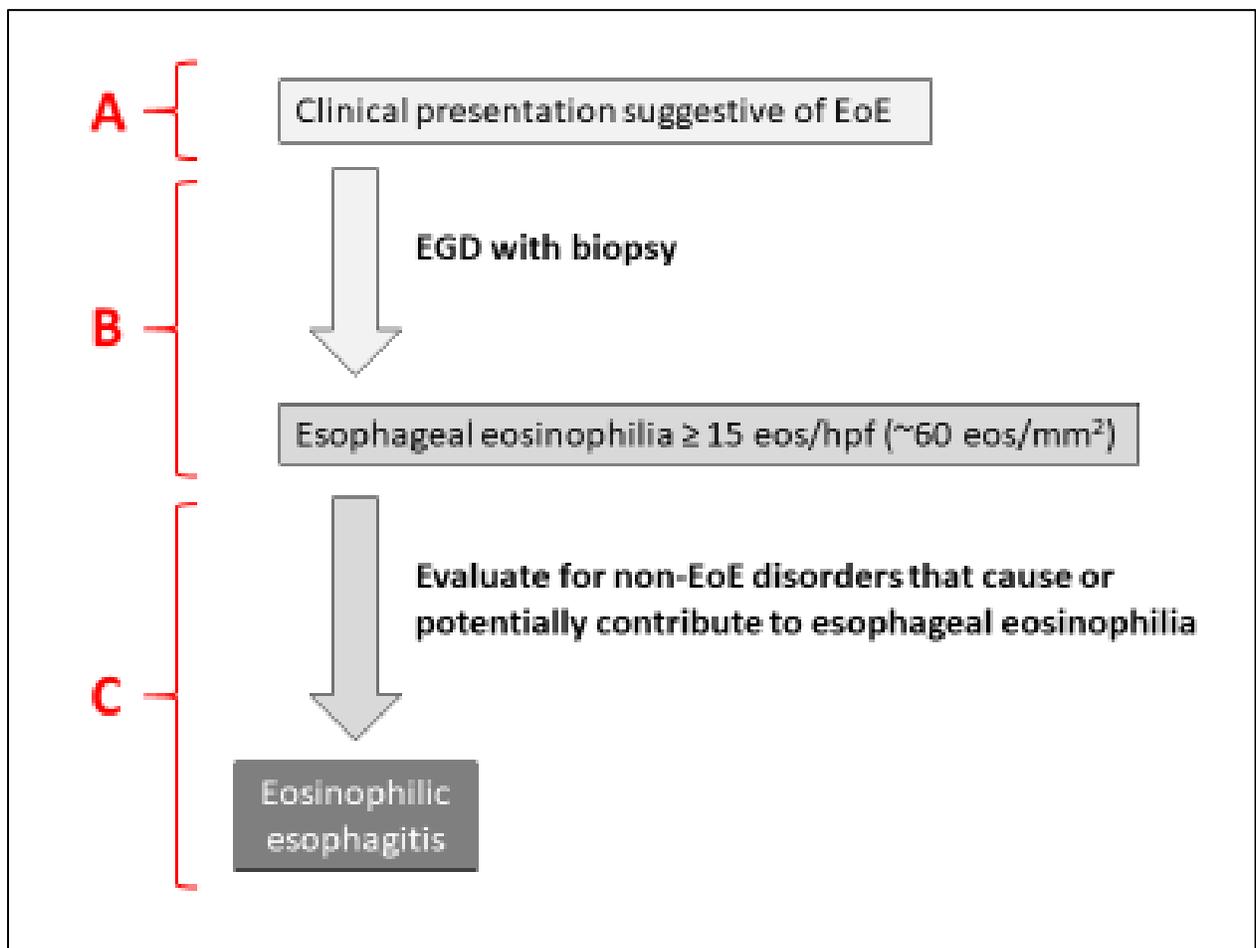


## SUPPLEMENTAL MATERIALS 2

### Illustrative cases of esophageal eosinophilia and EoE

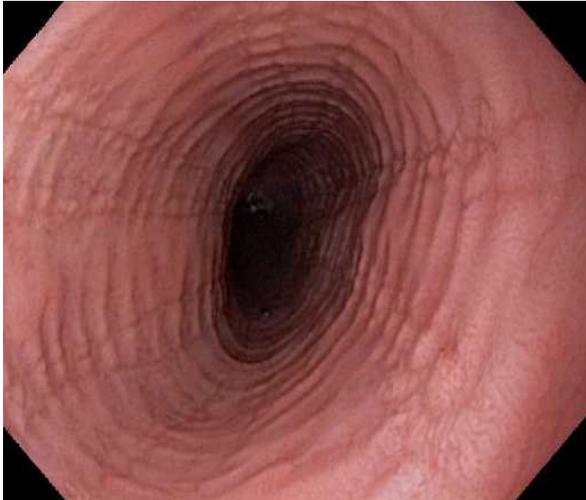
In this section, a series of brief case vignettes are presented, and each piece of information is linked to a specific point of the diagnostic algorithm figure (labeled from A-C, as below). This allows each decision point to be illustrated and used as a practical guide for EoE diagnosis over a number of potential clinical scenarios. However, given the format, not all diagnostic scenarios are presented. Additionally, these cases will not discuss subsequent treatment decisions beyond diagnosis, as this is beyond the scope of the current document.



***Presentations in adults/adolescents:***

1A – 30 year old man with seasonal allergies and 7 years of solid food dysphagia with transient food impactions.

