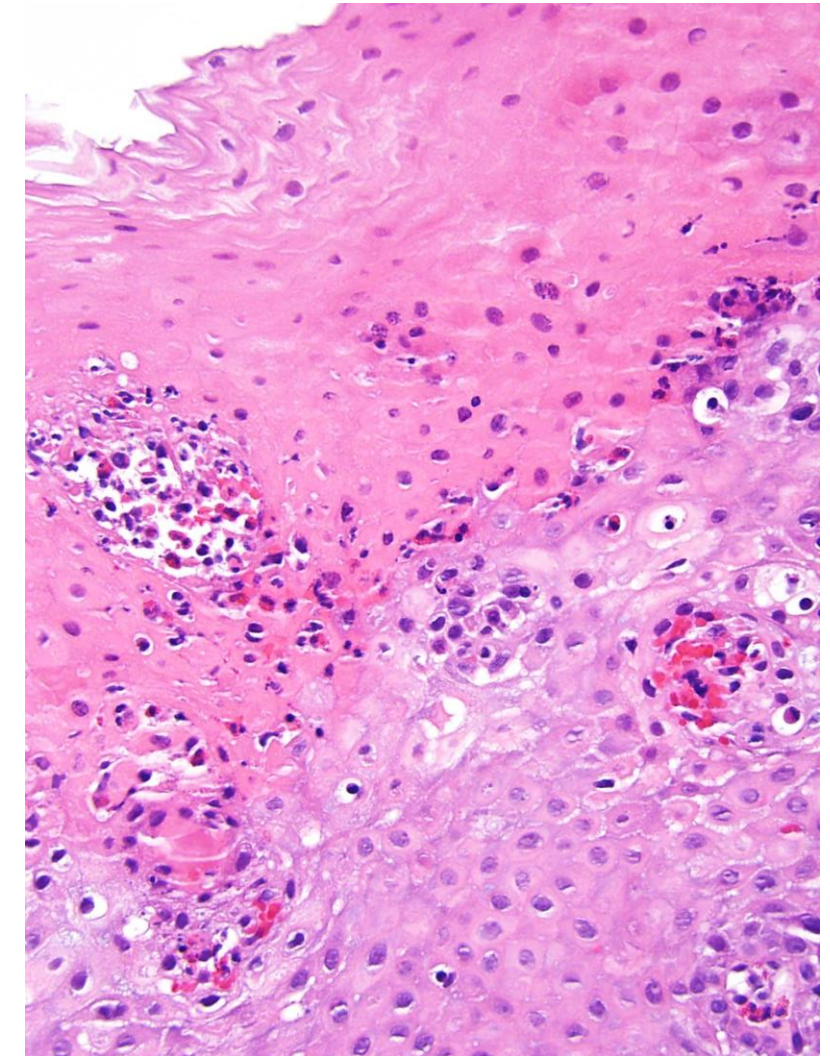


Corrosive and Contact Injuries

- **Pill esophagitis**
- **Esophagitis dissecans superficialis (sloughing esophagitis)**
- **“Black esophagus”**

Esophagitis Dissecans Superficialis

- Degeneration of squamous epithelium
- No inflammation
- Superficial necrotic zone detaches from deep viable zone
- Older patients 65 years (range 52-76)



Esophagitis Dissecans Superficialis: Clinical

- **No consistent clinical association – drugs in some instances**
- **Early reports were in men with debilitating illnesses (VA series) but in largest series, female preponderance (63%)**
- **Can be found incidentally or present with esophageal symptoms: dysphagia, heartburn**
- **Rare cases associated with blistering diseases such as bullous pemphigoid**
- **Rapid healing – eight weeks without complications**

Esophagitis Dissecans Superficialis: Pathogenesis

- **Acute injury?**
- **Associated with lots of different drugs, not necessarily aspirin and NSAIDs**
- **Selective serotonin reuptake inhibitors (SSRIs) in one study (73%); PPIs not protective**
- **Mechanism of injury is not apparent – no unifying hypothesis**
- **Underreported, so difficult to establish unbiased associations**

