Special Edition ACG Virtual Grand Rounds
WHAT PRIMARY CARE AND ER PHYSICIANS NEED TO KNOW ABOUT EOE:
ADVICE FROM 2 GASTROENTEROLOGISTS

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All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

Faculty

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Eosinophilic Esophagitis

- Chronic immune-mediated allergic condition
- Characterized by eosinophilic infiltration of esophageal mucosa
Eosinophilic Esophagitis

EoE: A Rare Disease?

Esophageal Eosinophilia with Dysphagia
A Distinct Clinicopathologic Syndrome

Small numbers of immunophagoid esophageal eosinophils (IEE) may be seen in 50% of patients with gastroesophageal reflux disease and occasionally in normal volunteers. High concentrations of IEE are rarely seen in either setting. During a two-year period we identified 12 adult patients with very dense eosinophil infiltrates in esophageal biopsies identified as >20 IEE/high-power field. Dysphagia was the presenting complaint in each, but no evidence of anatomical obstruction could be found. Endoscopic esophagitis was absent, but biopsies showed marked squamous hyperplasia and many IEE. Eleven patients had normal esophageal acid exposure on 24-hr pH monitoring. Esophageal manometry showed a nonspecific motility disturbance in 10 patients. For comparison. 90 patients with excess esophageal acid exposure on 24-hr pH monitoring were studied. Thirteen (14%) had motility disturbance, and 21 (23%) had dysphagia. Esophageal biopsies were devoid of IEE in 47 patients; none of the 47 with IEE had idiopathic eosinophilic esophagitis seen in the 12 study patients. The presence of high concentrations of IEE in esophageal biopsies from patients with dysphagia, normal endoscopy, and normal 24-hr esophageal pH monitoring represents a distinctive clinicopathologic syndrome not previously described.

KEY WORDS: eosinophilic esophagitis, motility disorder; allergic asthma, eosinophilic esophagitis}

American College of Gastroenterology
EoE: Incidence and Prevalence

- Incidence and prevalence both increasing worldwide
- Overall prevalence estimate is 0.5-1 cases / 1000 persons

EoE: A Global Disease

Eosinophilic Esophagitis

Endoscopy

Friability
Rings
Exudates
Luminal Narrowing
Pathology

Pathophysicsology: Simplified

- Immune cell infiltrate
- Epithelial damage
- Lamina propria fibrosis
Fibrosis: Leads to esophageal narrowing

- Natural response to injury
- Excessive collagen deposition leads to tissue stiffness and esophageal stricture

Normal esophagus  Trachealization  Stricture

Liacouras et al. JACI. 2011

Natural history of EoE

Schoepfer et al, Gastroenterology, 2013
Eosinophilic Esophagitis

Symptoms of esophageal dysfunction

- Dysphagia
- Food impaction
- Heartburn
- Regurgitation
- Vomiting
- Chest pain
Diagnostic Updates

Clinical Presentation Suggestive of EoE

EGD w/biopsies

Esophageal eosinophilia ≥15/hpf

No other cause for findings identified

Eosinophilic Esophagitis

Symptoms of esophageal dysfunction

Dysphagia

Regurgitation

Food impaction

Vomiting

Heartburn

Chest pain
Food Impaction

- ~15% of food impactions require emergent endoscopy (most resolve)
- 50% of pts with emergent food impaction requiring endoscopy have EoE
- <1% of patients will develop stasis/ulceration leading to perforation

Food Impaction: Glucagon

- Frequently used for emergent food impaction as a smooth muscle relaxant
- Success rates vary: reported range 12% - 50%
- Higher doses are not more effective in reducing LES pressure
- Less effective in patients with structural abnormalities
- Studies do show glucagon can shorten door to scope time
Emergent Endoscopy

- Timing: Typically with 24 hours, unless the patient is unable to manage secretions
- Airway Management is essential

Various techniques are used for endoscopic intervention (Roth net, graspers, push technique, pull technique, etc)

- Biopsies are essential
  - not yet routinely performed in 80% of cases(!)