1B – Endoscopy off PPI showed rings, furrows, and edema (E1 R2 Ex0 F2 S0), and biopsies showed a peak of 80 eos/hpf.



1C – No history of heartburn, reflux, regurgitation. No other GI, rheumatologic, or dermatologic symptoms. The patient is diagnosed with EoE.

2A – 14 year old boy with worsening intermittent solid food dysphagia for 3 years, and a transient impaction of a hot dog that cleared spontaneously during school.

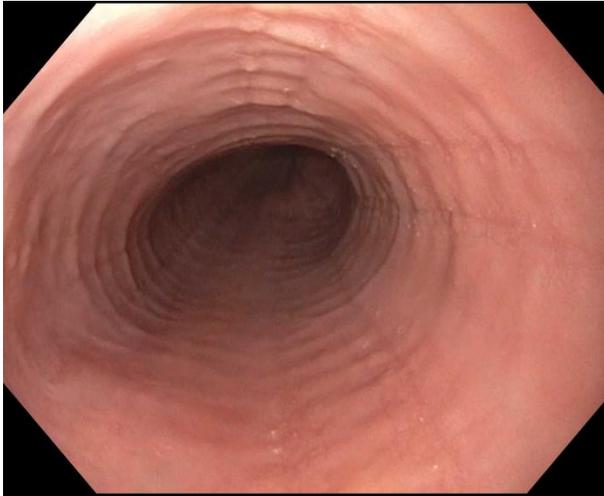
2B – Endoscopy off PPI showed edema, furrows, and white plaques (E1 R0 Ex1 F2 S0), and biopsies showed a peak of 60 eos/hpf.



2C - No history of heartburn, reflux, regurgitation. No other GI, rheumatologic, or dermatologic symptoms. The patient is diagnosed with EoE.

3A – 36 year old man with history of progressive solid food dysphagia, placed on omeprazole 20 mg twice daily after presenting to the ER with a food impaction that cleared prior to endoscopy, who follows-up after 8 weeks.