Esophagitis Dissecans Superficialis: Endoscopy

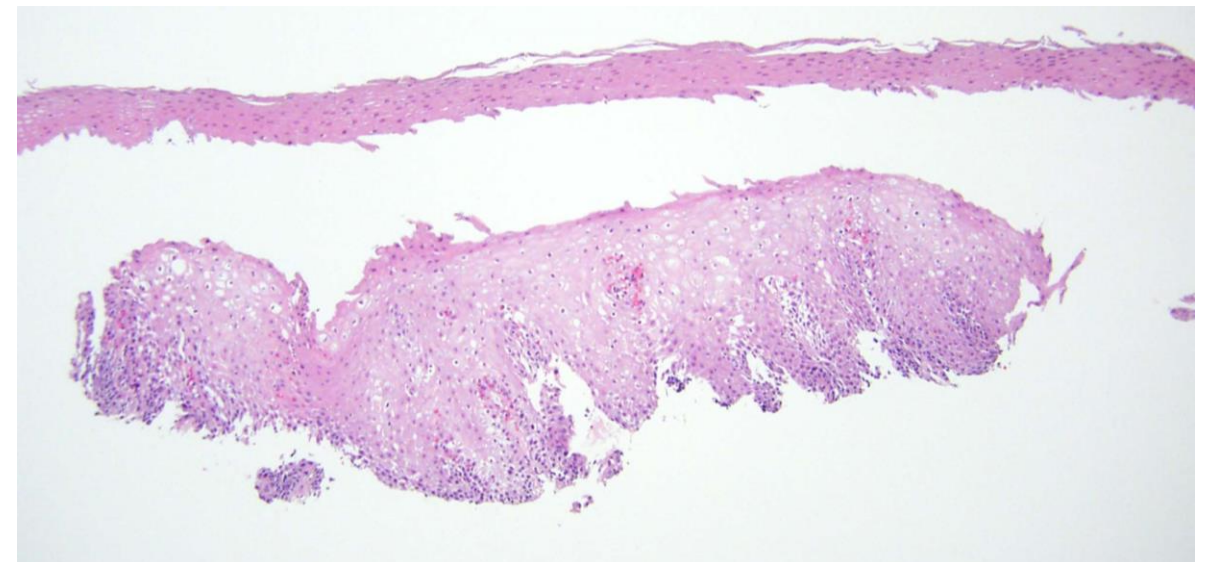
- Linear breaks with vertical strips of mucosal sloughing
- More common in distal esophagus
- May mimic or coexist with *Candida* esophagitis (typical white exudates)
- Detached mucosa peels away; underlying mucosa is normal
- No Barrett's esophagus
- Biopsy not necessary in classic cases