- Dilations are performed on an as-needed basis
Eosinophilic Esophagitis

Therapeutic Goals

Current goal of therapy: histologic remission. Overly simplistic?

Spectrum of response

**Non-response**
- Histology: Persistent eosinophilia ≥15 eos/hpf
- Symptoms: Persistent symptoms <30% decrease in symptom metric
- Endoscopy: Persistent endoscopic findings <30% decrease in EREFS

**Response**
- Histology: Reduced eosinophilia 7-14 eos/hpf 1-6 eos/hpf
- Symptoms: Decreased symptoms 30-90% decrease in symptom metric
- Endoscopy: Improved findings EREFS score ≥2 but less than baseline

**Complete normalization**
- Histology: Normal biopsy <3 eos/hpf
- Symptoms: Symptom resolution >90% decrease in symptom metric; EESAI score <20
- Endoscopy: Normal esophagus EREFS score <2
## Clinical Severity Index

<table>
<thead>
<tr>
<th>Points per features</th>
<th>1 point</th>
<th>2 points</th>
<th>4 points</th>
<th>15 points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>Weekly</td>
<td>Daily</td>
<td>Multiple x per day</td>
<td></td>
</tr>
<tr>
<td><strong>Complications</strong></td>
<td>Food impaction with ER visit or endoscopy</td>
<td>Hospitalization due to EoE</td>
<td>Esophageal perforation, BMI &lt;5th %ile, Elemental formula, systemic steroids</td>
<td></td>
</tr>
<tr>
<td><strong>Inflammatory (edema, furrows, exudates)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Endoscopy</strong></td>
<td>Localized</td>
<td>Diffuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td>15-60 eos/hpf</td>
<td>&gt;60 eos/hpf</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fibrostenotic (rings, strictures)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Endoscopy</strong></td>
<td>Present, but scope passes</td>
<td>Present but snug fit or requires dilation</td>
<td>Cannot pass standard upper endoscope, repeat dilations</td>
<td></td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td>BZH or LPF (or DEA/SEA)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total Score: <1: Inactive EoE; 1-6: Mild Active EoE; 7-14: Moderate Active EoE; ≥15: Severe Active EoE

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## EoE: Therapies

- **Diet**
- **Medications**
Dietary Therapy for EoE

• **Allergy Testing Guided Diet**
  - Limited to single-arm observational studies
  - Heterogeneous testing: skin-prick testing, serum-specific IgE testing, atopy patch testing, or combinations

Diet limitation based on IgE mediated testing is not currently recommended

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Dietary Therapy for EoE

• **Elemental Diet**
  - Elemental formulas are comprised of macronutrients broken down to their simplest forms including monosaccharides (carbs), medium chain triglycerides (fat), and amino acids (proteins)
  - They are formulated to meet full nutritional needs without supplementation
Dietary Therapy for EoE

• **Elemental Diet**
  - Limited prospective data in adults
  - 21 adults, 4 weeks
    - 17 adhered to diet
    - 71% histologic response ≤15 eos/hpf at 4 weeks
  - 29 adults, 4 weeks
    - 3 adults abandoned study on day 1
    - 8 adults with diet non compliance
    - 72% histologic response ≤10 eos/hpf at 4 weeks
  - After resuming a normal diet, eos ↑↑ in 3-7 days

The elemental diet is efficacious but difficult to maintain

Dietary Therapy for EoE

• **Six Food Elimination Diet (SFED)**
  - Wheat
  - Dairy/Cow’s Milk
  - Eggs
  - Nuts
  - Soy
  - Seafood/Shellfish

SFED for 6+ weeks, followed by an endoscopy with biopsies

If successful, reintroduce 1-2 food groups back in 6+ week intervals followed by an endoscopy each time