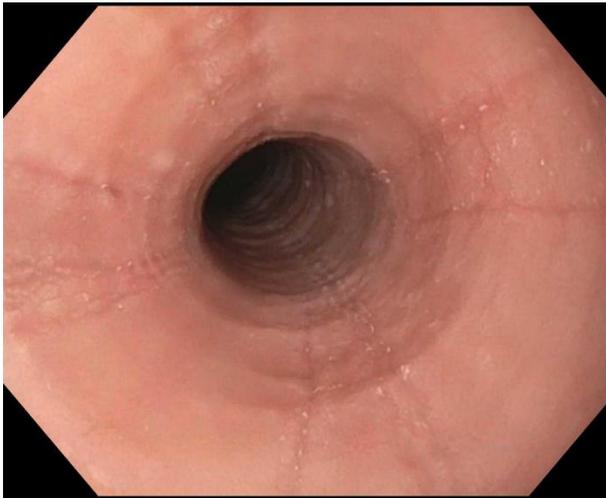
3B – Endoscopy on BID PPI shows rings, furrows, edema, exudates, and a stricture at the GEJ (E1 R2 Ex1 F1 S15), and biopsies showed 100 eos/hpf.



3C – No contribution of GERD by history. No other GI, rheumatologic, or dermatologic symptoms. The patient is diagnosed with EoE.

4A – 16 year old boy with food allergies, presents with longstanding dysphagia and transient food impactions, and a burning pain with swallowing. He was treated with a PPI for this latter symptom prior to endoscopy.

4B – Endoscopy on omeprazole 20 mg twice daily shows rings, esophageal narrowing, furrows, edema, exudates, and strictures proximally and at the GEJ (E1, R2, Ex 1, F1, S11). Biopsies showed 90 eos/hpf.



4C – No other GI, rheumatologic, or dermatologic symptoms. The patient is diagnosed with EoE.

5A – 22 year old man with seasonal allergies and solid food dysphagia.

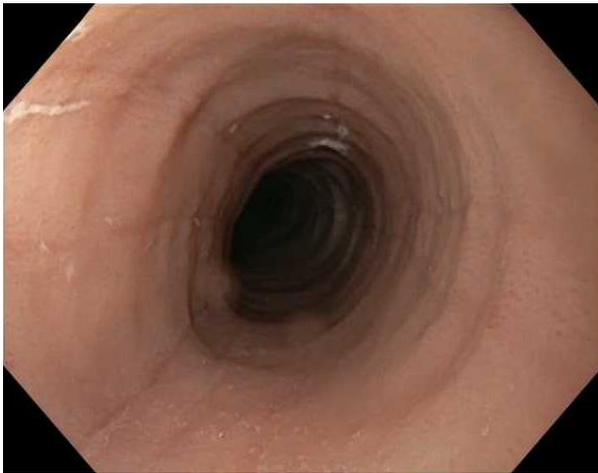
5B – Endoscopy off PPI shows rings and edema (E1 R2 E0 F0 S0). Biopsies show 45 eos/hpf.



5C – No history of heartburn, reflux, regurgitation. No other GI, rheumatologic, or dermatologic symptoms. The patient is diagnosed with EoE.

6A – 26 year old woman presents with heartburn, chest discomfort, and intermittent solid-food dysphagia.