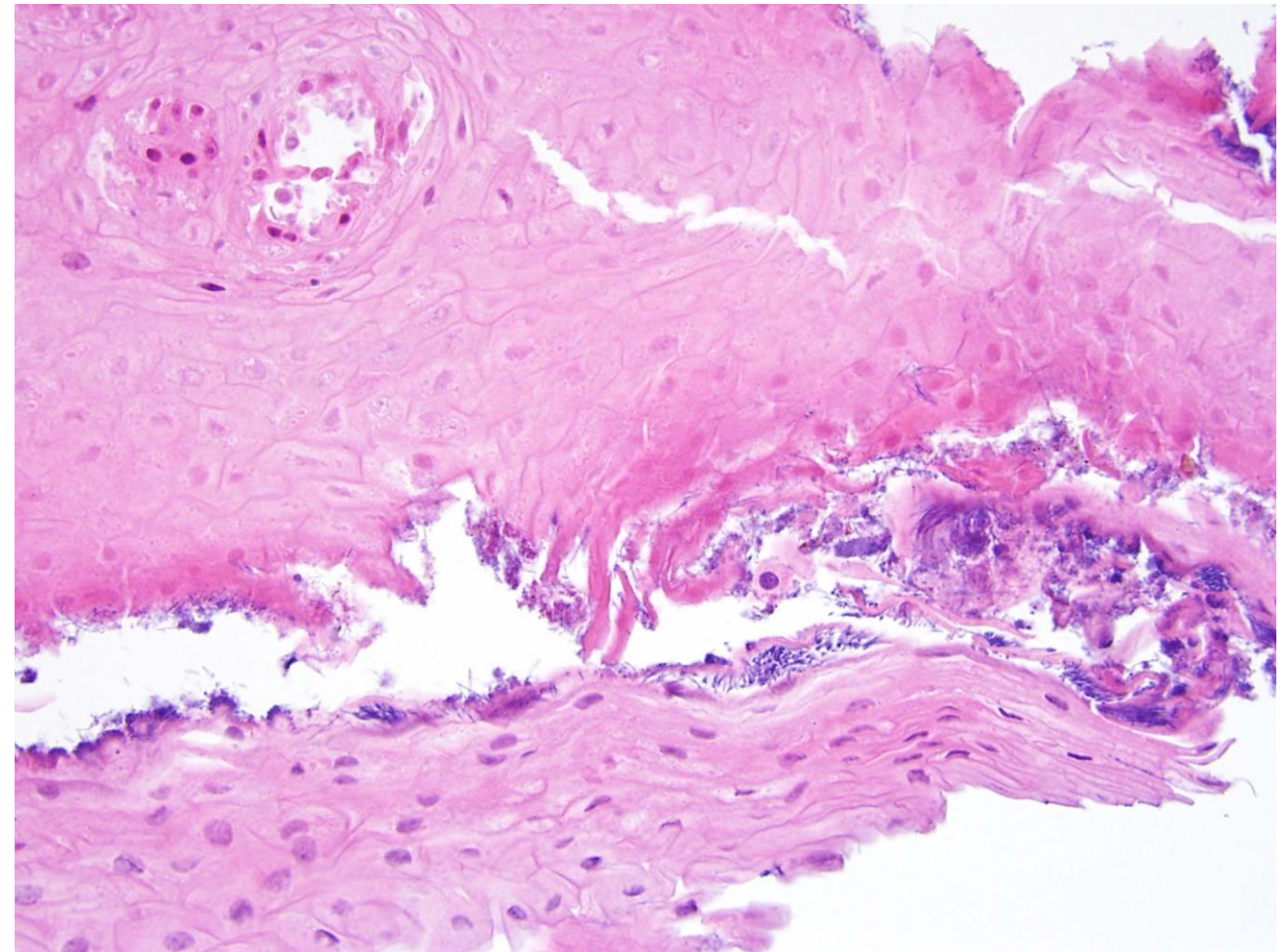
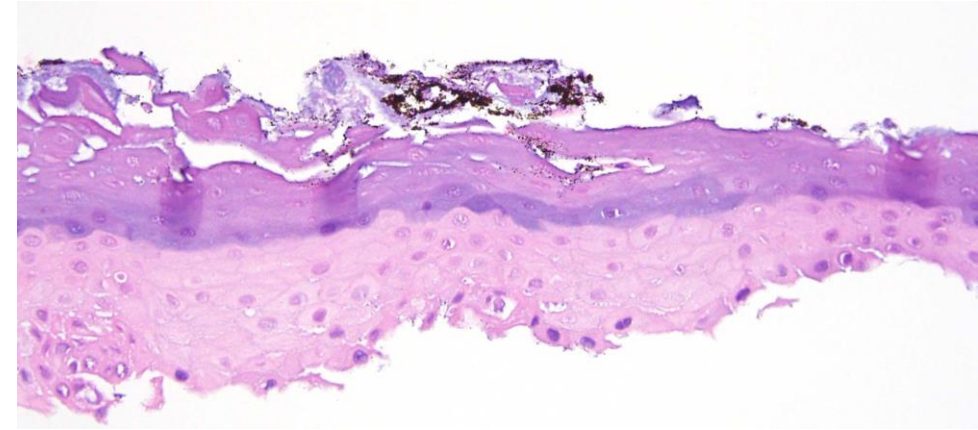
