Eosinophilic Esophagitis:
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ACG Clinical Guideline: 2013

- Genetic profiles support an allergic pathogenesis
  - TH2
- Symptoms related to esophageal dysfunction
- Peak eosinophil value >15/HPF
- Suggest a response to therapy
- Biopsy recommendations are 2-4 distally and 2-4 proximally
EoE Management

Treating Disease
- **Perfect**: Complete symptom and histologic remission
- Symptom and histological improvement don’t correlate
- Real Life: Improve symptoms and reduce esophageal eosinophilia

Avoiding Complications
- Chronic fibrotic stricture
- Food Impaction
- Esophageal rupture
- Minimize treatment side effects
- Med adverse effects
- Need for EGD
- Adverse effects QOL

Stricture is Dependent on Time

Types of the endoscopic features present at the time of EoE diagnosis stratified according to the length of diagnostic delay period.
Medical vs Dietary

- Medical
  - Dilation
  - PPI
  - Steroids
  - Future therapies

- Diet
  - Six food
  - Elemental
  - Allergy testing directed
  - Variations

Dilation in EoE

- 164 patients dilated 486 times
- 5% complication (post-procedural pain)
  - 0.4% pain requiring hospitalization
  - 1% with ED evaluation
- 58% required second dilation
  - 75% within 1 year

“Esophageal dilation did not result in additional improvement in dysphagia score compared with treatment with proton pump inhibitor and fluticasone alone. In patients with symptomatic esophageal eosinophilia without severe stricture, dilation does not appear to be a necessary initial treatment strategy.”

Kavitt R, Dia Esophagus 2015
PPI responsive Esophageal Eosinophilia (PPI-REE)

- Symptom response 25-80%
- Histologic resolution 33-61%
- Depends on definition of response

Response to PPI

- Esomeprazole (40 QD) versus fluticasone (440 mcg BID trial)
  - 58% response in PPI group, 31% response in fluticasone group

- Biopsies in 712 adults
  - N=35 Esophageal eosinophilia (>20 eos/HPF)
  - Rabeprazole 20 mg po BID for 2 months
  - 26 (75%) resulted in remission
  - Response occurred even in those with negative GERD profile

Fang and Peterson, Dig Dis Sci, 2009
Molina-Infante, Clin Gastroenterol Hepatol 2011
Randomized controlled trial comparing aerosolized swallowed fluticasone to esomeprazole for esophageal eosinophilia

- Prospective single-blinded randomized controlled trial
- stratified by GERD
- randomized to fluticasone 440 mcg BID or esomeprazole 40 mg QD for 8 weeks
- Primary outcome <7 eosinophils/hpf.

- 42 patients (90% male, 81% white, mean 38 ± 10)
- 19% (8/42) with GERD
- NO difference in resolution of eos between fluticasone and esomeprazole
  - (19 vs. 33%, P = 0.484).
  - Symptoms improved with PPI

Comparison of esophageal transcriptomes of study cohorts. A total of 114 samples from 5 centers were analyzed by using the EDP.

*Journal of Allergy and Clinical Immunology, Volume 135, Issue 1, 2015, 187–197.e4*
**Long-Term Loss of Response in Proton Pump Inhibitor-Responsive Esophageal Eosinophilia Is Uncommon and Influenced by CYP2C19 Genotype and Rhinoconjunctivitis.**

*Am J Gastroenterol.* 2015 Nov;110(11):1567-75

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**Topical Steroids**

- Swallowed, NPO
- Common Options
  - Fluticasone
  - Formulations include Flonase, blister pack, aerosol
  - Budesonide slurry
  - Not yet FDA approved
- Liquid formulations mixed with viscous solution (syrup, honey, Splenda)
- Contact time seems important
  - *Dellon E, Gastroenterol* 2012 1321
- Need to fast 30 minutes
- Mouth rinse
STEROIDS

- American College of Gastroenterology recommends TCS (fluticasone or budesonide) as first-line pharmacological treatment

- A randomized, placebo-controlled study in children using an oral suspension of budesonide
  - 53% response rate accounting for both symptomatology and histology with medium-dose and high-dose oral budesonide
  - 77% histological remission for high-dose oral budesonide.