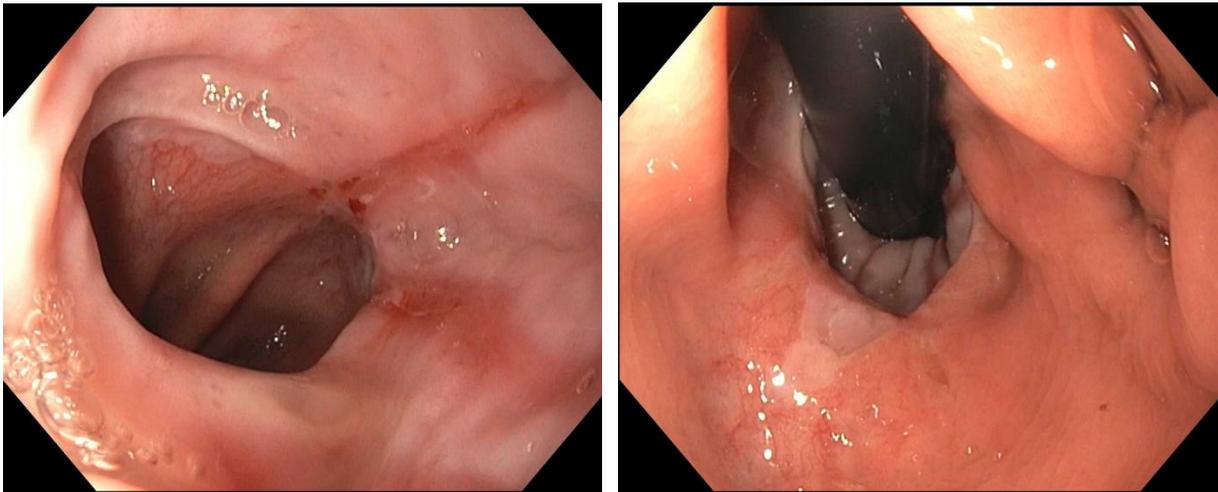
6B – Endoscopy off PPI shows rings, narrowing, edema, furrows, and exudates (E1 R2 Ex1 F1 S10) and dilation is performed. Biopsies show 60 eos/hpf.



6C - No other GI, rheumatologic, or dermatologic symptoms. The patient is diagnosed with EoE.

7A – 35 year old man with environmental allergies, atopic dermatitis, food allergies, heartburn, regurgitation, and dysphagia. Twice daily PPI is started for the heartburn and regurgitation symptoms.

7B – Endoscopy on PPI shows LA Grade B erosive esophagitis, a mild stricture at the gastroesophageal junction, and a medium-sized hiatal hernia, but the esophageal mucosa proximal to this is normal. Biopsies show 15 eos/hpf in the distal esophagus.

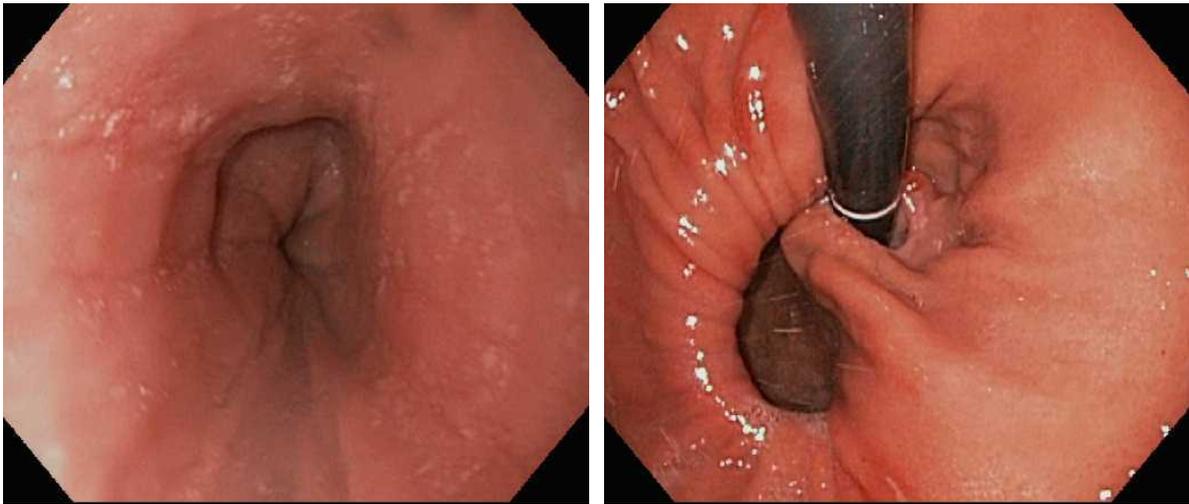


7C – Taking the entire clinical presentation into account, GERD complicated by erosive esophagitis is felt to be the cause, and the plan is to optimize anti-reflux therapy. EoE is not diagnosed.

8A – 38 year old man with food allergies, solid food dysphagia, heartburn and regurgitation.