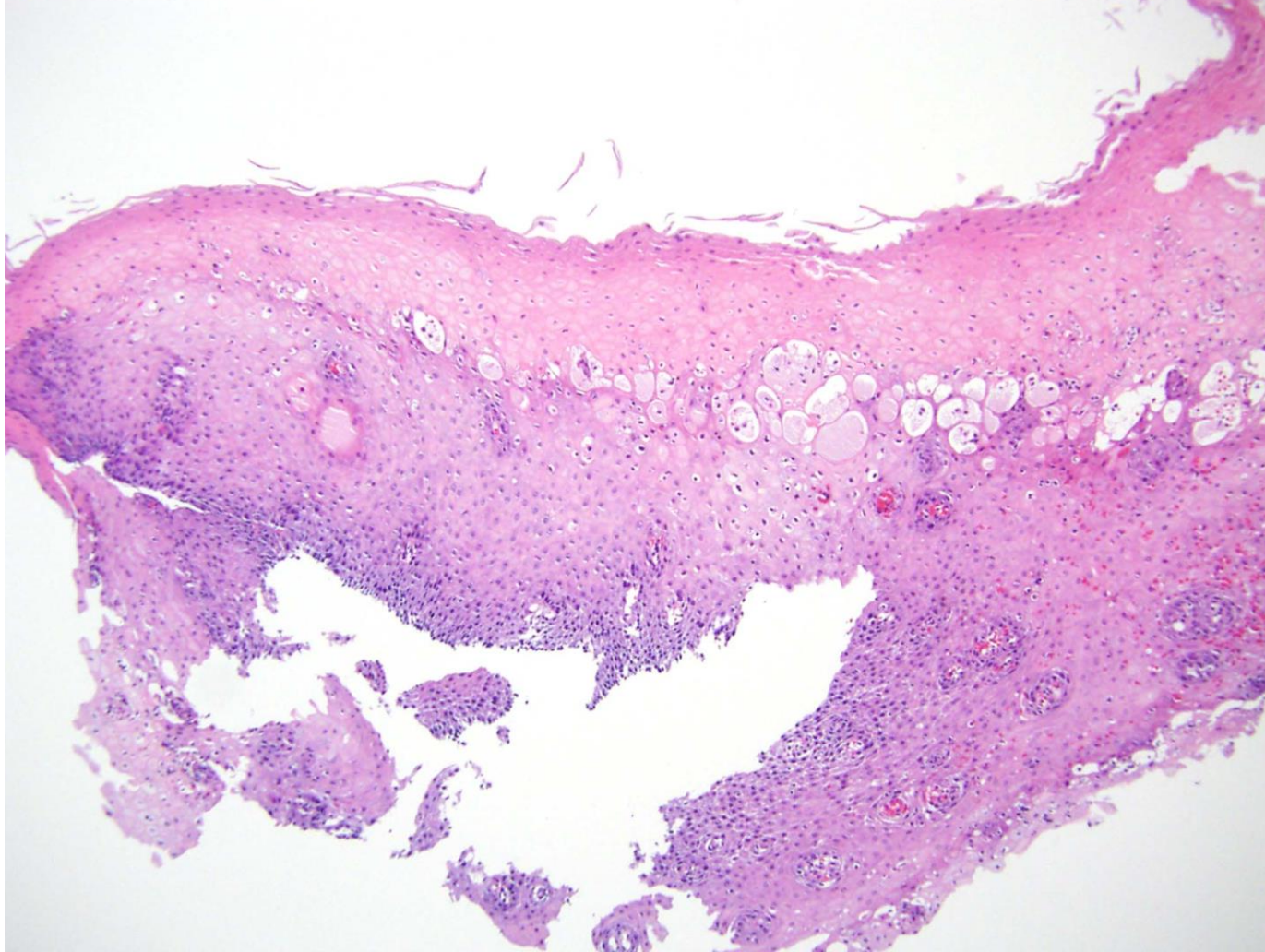