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**Budesonide**

Randomized, double blind, placebo controlled of oral budesonide 1mg BID for EoE

15 days

**Results:**
Eosinophil 68 to 5.5 c/t (62 to 57 in placebo).
Endoscopic reversal occurred as well.

Maintenance not as effective
50 week trial demonstrated return of eosinophils to 31

Straumann, Gastroenterology 2010
Dohil Clin Gastroenterol Hepatol 2010
Two week steroids

- European trial, RCT, blinded, 3 formulations
- Baseline and 2 week endoscopy
- Primary endpoint:
  - <15 eosinophils/HPF

Effect of treatment on eosinophilic load. BET1, effervescent tablets for orodispersible use 2×1 mg/day; BET2, effervescent tablets for orodispersible use 2×2 mg; BVS, budesonide viscous suspension 2×5 mL (0.4 mg/mL)/day; EoT, end of treatment; PLA, placebo.

Longevity of Response

Long term response versus long term risk
(dis)Advantages of TCS

**Advantages**
- Effectiveness
- Rapidity of response
- Low

**Disadvantages**
- required attention to administration (e.g. swallowing an inhalant)
- risk of candidal overgrowth
- cost
- Recurrent disease
- Long term safety
- Symptom relief?

**Unknown significance**
- long-term adrenal suppression
- growth impairment
- reduced bone density with use of corticosteroids.
- Unclear long term effect on fibrosis

Topical steroids - enough said?

Harel S reported up to 43%(6/14) of children on budesonide with AI – J Ped Gastro Nutrition 2015. Golekoh et al reported adrenal insufficiency (AI) in 10% of children with eosinophilic esophagitis treated with swallowed glucocorticoids for ≥6 months and suggest screening this population with low-dose adrenocorticotropic hormone stimulation testing (LDST). J Pediatrics 2016
Long Term Safety

- Long term safety in 54 children (mean fu 20 months) up to 5.7 years
- Growth rate normal
- Candida in 3/53
- Types:
  - Mometasone
  - Flonase
  - Budesonide

History of Diet

- First introduced in 1995 by Kelly et al.
  - 10 children with EoE showed improvement in symptoms and complete resolution of histological findings after exclusively taking amino acid formula for 6 weeks.

- Three main strategies.
  - Elemental diet - exclusively amino acid, carbohydrate, lipid, vitamin mineral based formula
  - Targeted elimination diet - based upon skin prick testing or atopy patch testing.
  - Empiric elimination - most common allergenic foods are avoided: cow’s milk, wheat, egg, soy, peanuts/treenuts, and seafood (fish/shellfish).

Elemental Diet in Adults

- 18 adults
  - Elecare 4 weeks
  - 2 week intervals

- Eosinophils from 54 to 10
  - $\leq 10$ eos/hpf: 72%

- Normal diet
  - eos ↑: 3-7 days

Effect of SFED on Esophageal Eosinophilia

- 64% achieved histologic response defined by < 5 eos/hpf

Peterson K Am J Gastroenterol Feb 2013
Recent studies on 4 food elimination diet 50-60% effective
  - Milk, soy, wheat, eggs
  - Not nuts or shellfish/seafood

Food Reintroduction – the basics

- After remission, foods are gradually reintroduced.
  - Begin with foods less likely to be allergens
  - Endoscopic evaluation may also be performed after introducing three to four low-allergic foods in a stepwise manner

- A multidisciplinary approach is vital in these patients to maintain quality of life
Meta-analysis of Dietary Interventions for Histologic Remission in EoE

**Overall effectiveness**
- Elemental: 90.8%
- SFED: 72.1%
- Food elimin: 45.5%

### Common Questions
- **Can I stop steroids?** Almost 100% thought to recur
- **What about mixups on diet?** Possible to still resolve but keep in mind
- **What if my patient cannot tolerate diet?** 2 weeks seems predictive
- **What about tolerance to foods?** Possible with hydrolyzed formula, more data needed
- **What about recurrent candida?** Can treat throughout
- **When do I stop evaluating them?** Unclear data
Newer Therapeutics

- IL-5 antibodies: eosinophil trafficking is IL5 dependent
- Dupilumab – binds to the alpha subunit of the interleukin-4 receptor (IL-4Rα). Through blockade of IL-4Rα, dupilumab modulates signaling of both the interleukin 4 and interleukin 13 pathway.
- RPC4046
  - recombinant humanized, high affinity, selective, anti–interleukin-13 (IL-13) monoclonal antibody.
Take Home Points

- PPI, TCS, Dilation, and Diet have all been shown to be effective strategies in Eosophageal Eosinophilia
- Longer duration of disease predicts a higher likelihood of requiring dilation
  - Dilation will not reduce underlying inflammation
- At one year, TCS appear safe
- Diet does not completely rule out reintroduction of inciting foods
- Therapeutic strategies should be tailored to the individual