Twice daily PPI is started for the heartburn and regurgitation symptoms.

8B – Endoscopy on PPI shows edema, exudates, and furrows (E1 R0 Ex1 F1 S0), as well as a hiatal hernia with a paraesophageal component. Biopsies show 80 eos/hpf.

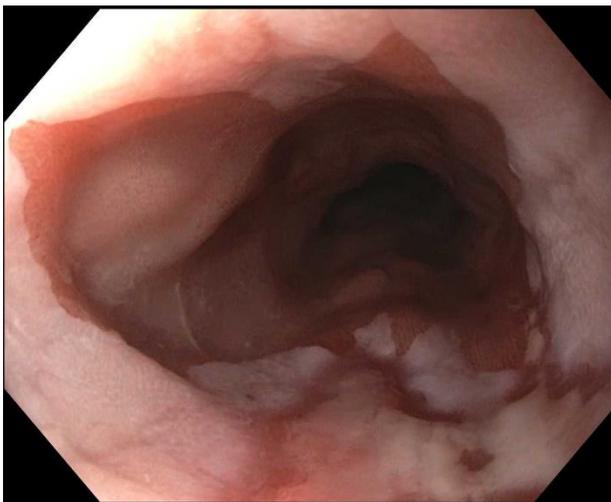
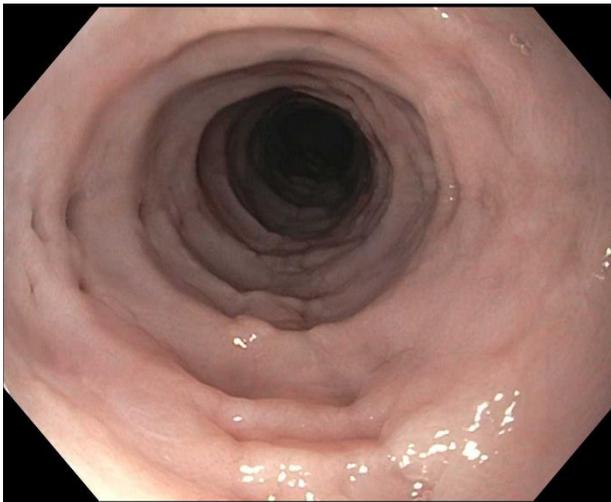


8C – Given the mixed symptom presentation concerning for GERD as well as the anatomic abnormality, the patient is referred for hiatal hernia repair and fundoplication. EoE remains a diagnostic consideration but is not confirmed. Repeat endoscopy 3 months post-operatively off PPI shows normalization of the esophagus and biopsies show 2 eos/hpf. EoE is not diagnosed.



9A – 57 year old man with longstanding dysphagia, heartburn, regurgitation, and rheumatoid arthritis, as well as asthma and environmental allergies. Has been maintained on esomeprazole 40 mg twice daily without symptom response.

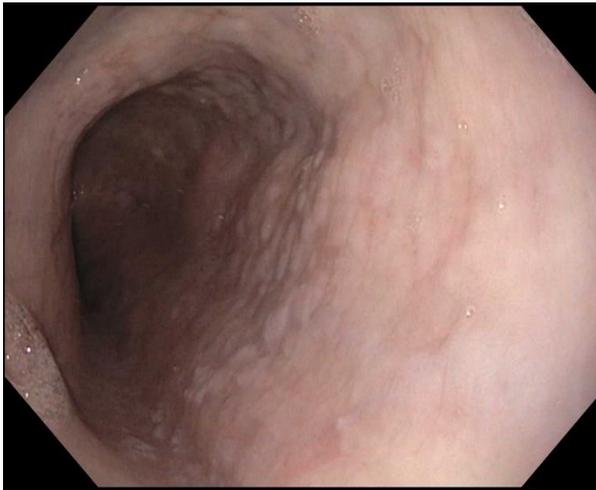
9B – Endoscopy on PPI shows edema, rings, furrows, narrowing, and pseudodiverticulosis proximally (E1 R2 Ex0 F1 S0). The squamocolumnar junction is found at 30 cm, with associated grade B erosive esophagitis. Distal to 30 cm, there is salmon-colored mucosa with squamous islands suggested of Barrett’s esophagus. Biopsies show a peak of 62 eos/hpf in the proximal esophagus, and confirm non-dysplastic BE in the distal esophagus.