Esophagitis Dissecans Superficialis: Histology

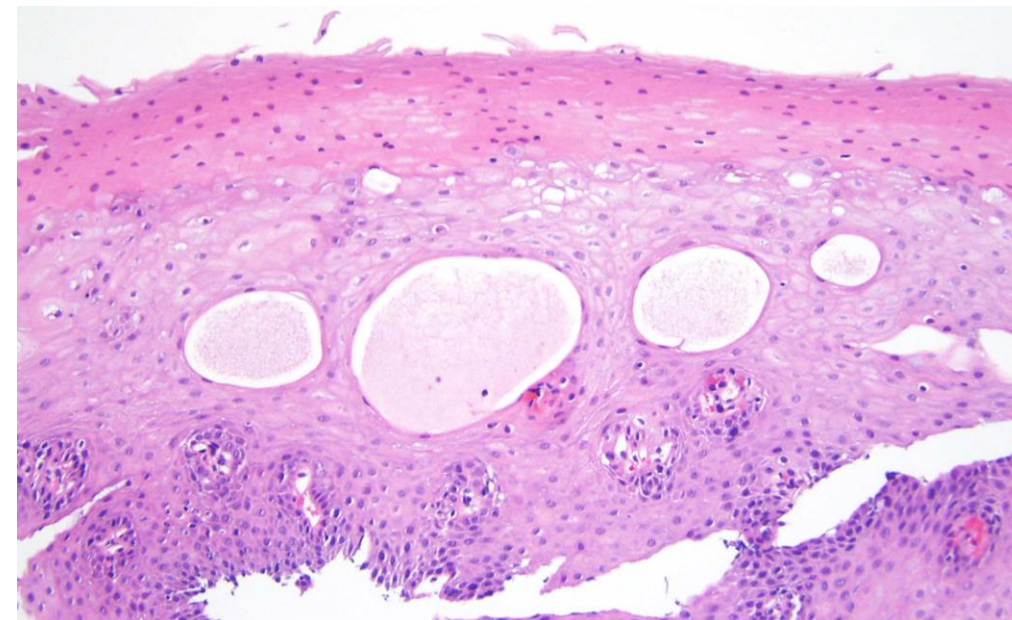
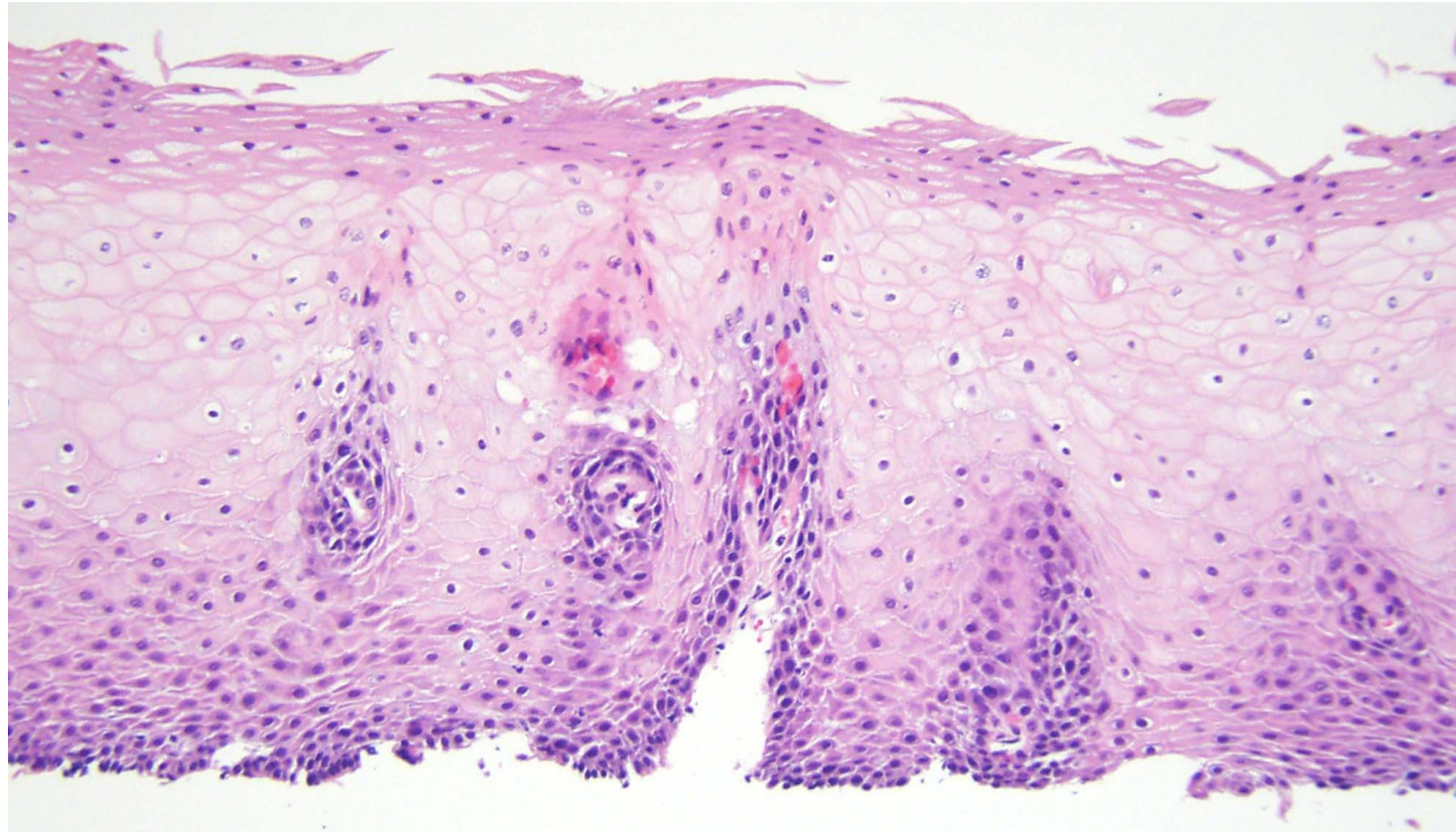
- Long detached fragments of superficial epithelium
- Intraepithelial splitting above the basal layer
- Minimal inflammation
- Parakeratosis, two-toned appearance
- Clefts between layers
- May show fungal and bacterial colonization