Peterson KA et al. Am J Gastroenterol. 2013
Warners MJ et al. Aliment Pharmacol Ther. 2017
Dietary Therapy for EoE

**PROS**
- Medication free therapy for a chronic disease

**CONS**
- Costly
- Time consuming
- Multiple endoscopies
- Socially limiting
- Difficult to maintain
EoE: Therapies

Diet

Medications

Medical Therapy for EoE: Response

Table. Current Treatment Options for Eosinophilic Esophagitis

<table>
<thead>
<tr>
<th>Treatment approach</th>
<th>Dose or methods</th>
<th>Pooled histologic response</th>
<th>Adverse effects</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proton pump inhibitors*</td>
<td>Omeprazole or equivalent, 20 mg, twice daily</td>
<td>41.7% in a systematic review of observational data of 1051 participants compared with a historical placebo comparison group of 13.3%12</td>
<td>Acute: Headache &lt;5%13</td>
<td>Low cost</td>
</tr>
<tr>
<td></td>
<td>Pantoprazole, 40 mg, twice daily</td>
<td></td>
<td>Diarrhea &lt;5%13</td>
<td>Readily available</td>
</tr>
<tr>
<td></td>
<td>Lansoprazole, 30 mg, twice daily</td>
<td></td>
<td>Enteric infections (1.4% in 53 152 patient-years of follow-up)14</td>
<td>Ease of administration</td>
</tr>
<tr>
<td></td>
<td>Rabeprazole, 20 mg, twice daily</td>
<td></td>
<td>Proposed chronic17:</td>
<td>Well tolerated</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Chronic kidney disease (0.1%-0.3%/patient/y)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bone fracture (0.1%-0.5%/patient/y)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Dementia (0.07%-1.5%/patient/y)</td>
<td></td>
</tr>
<tr>
<td>Topical corticosteroids</td>
<td>Fluticasone, 440-880 µg, twice daily</td>
<td>64.9% in 8 randomized clinical trials of 437 patients compared with 13.3% treated with placebo12</td>
<td>Esophageal candida (12%-16%)15</td>
<td>Off-label use of asthma medications results in need to repurpose as slurry for fluticasone</td>
</tr>
<tr>
<td></td>
<td>Budesonide, 1-2 mg, twice daily</td>
<td></td>
<td>Oral thrush (2%-3%)16</td>
<td>Cost may be considerable because it is not always covered by insurance</td>
</tr>
</tbody>
</table>

*An upper endoscopy is necessary to assess histologic response

Muir Falk JAMA 2021
Pharmacologic therapy

Topical swallowed steroids

- Fluticasone (Inhaler)
- Budesonide (Slurry)

RCT, 129 patients

- Budesonide (slurry) 1 mg BID vs.
- Fluticasone (inhaler) 880 μg BID

- Post treatment max eos/hpf:
  - OVB: 15 eos/hpf
  - MDI: 21 eos/hpf
  - p = .31

Overall topical steroids are an effective primary therapeutic option

Pharmacologic Therapy: Topical Steroids

Emerging Therapies

- Novel Steroid Formulations
  - Budesonide Suspension – Dec 2021 not approved by the FDA
  - Fluticasone disintegrating tablet – studies ongoing
  - Budesonide orodispersible tablet- approved for use in Europe, Canada, and Australia

Pharmacologic Therapy: Dupilumab

- IL-4Rα subunit receptor antagonist
- Phase 3 Study: Dupilumab 300 mg weekly (or Qoweek) vs placebo
- Dysphagia score and peak eosinophil count were significantly lower in the dupilumab weekly group
Pharmacologic Therapy: Dupilumab

Most sAEs were not considered related to the trial, except 1 sAE of systemic inflammatory response syndrome.

Most common AEs involved injection site.