9C – The patient is diagnosed with EoE overlapping with GERD/BE.

10A – 52 year old woman with dysphagia to solids more than liquids, heartburn, and regurgitation.

10B – Endoscopy on PPI shows edema, congestion, granularity and furrows in the distal half of the esophagus, as well as a question of decreased peristalsis. Biopsies show 26 eos/hpf distally, but are normal proximally.

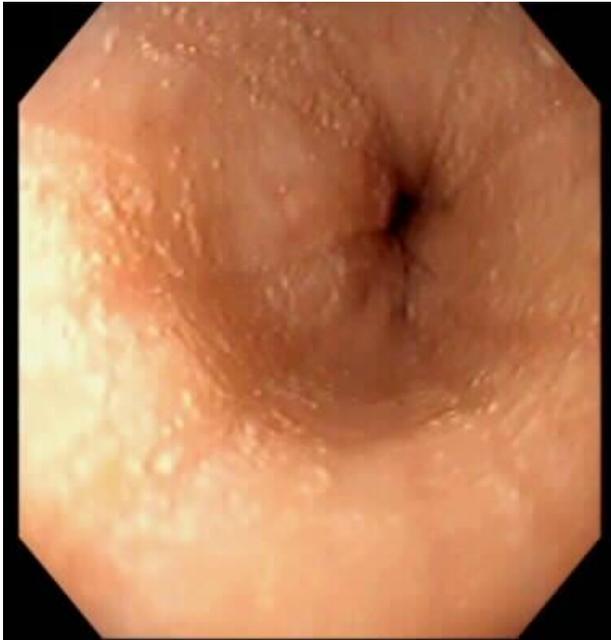


10C – Esophageal manometry confirms type I achalasia as the cause of esophageal dysmotility.

***Presentations in children:***

11A – 5 year old with 6 months of increased chest pain and vomiting twice a week. Atopic history with mild intermittent asthma, IgE food allergy to peanut. No history of other GI symptoms, failure to thrive, infant reflux or prematurity, but he is missing school because of his symptoms.

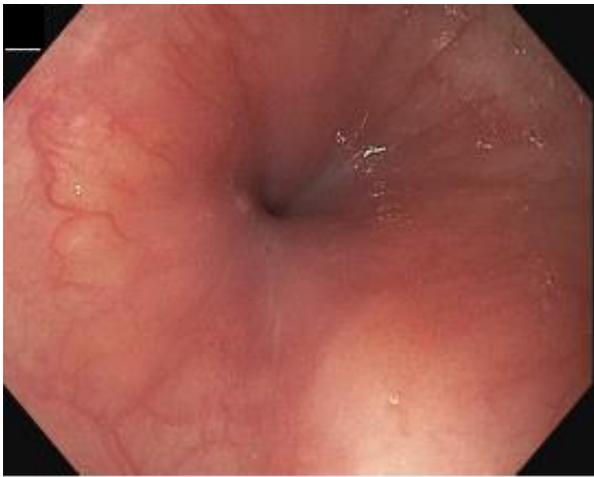
11B – Endoscopy shows an inflamed esophagus with edema, furrows, and exudates (E1 R0 Ex1 F1 S0) and biopsies show a peak count of 45 eosinophils/HPF isolated in the esophagus.



11C – EoE is diagnosed.

12A – 3 year old with history of vomiting since 4 months of age. Started on ranitidine x 2 months without improvement, and then started on omeprazole 10 mg BID with resolution of vomiting. PPI therapy could not be weaned without a recurrence of symptoms. In addition, the patient began to lose weight. Endoscopy was performed on PPI therapy.