Sloughing Esophagitis



Sloughing Esophagitis

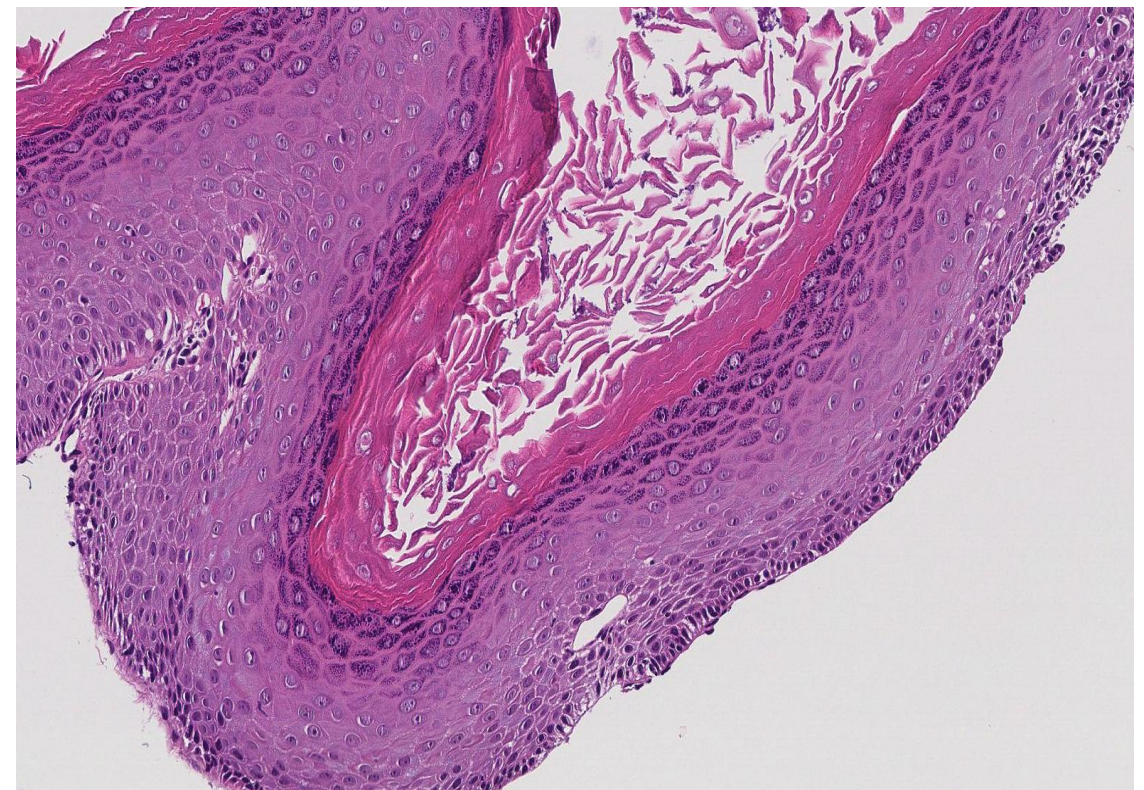


Esophagitis Dissecans Superficialis: DDx

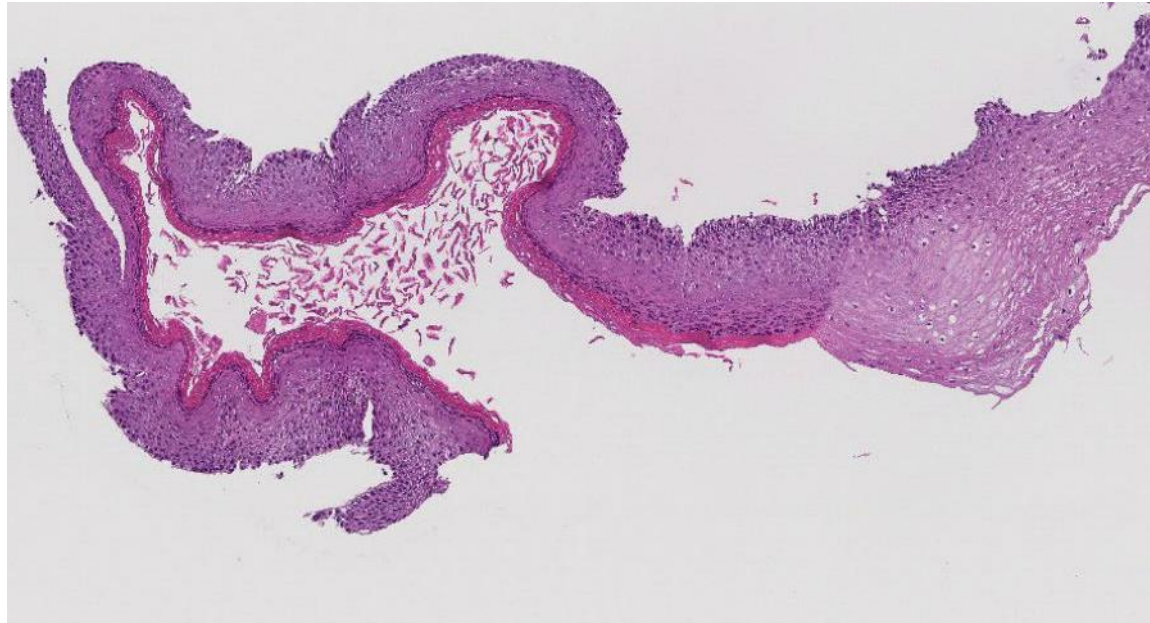
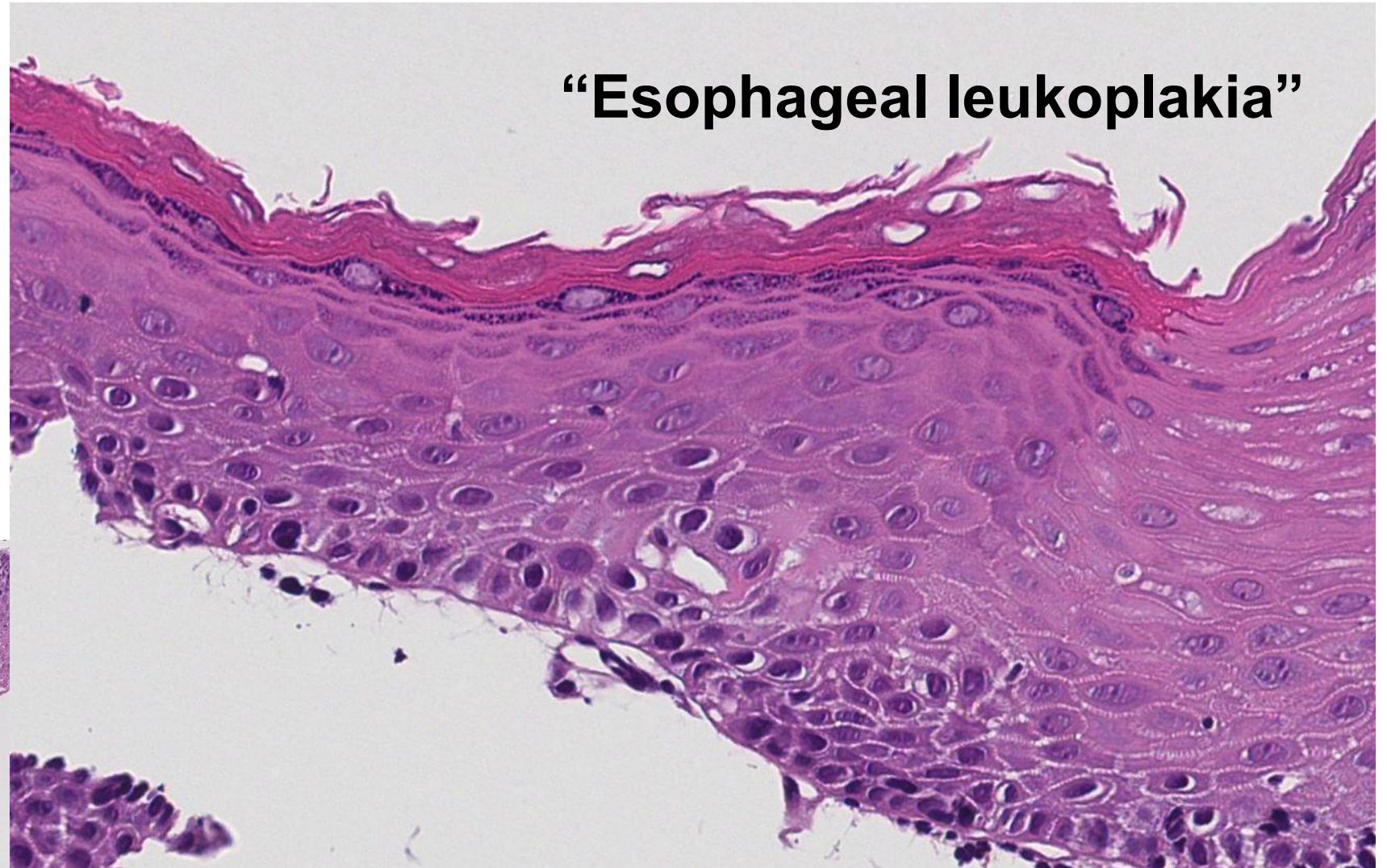
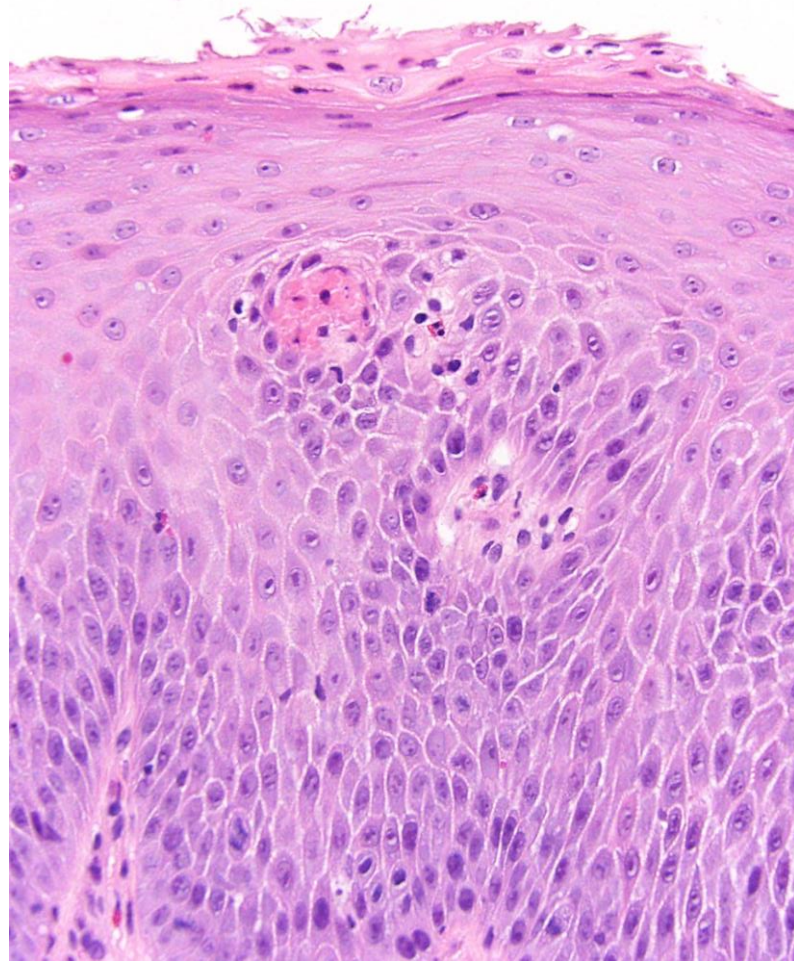
- **Candidiasis** – isolated white plaques but can be confluent when severe
- **Lichen planus** – plaque-like appearance, not thin sheets of epithelium; LP is associated with stricture, narrow caliber, extraesophageal manifestations
- **Scope trauma**
- **Histologic DDx (parakeratosis):**
 - Chemical or thermal injury
 - Pill esophagitis
 - GERD, stricture (usually very thin layer of parakeratosis)
 - Lichen planus
 - Achalasia

Differential Diagnosis: Epidermoid Metaplasia

- White esophageal plaque (leukoplakia)
- Rare finding, less than 1% of biopsies
- Distinguished from parakeratosis by granular layer and presence of keratosis
- Associated with squamous neoplasia, but unclear if it is a precursor
- Genetic alterations have been reported in some cases (mostly *TP53*)