<table>
<thead>
<tr>
<th>Event</th>
<th>Part A</th>
<th>Part B</th>
<th>Part A-C Group in Part C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dupilumab, 300 mg weekly (N=42)</td>
<td>Placebo (N=39)</td>
<td>Dupilumab, 300 mg every 2 wk (N=81)</td>
</tr>
<tr>
<td>Deaths</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Adverse event</td>
<td>16 (36)</td>
<td>12 (32)</td>
<td>67 (84)</td>
</tr>
<tr>
<td>Serious adverse event†</td>
<td>2 (5)</td>
<td>0</td>
<td>5 (6)</td>
</tr>
<tr>
<td>Adverse event leading to dis-</td>
<td>1 (2)</td>
<td>0</td>
<td>2 (2)</td>
</tr>
<tr>
<td>continuation†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse event occurring in ≥10% of patients in any group†</td>
<td>7 (17)</td>
<td>4 (10)</td>
<td>16 (20)</td>
</tr>
<tr>
<td>Injection-site reaction</td>
<td>3 (7)</td>
<td>5 (13)</td>
<td>8 (10)</td>
</tr>
<tr>
<td>Injection-site erythema</td>
<td>4 (10)</td>
<td>3 (8)</td>
<td>7 (9)</td>
</tr>
<tr>
<td>Injection-site pain</td>
<td>3 (7)</td>
<td>1 (2)</td>
<td>10 (12)</td>
</tr>
<tr>
<td>Injection-site swelling</td>
<td>5 (12)</td>
<td>4 (10)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>4 (10)</td>
<td>6 (8)</td>
<td>5 (6)</td>
</tr>
<tr>
<td>Headache</td>
<td>0</td>
<td>1 (2)</td>
<td>0</td>
</tr>
<tr>
<td>Acne</td>
<td>0</td>
<td>4 (10)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Rash</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Emerging Therapies

**Biologics**
- Cendakimab
- Mepolizumab
- Lirentelimab
- Vedolizumab
- Tezepelumab
- Barzolvolimab

**Non-biologics**
- Vonoprazan
- Etrasimod
Special Considerations in Pediatrics

Case Report #1

- 17 year old male presents to the ED with a food stuck in his throat
- He is unable to swallow his secretions and is spitting into a basin
- He is retching but only saliva is coming up
- He is able to speak and breathe comfortably
- PMH: allergic rhinitis
- Exam: normal growth, allergic shiners, CTA
- He undergoes emergency endoscopy
- Biopsy reveals 60 eos/hpf in esophagus; normal antrum and duodenum
Case Report #2

• 5 year old female with eczema, IgE mediated food allergy to egg and peanut, asthma, and allergic rhinitis presenting for allergy follow up.
  • She had outgrown her IgE milk allergy 2 years ago and eats yogurt and ice cream regularly.
• As an aside her mother reports that for the last 6 months she has daily abdominal pain, gastroesophageal reflux and regurgitation
• Allergist notices her weight percentiles decreased from 50th percentile to 30th percentile
• She is referred to GI for evaluation
  • Initially started on proton pump inhibitor and constipation addressed
  • Symptoms persisted and EGD revealed > 100 eos/hpf

Symptoms of EoE

• Vomiting
• Feeding refusal
• Failure to thrive
• Abdominal pain
• Heart burn
• Dysphagia
• Food impactions

Younger children

Adolescents or Adults
Coping Mechanisms

- Overchewing
- Slow meal eating
- Lubrication
- Increased drinking
- Avoiding “tough” foods

Multi-disciplinary Approach

- Patient and family
- Allergy
  - Role of atopy
  - Recognition and treatment of other atopic conditions
- Gastroenterology
  - Concomitant reflux, constipation, delayed gastric emptying
  - Procedures
- Nutrition
  - Ensure proper nutrition micro and macronutrient level
- Feeding therapist
- Psychologist
More common in patients with other forms of allergy