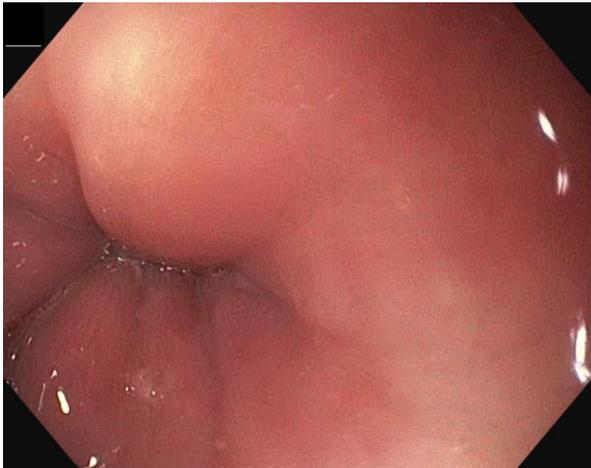
12B – Upper endoscopy has a normal appearance (E0 R0 Ex0 F0 S0) and biopsies show a peak count of 75 eosinophils/HPF isolated in the esophagus.



12C – Upper GI radiographic study shows no anatomical issues and a sweat test is normal. A diagnosis of EoE is made.

13A – 6 year old boy with a history of chronic, intermittent vomiting since 4 months of age. At one week of age, his PCP switched him to a soy-based formula with a decrease of vomiting to once a week, but his weight decreased from the 50<sup>th</sup> to the 25<sup>th</sup> percentile. When he was one year of age, he was started on a daily dose of 7.5 mg of omeprazole. His vomiting decreased to once a month. Upon reintroduction of milk into his diet, he experienced vomiting daily. At his 2 year visit, his weight was noted to be at the 3<sup>rd</sup> percentile. He was eventually referred to a gastroenterologist off of his omeprazole for 6 month because of parental concerns about its safety.

13B – Upper endoscopy had findings of edema only (E1 R0 Ex0 F0 S0) and biopsies showed 50 eosinophils/hpf.



13C – Omeprazole 10 mg twice daily therapy was started. After 3 months of treatment, his symptoms resolved and endoscopy revealed normal appearing esophageal mucosa and biopsies showed 0 eos/hpf. This patient could have either GERD or EoE and will need further follow up to eventually make final diagnosis. This is a situation where molecular profiling of an esophageal biopsy with a gene expression panel could have utility.

14A – 16 year old girl presented with a 2 year history of progressive dysphagia and worsening fatigue. No history of lower GI symptoms was reported. She had a history of cough and shortness of breath that respond to albuterol and inhaled steroids, with a previous diagnosis of asthma.

14B – Endoscopy shows edema, rings, plaques, and furrows (E1 R1 Ex1 F2 S0) and esophageal biopsy shows 75 eos/hpf in the esophagus.



14C – Given the systemic symptoms, as well as symptoms related to decreased circulation to the hands and toes, she had additional work-up. This showed positive anti-SCL-70, 10% peripheral eosinophilia, and a restrictive pattern of lung function. The patient was diagnosed with scleroderma, with esophageal eosinophilia due to stasis from dysmotility.

15A – 1 year old girl with eczema presents for evaluation of chronic coughing during and after eating as well as a history of multiple viral infections. The patient drank dairy based infant formula as well as purees and had not been treated with any medications including PPIs or H2 receptor antagonists. Family history was negative for atopic disease, reflux, or esophageal dilations. During a multidisciplinary evaluation for the cough a laryngoscopy, bronchoscopy and esophagogastroduodenoscopy was performed.

15B – Upper endoscopy shows an esophagus with exudates, edema, and furrows (E1 R0 Ex1 F1 S0) and biopsies show 150 eos/hpf field at 3 levels throughout the esophagus.



15C – The patient is diagnosed with EoE.