Epidermoid Metaplasia: Histology

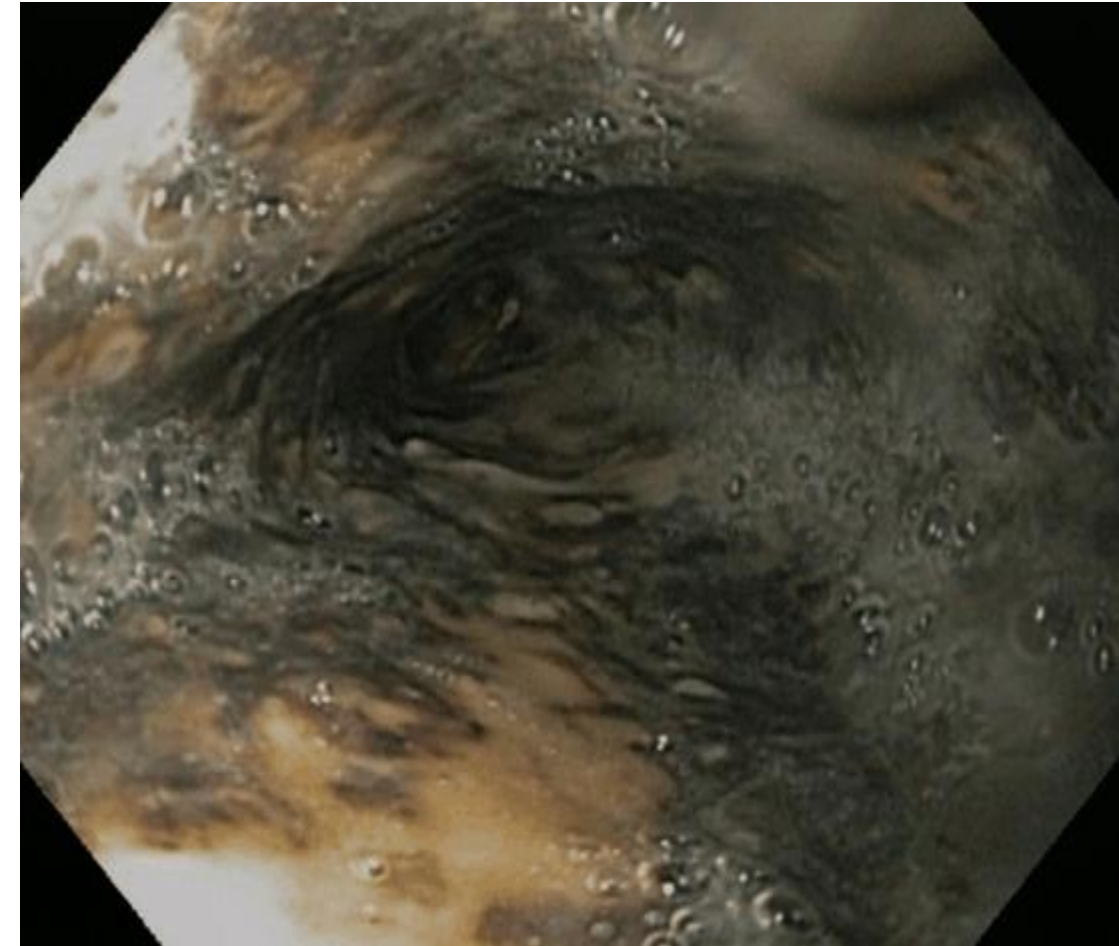


Corrosive and Contact Injuries

- **Pill esophagitis**
- **Esophagitis dissecans superficialis (sloughing esophagitis)**
- **“Black esophagus”**

“Black Esophagus”

- Acute esophageal necrosis
- Black color is due to hemorrhage
- Due to ischemia – associated with long-standing diabetes, coronary artery disease
- Biopsy is not needed
- May be seen at autopsy



Ghoneim S, Shah A, Delal S, et al. Black esophagus in the setting of diabetic ketoacidosis: a rare finding from our institution. *Case Rep Gastroenterol*. 2019;13(3):475-480. Licensed under [CC BY 3.0](https://creativecommons.org/licenses/by/3.0/)

Closing Comments & Summary: Pathology Pearls

- **Reflux esophagitis has a characteristic constellation of histologic features, but the lower threshold for diagnosis is not well defined.**
- **Eosinophilic esophagitis diagnosis relies upon histology.**
 - **Include number of eosinophils per high power field**
 - **Mention basal layer hyperplasia, spongiosis, eosinophilic microabscesses, lamina propria fibrosis**
- **Lichenoid esophagitis pattern of injury is probably underrecognized but is not specific for lichen planus. Lymphocytic esophagitis is often a manifestation of collagen vascular disease.**
- **Medications commonly injure the esophagus; features are not specific, but the diagnosis can be suspected.**



Questions?