<table>
<thead>
<tr>
<th>Author/population</th>
<th>IgE-Mediated Food Allergy</th>
<th>Asthma</th>
<th>Allergic Rhinitis</th>
<th>Atopic Dermatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Population</td>
<td>3%</td>
<td>8.5%</td>
<td>25%</td>
<td>10%</td>
</tr>
<tr>
<td>EoE patients</td>
<td>5.7%</td>
<td>33-66%</td>
<td>30-90%</td>
<td>19-55%</td>
</tr>
</tbody>
</table>

• In terms of allergic rhinitis, seasonal variations may exist.
  • 30% of patients have environmental allergies contribute to EoE
  • Few patients where only cause


Psychosocial and Quality of Life

• Recognize stressors on patient and family
  • Symptom standpoint
    • Are there ways to help
  • Treatment itself
  • Financial standpoint

• Seek ways to help with stressors

• APFED, CURED, ACAAI, AAAAAI, EAACI

Klinnert MD et al. JPGN 2014;59: 308–316.
Therapy options

• Offer choices
  • Therapy that you pick now does not have to be your forever therapy

• What therapy are you going to be able to adhere to?

• If diet is already limited, can you feasibly limit any more?
  • Feeding disorders

Monitoring

• Coping mechanisms make assessing symptoms difficult
• Non-response rates are 20 to 60%
• Need to assess by repeat endoscopy
Special patient groups

- Outside of patients with known atopy, other “higher risk groups”
  - Outgrowing IgE mediated food allergy
  - Outgrowing FPIES trigger foods
  - Undergoing oral immunotherapy

Monitoring for disease: transnasal endoscopy

- Retrospective study 190 patients (3 to 22 years)
- Underwent video goggle or virtual reality-based unsedated TNE
- 294 of 300 attempts successful
  - 54 underwent multiple TNE
- Reduced cost by 54% from $9400 to $4400
- Side effects:
  - 11 epistaxis, 9 spit up, 8 vomiting, 1 nausea, 1 sneeze (tracheal intubation)
  - 264 tolerated

The future

- Better monitoring
  - Esophageal String Test
  - Cytology sponge
  - Esophageal Brush
  - Endoflip

- Different treatment options
  - Medications directed against specific chemokines, cytokines and inflammatory mediators

- More research
  - Role of organoids and personalized medicine

Following up

- One must have a repeat endoscopy to truly know what is going on in esophagus
  - Whatever plan is patient must be following OR EGD will not answer question at hand
  - Can still have esophageal eosinophils without symptoms...
  - If a patient needs systemic steroids for any reason, typically wait a month before repeat EGD
  - Once there is a normal EGD, how often does one need to repeat it?
Case Report #1—what happened?

• 17 year old male presents to the ED with a food stuck in his throat
• Biopsy reveals 60 eos/hpf in esophagus; normal antrum and duodenum
• Initially placed on high dose PPI (compliant) and repeat endoscopy improved but still abnormal.
• Swallowed steroids started along with PPI led to remission
• Over time, may consider Dupilumab

Case Report #2: what happened?

• 5 year old female with eczema, IgE mediated food allergy to egg and peanut (outgrew milk allergy), asthma, and allergic rhinitis presenting for allergy follow up.
• Endoscopy revealed >100 eos/hpf in esophagus while on PPI
• Variety of options offered but ultimately removed dairy with resolution in symptoms and normalization of esophageal eosinophils
Conclusions

- EoE is a chronic immune-mediated allergic condition
- It can affect people of all ages
- Over 60% of patients have comorbid atopic condition
- Presenting symptoms in adults include heartburn, dysphagia, and food impaction
- Small children have vomiting and failure to thrive

Conclusions

- 50% of pts with food impaction requiring EGD have EoE
- Medical therapy includes proton pump inhibitors, topical swallowed steroids, and dupilumab
- Elimination diets are the most common form of dietary therapy in adults
- Long-term therapy is recommended
Questions?

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